INVESTIGATION OF IMPROVED FIXATION IN
MASSIVE ENDO-PROSTHETIC REPLACEMENTS
OF THE LOWER LIMB

by

PAUL SIMON UNWIN

SUBMITTED FOR THE DEGREE OF DOCTOR OF PHILOSOPHY IN THE
UNIVERSITY OF LONDON

OCTOBER 1996

DIVISION OF BIOMEDICAL ENGINEERING, INSTITUTE OF
ORTHOPÆDICS
UNIVERSITY COLLEGE LONDON
ROYAL NATIONAL ORTHOPÆDIC HOSPITAL
STANMORE, MIDDLESEX
Abstract

This retrospective study of 1149 of cemented intra-medullary stemmed Stanmore bone tumour lower limb massive endo-prostheses, identified that aseptic loosening was the most common form of implant related failure.

Revision for aseptic loosening occurred in 14.5% of the 1149 cases. The probability of surviving aseptic loosening for 10 year for proximal femoral, distal femoral and proximal tibial replacements was 87.9%, 65.1% and 51.5% respectively. Patients at greatest risk of loosening were young patients with a distal femoral or proximal tibial replacement, or patients with extensive resections of the distal femur or proximal tibia. Those patients with short proximal femoral resections were at greater risk than those with extensive resections.

Clinical and radiographic evaluations of patients were poor predictors of loosening. However, there was a correlation between pain and radiographic radiolucent lines.

This study provided impetus to develop three new method of improving implant fixation. These were -

1. enhanced fixation of cemented intra-medullary stemmed replacements using porous beaded collars or hydroxyapatite coated collars. Bony bridging did not occur with porous collared replacements but did with 81.8% of hydroxyapatite coated replacements.

2. uncemented intra-medullary fixation using press-fit, hydroxyapatite coated custom-made stems. After laboratory and cadaveric studies, a clinical trial of
20 patients was undertaken. Early radiographic results of target groups were encouraging.

3. extra-cortical fixation using hydroxyapatite coated extra-cortical plates. Inspired by the first Stanmore replacements, extra-cortical plated fixation was investigated using a goat model. Histological results of mid-shaft tibial replacements identified osseointegrated encompassed plates. The success of the animal model, led to the insertion of an extra-cortical plated distal femoral endo-prosthesis.

All three methods of improving the fixation showed encouraging results. The acceptance and increasing use of enhanced methods of fixation has reinforced the value of this work.
I am greatly indebted to my supervisor, Professor Peter Walker, for direction and stimulating discussion throughout this work. Without Professor Walker's guidance and trust in my abilities I believe that the developments achieved in this work would have been far less.

In addition, I would like to take this opportunity to acknowledge the tremendous support from Dr Gordon Blunn throughout my time at Stanmore. All of my past colleagues at the Division of Biomedical Engineering have contributed to this work through their friendship and support. In particular I would like to single out Hugh Crawford, Ron Ansel and Peter Lilley.

I would like to thank all the surgeons past and present of the Supra Regional Bone Tumour Treatment Services. They allowed me to have access to their patients, that provided me with invaluable data. All the surgeons were supportive and paid great interest in the developments that they let us introduce to enhance the fixation of the endo-prostheses. Justin Cobb deserves a special thank you. His enthusiasm, encouragement and dedication to his patients, led me to persevere with the developments of the uncemented intramedullary stemmed and extra-cortical fixation methods. Justin's sense of humour whilst in clinics, the operating theatre or at meetings will always be remembered.

A thank you must go to all the patients I met whilst attending clinics both in Birmingham and London. I met many patients who were so grateful to the team who saved their limb. It is an honour to have been a part of that team and it saddens me to think that we have not achieved the success in terms of fixation that we would wish. The patients and their families were a source of
motivation and it is of great sadness to me that some patients have not survived their disease.

I would like to thank my family for their constant support. My parents along with my wife Diane, took on the horrendous job of proof reading this thesis. Diane provided much valued moral support.

Finally, I would like to acknowledge the financial contribution of the Bristol Myers Squibb Foundation and the Medical Research Council in support of this work.
# Contents

Abstract ..........................................................................................................................2

Acknowledgements .....................................................................................................4

Contents .......................................................................................................................6

List of Tables .................................................................................................................15

List of Figures ...............................................................................................................17

List of Plates ..................................................................................................................25

Chapter 1. Introduction to bone tumour limb salvage ............................................29

1.1. Aim of the study ....................................................................................................30

1.1.1. The Division of Biomedical Engineering, Institute of Orthopaedic, University College London .................................................................32

1.2. Layout of the thesis ..............................................................................................33

1.3. Forms of limb salvage ..........................................................................................34

1.3.1. Allografting .....................................................................................................34

1.3.2. Composites (Implant plus grafting) .................................................................36

1.3.3. Bone transport ................................................................................................36

1.3.4. Rotationplasty ................................................................................................37

1.3.5. Amputation ......................................................................................................37

1.4. Massive custom-made replacements ...................................................................38

1.5. Stanmore custom-made replacements ................................................................38

1.5.1. The first Stanmore custom-made replacements .............................................39

1.5.2. The Stanmore intra-medullary stemmed massive endo-prosthetic replacements ............................................................39

1.5.2.1. Proximal femoral .....................................................................................40
Chapter 2. Investigations of aseptic loosening in 1149 bone tumour limb salvage cases

2.1. Introduction

2.2. Materials and Methods

2.2.1. Selection criteria

2.2.2. The study group

2.2.2.1. Diagnosis
Chapter 3. Clinical assessment of patients with cemented intramedullary endo-prostheses of the lower limb

3.1. Introduction

3.2. Methodology

3.2.1. ISOLS clinical evaluation

3.2.1.1. Modification to the ISOLS system

3.2.2. Biomedical Engineering clinical evaluation

3.2.3. Selection criteria

3.3. Results

3.3.1. Overall Grade

3.3.2. The sections of the ISOLS and BME clinical grading systems

3.3.3. Functional activity

3.3.3.1. Patient age

3.3.3.2. Percentage of bone resected

3.3.3.3. Walking distance

3.3.3.4. Stairs

3.3.3.5. Walking aid

3.3.3.6. Activity of daily living

3.3.3.7. Level of activity

3.3.4. Instability

3.3.5. Pain

3.3.6. ROM Knee
Chapter 4. Radiographic assessment of cemented intra-medullary stemmed endo-prostheses

4.1. Introduction

4.1.1. Aim

4.1.2. Purpose

4.1.3. Radiographic grading system

4.1.3.1. The ISOLS implant radiographic evaluation

4.1.3.2. The BME radiographic score

4.1.3.3. Constructive

4.1.3.4. Adverse

4.1.3.5. Scoring

4.2. Methodology

4.2.1. Data collection

4.2.2. Radiographic zones

4.3. Results

4.3.1. Radiographic study group

4.3.1.1. Grades

4.3.2. BME Grading system parameters

4.3.2.1. Constructive
4.3.2.2. Increased shaft diameter .............................................. 150
4.3.2.3. Adverse bony remodelling parameters .......................... 150
4.3.2.4. Radiolucent lines ....................................................... 150
4.3.2.5. Reduced shaft diameter ............................................. 158
4.3.2.6. Cavitation ................................................................. 159
4.3.2.7. Reduced bone density ................................................. 160
4.3.2.8. Plateau gap ............................................................... 160
4.3.3. Indicators of aseptic loosening ......................................... 162
4.3.4. Correlation between clinical and radiographic assessments ......................................................................................... 162
  4.3.4.1. Radiolucent line and clinical grade
  correlation ........................................................................... 163
4.4. Discussion ....................................................................................... 163

Chapter 5. The use of the new bone formation to enhance the fixation of cemented replacements ........................................... 195

  5.1. Introduction ............................................................................. 196
  5.2. Purpose .................................................................................. 197
  5.3. Investigations of the Pedicle Formation ..................................... 197
    5.3.1. Materials and Method .................................................... 197
    5.3.2. Results ........................................................................ 198
      5.3.2.1. Pedicle Frequency ................................................... 198
      5.3.2.2. Distribution ............................................................. 198
      5.3.2.3. Number of quadrants ............................................. 198
      5.3.2.4. Dimensions of the pedicle .................................... 198
      5.3.2.5. Resection ............................................................... 199
      5.3.2.6. Patient age ............................................................ 200
      5.3.2.7. Radiolucent lines versus Pedicle formation ............ 201
      5.3.2.8. Duration ............................................................... 201
5.3.2.9. Discussion of pedicle associated with uncoated replacements ............................................................202
5.3.2.10. The formation of the pedicle .................................................202

5.4. Enhancing the fixation ............................................................................203
5.4.1. Porous collared replacements ..................................................203
5.4.1.1. Materials and patients ................................................204
5.4.1.2. Results ..........................................................................205
5.4.2. Discussion - the use of porous collars on massive endo-prostheses ....................................................206
5.4.3. Hydroxyapatite coated replacements .....................................207
5.4.3.1. Materials and patients ................................................208
5.4.3.2. Results ..........................................................................210
5.4.4. Discussion - bony ingrowth associated with hydroxyapatite collared replacements ..............................................213
5.4.4.1. A comparison of hydroxyapatite, porous collared and uncoated femoral replacements .......................215

5.5. Discussion - methods of enhancing the fixation. .................................216

5.6. Future work ..............................................................................................217

Chapter 6. Uncemented intra-medullary stemmed fixation...............................238

6.1. Introduction ..............................................................................................239
6.1.1. The use of uncemented massive replacements .................................240
6.1.2. Aim ...............................................................................................241
6.2. Methodology ............................................................................................241
6.3. Design Rationale ......................................................................................242
6.3.1. Pre-clinical trials ...........................................................................243
6.3.1.1. Fatigue testing .........................................................................247
6.3.1.2. Sectioning of fatigued implants ...........................................248
6.3.2. Experimental Studies ........................................................................249
6.3.3. Clinical studies ............................................................ 249
   6.3.3.1. Patients .........................................................................249
   6.3.3.2. Implant design ............................................................249
   6.3.3.3. Technical problems inserting the replacements 251
6.3.4. Results .........................................................................................253
   6.3.4.1. Clinical follow-up .......................................................253
   6.3.4.2. Radiographic follow-up .............................................254
6.3.5. Discussion - use of uncemented intra-medullary fixation 255
6.3.6. The future of uncemented intra-medullary fixation 260

Chapter 7. Extra-cortical plated massive endo-prosthetic replacements 278
7.1. Introduction ...............................................................................................279
   7.1.1. Extra-cortical fixation of the first Stanmore massive replacements 279
   7.1.2. Aim ...............................................................................................280
   7.1.3. Purpose ........................................................................................281
   7.1.4. Intra-medullary versus Extra-cortical 281
7.2. Design Rationale .......................................................................................282
   7.2.1. Plated design ..................................................................283
   7.2.1.1. Basket design ...............................................................285
7.3. Experimental Studies ..............................................................................286
   7.3.1. Laboratory ...................................................................................286
   7.3.2. Animal model ...........................................................................286
   7.3.2.1. Methodology. The goat study ..................................287
   7.3.2.2. Surgical procedure ......................................................288
   7.3.2.3. In vivo ...........................................................................289
   7.3.2.4. Retrieval study and blood supply labelling 289
List of Tables

Table 1.1. A summary of aseptic loosening in 23 studies from centres throughout the world. .........................................................................................................59

Table 2.1. Patient age and percentage of bone resected with respect to the commonest tumour for each implant group. ............................................................105

Table 2.2. The status of the 1149 patients, highlighting those who underwent revision. .............................................................................................................106

Table 2.3. The form of implant related failure with respect to implant type, highlighting aseptic loosening. ................................................................................107

Table 2.4. The percentage of cases that failed from aseptic loosening and the mean time to failure with respect to patient age, gender and the percentage of bone resected. ..............................................................108

Table 3.1. A comparison of the clinical grading scores of patients that were revised because of aseptic loosening within 12 months of the clinical assessment and those patients that were not known to have failed from aseptic loosening. .............................................................................141

Table 4.1. The scoring system for the radiographic parameters. .................................................................................................................................193

Table 4.2. A comparison of the radiographic parameters scores between those cases that failed and those that did not ........................................................................194

Table 4.3. The probability of a correlation between clinical grading parameters and radiographic score. ..................................................................................194

Table 5.1. The number of cases with no pedicle, those with pedicle that had no ingrowth, some pedicles with ingrowth and all pedicles with ingrowth with respect to implant. .................................................................236
Table 5.2. The number of cases with pedicle and pedicle ingrowth with respect to implant ................................................................. 236

Table 5.3. A comparison of the uncoated (control), porous collared and hydroxyapatite coated replacements .................................................. 237

Table 6.1. The status of the 20 patient with uncemented massive replacements ............................................................................................ 275

Table 6.2. The overall radiographic and individual parameter scores of the uncemented intra-medullary stemmed replacements ........................................ 276

Table 6.3. A matched comparison of radiographs of uncemented and cemented replacements .................................................................................. 277

Table 7.1. A summary of the extra-cortical plated replacements ......................................................................................................................... 308

Table 7.2. A summary of the bone remodelling at the plateau, mid-section and tip regions of the extra-cortical plates ...................................................... 309

Table 7.3. Bony apposition around the extra-cortical plates using the zones illustrated in Figure 7.4 ................................................................. 310
List of Figures

Figure 1.1. Intra-medullary stemmed endo-prostheses for the replacement of the proximal femur (left), distal femur (centre) and proximal tibia (right). .......................................................... 53

Figure 1.2. The number of bone tumour custom-made Stanmore endo-prostheses inserted between 1950 and 1993, highlighting important events. ........................................................................ 54

Figure 1.3. The skeletal locations of 1686 Stanmore custom-made bone tumour endo-prostheses inserted between 1950 and 1993. ................................................................. 55

Figure 2.1. The age distribution of the patients with respect implant. There was a significant difference in the age of the patient with respect to skeletal location ........................................... 87

Figure 2.2. The distribution of the percentage of bone resected with respect implant. There was no significant difference in the percentage of bone resected with respect to skeletal location ........................................... 87

Figure 2.3. The percentage of bone resected with respect to patient age and implant. .................................................................................................................. 88

Figure 2.4. The percentage of bone resected (mean ± S.E.) with respect to method of biopsy type and implant ...................................................................................... 89

Figure 2.5. The probability of surviving aseptic loosening with proximal, distal femoral or proximal tibial replacement that used cemented intra-medullary stemmed fixation (upper). The probability of surviving (middle) and cumulative hazard (lower) of aseptic loosening with uncoated proximal femoral, uncoated distal femoral replacements with a Stanmore knee or uncoated proximal tibial replacements with a Stanmore knee. .................................................. 90
Figure 2.6.a. The probability of surviving aseptic loosening (upper) and cumulative hazard (lower) of uncoated distal femoral replacements with respect to age. ................................................................. 91

Figure 2.6.b. The probability of proximal femoral (upper) and proximal tibial (lower) surviving aseptic loosening with respect to age ................................................................. 92

Figure 2.7.a. The probability of surviving aseptic loosening (upper) and cumulative hazard (lower) of uncoated distal femoral replacements with respect to the percentage of bone resected ........................................................................................................ 93

Figure 2.7.b. The probability of proximal femoral (upper) and proximal tibial (lower) surviving aseptic loosening with respect to the percentage of bone resected ........................................................................................................ 94

Figure 2.8.a. The probability of surviving aseptic loosening with uncoated proximal femoral replacements (upper) and distal femoral replacements (lower) with respect to gender ........................................................................................................ 95

Figure 2.8.b. The probability of surviving aseptic loosening with uncoated proximal tibial replacements with respect to gender ........................................................................................................ 96

Figure 2.9. The probability of surviving aseptic loosening for young (upper), middle aged (middle) and elderly (lower) patients with uncoated distal femoral replacements (Stanmore knee hinge), with respect to the percentage of bone resected ........................................................................................................ 97

Figure 2.10. The probability of patients with uncoated distal femoral replacements (Stanmore knee hinge), surviving aseptic loosening with respect to the year of insertion ........................................................................................................ 98

Figure 2.11. The probability of patients who were administered chemotherapeutic drugs with uncoated distal femoral replacements (Stanmore knee hinge), surviving aseptic loosening compared that were
not, for all age groups (above) and those patients aged between 20 and
60 years (below).................................................................99

Figure 2.12. A comparison of the survivorship curves of the two
surgeons, illustrating the probability of surviving aseptic loosening for
patients with uncoated distal femoral replacements who had
osteosarcoma, were aged between 20 and 60 years and had between 40
and 60% of the distal femur resected. ......................................................100

Figure 2.13. The probability of patients with distal femoral knee
replacements surviving aseptic loosening with respect to knee hinge
configuration........................................................................101

Figure 2.14. The offset distance between the line of force and the long
axis of the femur........................................................................102

Figure 2.15. A comparison of the offset distance at the tip of the intra-
medullary stem of a proximal femoral replacement (left) and a distal
femoral replacement (right). Both implants replace 50% of the femur. ...............103

Figure 3.1. The number of assessments performed with respect to
implant duration and implant type..............................................131

Figure 3.2. The distribution of the ISOLS clinical grades with respect to
implant type..............................................................................131

Figure 3.3. Clinical score (ISOLS) with respect to duration and implant. ..........132

Figure 3.4. The ISOLS (upper) and BME (lower) clinical grading scores
with respect to patient age and implant........................................133

Figure 3.5. The ISOLS (upper) and BME (lower) clinical grading scores
with respect to the percentage of bone resected and implant.................134
Figure 3.6. The distribution of grades of the six sections that comprise to form the ISOLS clinical evaluation grade. ..............................................................135

Figure 3.7. The distribution of grades of the three sections that comprise to form the BME clinical evaluation grade. ..............................................................136

Figure 3.8. The individual clinical parameters that together form the Function Activity section of the clinical evaluation systems. ........................................137

Figure 3.9. The level of activity of the patient with respect to implant type. .........................................................................................................................138

Figure 3.10. Leg length discrepancy comparing the length of the limb salvaged leg with the contra-lateral, with respect to implant type. ......................139

Figure 3.11. The degree of limp with respect to implant. .................................................................................................................................140

Figure 3.12. Pain scores with respect to those classed as survivors or failures. ..................................................................................................................140

Figure 4.1. A diagrammatic transverse section through a bone, with the quadrants defined. .........................................................................................168

Figure 4.2. A diagrammatic representation of the parameters measured on radiographs. ..........................................................................................169

Figure 4.3. A diagrammatic representation of the BME radiographic evaluation program to score radiographs. ...............................................................170

Figure 4.4. The radiographic zones. ........................................................................171

Figure 4.5. The BME radiographic grades of 367 cemented intra-medullary stemmed endo-prostheses. .................................................................172

Figure 4.6. The ISOLS radiographic grades with respect to the implant type. ..................................................................................................................172
Figure 4.7. The percentage of radiographs showing constructive bony remodelling.

Figure 4.8. The frequency (%) and score of increased shaft diameter with respect to implant type and age of the patient.

Figure 4.9. The frequency (%) and score (±S.E.) of increased shaft diameter with respect to implant type and the percentage of bone resected.

Figure 4.10. The frequency and score of increased shaft diameter for each quadrant with respect to the percentage of bone resected and implant.

Figure 4.11. The percentage of cases with increased shaft diameter with respect to the location of the radiolucent line.

Figure 4.12. The percentage of radiographs showing adverse bony remodelling features.

Figure 4.13. Distribution of the total RLL scores with respect to implant.

Figure 4.14. The frequency (%) and score (±S.E.) of radiolucent lines with respect to age of the patient and implant.

Figure 4.15. The frequency (%) and score of radiolucent lines for each quadrant with respect to patient age and implant.

Figure 4.16. The frequency and score (±S.E.) of radiolucent lines with respect to the percentage of bone resected and implant.

Figure 4.17. The frequency (%) and score of radiolucent lines for each quadrant with respect to the percentage of bone resected and implant.
Figure 4.18. The percentage of cases with radiolucent lines with respect to the location of the radiolucent line and implant .........................................................184

Figure 4.19. The frequency (%) of RLLs along the stem length with respect to the percentage of bone resected and implant .....................................................185

Figure 4.20. The frequency and score of radiolucent lines with respect to duration and implant .................................................................................................186

Figure 4.21. The frequency and height (±S.E.) of the plateau gap with respect to quadrant and implant .......................................................................................187

Figure 4.22. Radiolucent line scores with respect to those that failed and those that did not .................................................................................................................188

Figure 4.23. The frequency of increased and decreased shaft diameter along the stem length for each quadrant with respect to the percentage of bone resected and implant .............................................................................189

Figure 5.1. The frequency (%) of pedicle with respect to quadrant and implant .................................................................................................................................218

Figure 5.2. The number of quadrants with pedicle present with respect to quadrant and implant ..................................................................................................................219

Figure 5.3. The frequency of pedicle with respect to implant and percentage of bone resected .................................................................................................................220

Figure 5.4. The frequency (%) of pedicle and mean pedicle score (±S.E.) with respect to quadrant, the percentage of bone resected and implant .............................................................................221

Figure 5.5. The frequency of pedicle with respect to implant, quadrant and the age of the patient .................................................................................................................222
Figure 5.6. The frequency (%) of pedicle and pedicle length (±S.E.) with respect to implant, quadrant and the age of the patient at the time of limb salvage. .................................................................223

Figure 5.7. The presence of pedicle with respect to duration and implant ..................................................................................................................................224

Figure 5.8. The number of quadrants with pedicle present with respect to implant ..............................................................................................................................225

Figure 5.9. The number of radiographs assessed with and without pedicle, in each time interval .................................................................................................................................226

Figure 5.10. The mean length of the pedicle (±S.E.) with respect to quadrant and implant .................................................................................................................................226

Figure 5.11. The percentage of cases with a plateau gap with respect to the presence or absence of a cement layer on the prosthesis plateau, with respect to quadrant .................................................................................................................................227

Figure 5.12. The rectangular shaped grooves (left) of the present design exhibited bony stress shielding. The triangular shaped grooves (right) as illustrated by Heimke result in a more evenly distributed stresses leading to greater bony contact .................................................................................................................................228

Figure 6.1. The design of the original proposed uncemented intra-medullary stemmed replacement .................................................................................................................................262

Figure 6.2. The ovality of the intra-medullary canal at 10% increments along the length of 10 femora ..................................................263

Figure 6.3. The design of the shaped plateau. The concave design was designed to reduce the possibility of longitudinal fracture of the bone..............264
Figure 6.4 The cross-section of femur illustrating the canal widths as described in the text. .................................................................265

Figure 7.1. The cross-section of a femur with a lateral and medial extracortical plate demonstrating that with a antero-posterior force the fixation screws are subjected to a shear force. .................................................................296

Figure 7.2. The design of the extra-cortical plated replacement for use in the animal model. .................................................................297

Figure 7.3. The designs of the cylindrical (left) and anatomic shaped extra-cortical basket (right) components. .................................................................298

Figure 7.4. A cross-section of an extra-cortical plate showing the bone apposition zones. .................................................................299

Figure 7.5. The 3 plated design used for reconstruction of the right distal femur of a 10 year old girl with osteosarcoma. .................................................................300
List of Plates

Plate 1.1. The first all metal distal femoral endo-prosthesis. Extra-cortical plates were used for fixation. This replacement remained in situ for 21 years. ..................................................................................................................56

Plate 1.2. Custom-made Stanmore proximal femoral (left), and proximal tibial (centre), distal femoral (right) replacements. These types of replacement were used extensively throughout the 1970s and 1980s. ..............................57

Plate 1.3. A chondrosarcoma of the proximal femur. The dimensions on the radiograph were scribed when the engineer was designing the proximal femoral replacement.................................................................58

Plate 2.1. A radiograph of an extendible distal femoral replacement showing aseptic loosening and pivoting of the femoral intra-medullary stem. This replacement had been in situ for four years. ..............................................104

Plate 4.1. A typical radiograph of a distal femoral replacement (implant duration = 14 months). Note the extensive medial pedicle, the small lateral pedicle and the shape of the plateau gaps..........................................................191

Plate 4.2. A radiograph of a loosened distal femoral replacement, showing radiolucent lines between the cement mantle and bone. (Implant duration = 21 months). Note the extensive RLLs on both the medial and lateral aspects. However, the RLLs do not penetrate the proximal cement mass.......................................................................................................192

Plate 5.1. Typical pedicle formation on a distal femoral endo-prosthesis. Note the extensive pedicle on the medial aspect of the replacement and the absence of pedicle on the lateral. There is a well defined radiolucent line between the pedicle and implant shaft, the resected bone and the prosthesis plateau and at the cement/bone interface. (Implant duration = 34 months)..................................................................................................229
Plate 5.2 a & b. A porous collared proximal femoral replacement (upper) and close up of the titanium beaded collar (lower). ........................................230

Plate 5.3. A radiograph of a porous collared replacement. Note the gap between the pedicle and the porous collar. (Implant duration = 2 years) .....................................................................................................................................231

Plate 5.4. A transverse section through the retrieved distal femoral implant. (Implant duration = 7 months). The band of aligned fibrous tissue (yellow) is interpositioned between the porous collar (black) and pedicle bone (brown)..........................................................................................................232

Plate 5.5. A hydroxyapatite coated distal femoral replacement. ........................................233

Plate 5.6. A lateral radiograph showing a well developed posterior pedicle ingrown into the hydroxyapatite coated grooves of a distal femoral replacement. The anterior pedicle does not appear to have fully incorporated into the grooved structure. (Implant duration = 22 months)..........................................................................................................234

Plate 5.7. a and b. Radiographs showing the change in the pedicle structure. Note the fine trabecularisation occurring in the later radiograph. The upper radiograph shows the pedicle formation after an implant duration of 13 months and the lower after 20 months............................235

Plate 6.1. A trial uncemented replacement and associated custom-made tools.......................................................................................................................................266

Plate 6.2. A custom-made miller with a precisely fitting pilot to prevent toggle whilst operating the device was used to produce a flat resected bone surface perpendicular to the long axis of the bone shaft..................................................................................267

Plate 6.3. Anti-rotation lugs were used on the uncemented replacements in the later clinical cases. Specialised tooling was
required to produce a recess. A close fit was considered essential to obtain initial implant stability

Plate 6.4. A proximal femoral replacement inserted into a cadaveric femur, undergoing fatigue testing to ensure that the intra-medullary will not fracture under normal use.

Plate 6.5. The first uncoated un cemented endo-prosthesis. This proximal humeral replacement had a screw passed through the aperture in the intra-medullary stem to prevent rotation. The intra-medullary stem was not hydroxyapatite coated.

Plate 6.6. An un cemented extendible distal femoral replacement with hydroxyapatite coating. Note the two sectioned stem, anti-rotation lugs and that the proximal section of the stem has been curved posteriorly to prevent contacting of the anterior endosteal surface of the femur.

Plate 6.7 a & b. Radiographs of a revision distal femoral replacement 1 day (upper) and 9 months (lower) following insertion of the implant. The later radiograph shows extensively bone remodelling with infilling distally and an increase in bone girth adjacent to the junction of the proximal and distal stem sections.

Plate 6.8. The frontal radiograph of case 4, showing the helical fracture and some bony remodelling. (Implant duration = 2 months). There has been remodelling around the anti-rotation lug, the tip of the intra-medullary stem and a small medial pedicle has developed but has not ingrown.

Plate 6.9. The radiograph of case 5, showing the general lack of remodelling after an implant duration of 14 months. There has been a small reduction in bone girth distally and a slight increase in girth adjacent to the junction of the proximal and distal stem sections.
Plate 7.1. A radiograph of a extra-cortical plated distal femoral replacement (Implant duration 18 years). The femoral and tibial plates were secured with transverse bolts. Bone had encased the proximal tip of the medial femoral plate.

Plate 7.2. A extra-cortical plated mid-shaft tibial replacement with 3 proximal plates and a distal intra-medullary stem. The hydroxyapatite coating covered all plate surfaces, the plateau and the proximal shaft.

Plate 7.3. An anatomically shaped basket viewed looking into the basket. This trial was fabricated in polyethylene and machined by computer controlled milling machine. (Top = proximal, right = medial)

Plate 7.4. A disassembled anatomically shaped basket fabricated in titanium alloy and coated in hydroxyapatite ceramic.

Plate 7.5. A radiograph of a extra-cortical plated mid-shaft tibial replacement in a goat model. This three plated design was secured to the proximal tibia with uni-cortical screws. Bone has begun to developed over the posterior plate and around the implant shaft. (Implant duration = 3 months).

Plate 7.6. A contact radiograph of a transverse section through a retrieved extra-cortical plated mid-shaft tibial replacement. The goat was culled 6 months following implantation. Note the bony attachment of the antero-medial plate (upper right), and the vascularisation of the cortex adjacent to the inner surfaces of the posterior and lateral plates.

Plate 7.7. A radiograph of the extra-cortical plated distal femoral replacement that was the first of its kind to be used for over 3 decades (implant duration = 4 months). There was some periosteaal activity with some bone forming around but not into the anterior plate.
Chapter 1

Introduction to bone tumour limb salvage
Custom-made massive endo-prosthetic replacements in comparison to standard joint replacements are used infrequently. During the last two decades the use of massive endo-prosthetic replacements has become increasingly important in limb salvage surgery, predominantly for the treatment of bone tumours. Unlike the majority of joint replacement patients who are elderly, bone tumour patients are frequently in their second or third decades of life and therefore any method of limb salvage may be required to function for many decades. Until recently, there had been few studies undertaken concerning massive replacements, largely as a result of the small number used. Early studies did not identify aseptic loosening as a major cause of implant related failure, often because of the relatively short follow-up. These studies highlighted the short-term complications such as fatigue fracture and infection. Until recently, the longer term complications have not been possible to identify.

In addition, whilst designing and manufacturing the custom-made replacements within the Division of Biomedical Engineering, it was becoming clear that aseptic loosening was an ever increasing problem. It has now been recognised that aseptic loosening is singly the most common cause of an implant related failure with cemented intra-medullary stemmed massive endo-prostheses.

However, it was unacceptable to identify that aseptic loosening was the predominant mode of failure with massive endo-prostheses without identifying factors that influenced loosening and putting forward possible solutions.

1.1. Aim of the study

The principal aims of this research were to -

- identify the factors related to aseptic loosening
- develop new methods of fixation to improve the longevity of massive endo-prosthetic replacements.
In greater detail, the undertakings were -

1. An extensive clinical and radiographic review of patients with one of the three most commonly used lower limb custom-made endo-prosthetic replacements. These replacements were the proximal femoral, distal femoral and proximal tibial replacements, designed and manufactured individually at the Division of Biomedical Engineering located at the Royal National Orthopaedic Hospital, Stanmore. The data collected in the review formed the underpinning basis from which all future modifications to the implant design were to be measured against.

The reasons for studying these 3 implants were -

- they were the most commonly used replacements. This was because malignant bone tumours occur most frequently in the lower limb.
- aseptic loosening predominated in the lower limb compared to the upper limb.
- the three skeletal locations differed in the biomechanics. The long axis of the femur is angled towards the medial line and is bowed anteriorly in the sagittal plane whereas the long axis of the tibia has a vertical orientation and relatively straight.

2. Based upon the data obtained above, a number of modifications to existing designs and new fixation methods were developed. The aim was to reduce the rate of aseptic loosening and prolong the life of endo-prostheses. The developments can be sub-divided into three sections, and were the -

- enhancement of the fixation of existing cemented intra-medullary designs. Using technologies developed for uncemented joint replacement and dental restoration, proposed methods to improve the fixation were introduced that later underwent clinical trials.
• introduction of an uncemented intra-medullary stemmed endoprosthetic replacement. The development required pre-clinical trials and culminating in clinical evaluations. The design rationale required input from the extensive review of patients with cemented intra-medullary replacements and those with implants that had enhanced fixation features.

• investigation of extra-cortical fixation.

1.1.1. The Division of Biomedical Engineering, Institute of Orthopaedic, University College London.

The location of this research was at the Division of Biomedical Engineering, situated at the Royal National Orthopaedic Hospital, Stanmore. This was an ideal location because -

1. The founding work in limb salvage devices in Britain was carried out under the direction of Prof. J.T.Scales, who headed the Division for over 3 decades.

2. Records of all Stanmore custom-made replacement cases have been kept, providing a wealth of invaluable long-term data that is unsurpassed anywhere in the world. The number of Stanmore custom-made massive endo-prostheses inserted by late 1994 was over 2,500, and is considered to be the largest of its kind in the world.

3. The synergy of research and development with the service commitment of the design and manufacture of custom-made endo-prostheses directed by Prof. P.S.Walker, provides opportunity to put forward new ideas and test hypotheses. In addition, debate and paper presentations at national and international meetings is widely encouraged.
4. The Division works in close collaboration with orthopaedic surgeons of the two Supra-regional Bone Tumour Treatment Centres who provide valuable input and actively encourage and assist in the R&D programme.

5. Within the Division there are a number of other inter-related projects such as the telemetry of strain-gauged massive endo-prostheses and the development of a non-invasive extendible massive endo-prosthetic replacements.

1.2. Layout of the thesis

The thesis has been laid out with an introduction that describes briefly the biomechanics of the lower limb and the most commonly occurring bone tumours. Methods of limb salvage, forms of fixation and factors relating to aseptic loosening are discussed. In addition, the results from other limb salvage centres throughout out the world have been presented.

After the introductory chapter the remainder of the thesis has been sub-divided into four sections. The four sections are -

• An extensive survival study of 1149 primary intra-medullary stemmed lower limb endo-prosthetic cases provided data from which to compare developments put forward in this research and for use in future developments. The survival studies were supplemented by radiographic and clinical assessments of patients. This extensive review identified parameters that influenced aseptic loosening and led to the development of theories on loosening. (Chapters 2-4).

• Methods of enhancing the fixation of cemented intra-medullary stemmed endo-prosthetic replacements were introduced using technology transfer from recent developments in total joint replacement. (Chapter 5).

• Uncemented intra-medullary stemmed fixation was developed using knowledge gained enhancing the fixation and from total joint
replacement technology. This chapter detailed the development of the uncemented intra-medullary stemmed endo-prostheses. (Chapter 6).

- Experimental methods of extra-cortical fixation were investigated using an animal model. Inspired by the results of the extra-cortical plated fixation of the earliest Stanmore massive endo-prostheses, modifications and novel designs were selected and tested. (Chapter 7).

Each chapter has its own introduction, methodology, results and discussion.

The thesis was completed with a summary and conclusions, highlighting the major findings. (Chapter 10).

1.3. Forms of limb salvage

The predominant method of limb salvage reconstruction for malignant neoplasia of bone in the UK has been the massive endo-prosthesis. Prior to the introduction of adjuvant chemotherapy, amputation was used frequently, endeavouring to save the life of the patient. However skeletal reconstruction has not been restricted solely to the use of metallic endo-prostheses. Throughout the world there are a number of alternative limb salvage techniques being used currently.

1.3.1. Allografting

Allografting, the most common alternative limb salvage technique to endoprosthetic limb reconstruction has been popular in the USA and Europe. The allografting technique used predominantly in bone tumour surgery has also been used for revision of failed standard total knee replacements (Tsahakis et al 1994). Studies of this limb salvage method identified that complication rates were relatively high. One study of 83 massive distal femoral osteoarticular allografts showed that complications included fractures (14%), non-unions (12%), arthritis (10%), joint instability (7%), infections (6%) and resorption (6%)
Mnaymneh et al (1994). Other similar studies also recorded high complication rates, predominantly as a result of fracturing (Delloye et al 1995, Donatti et al 1995) or non-union (Capanna et al 1993). Using an intra-medullary nail to improve the stability of the graft had its own complications. Wolf noted that intra-medullary nails fractured usually 2 to 3 years after insertion or in the longer term, migrated (Wolf et al 1995).

Chemotherapy has been linked to the complication rate. Mnaymneh report infection in 13% and non-unions in 23% of allograft patients who had chemotherapy, but for those who had no chemotherapy, infections occurred in 2% and non-unions in 6% (Mnaymneh et al 1994).

Other forms of complications including disease transmission (Buck et al 1989) such as hepatitis C (Conrad et al 1995), and the possibility of an immune reaction (Berrey et al 1990) have been raised. Disease transmission and rejection can be eliminated by autografting and furthermore, a more rapid union that is less dependant on osteosynthesis devices can be obtained (Capanna et al 1991a). However, autografting suffers from the limitation of graft size (Zatsepin and Burdygin 1994), the inability to obtain an osteoarticular graft, and additional complications at the site of harvest (Capanna et al 1991a). The most common donor site has been the fibula, which can be used either revascularised (Ceruso et al 1995) or not (Lindner et al 1995). An extensive series of 111 free fibula grafts reported that 7 cases had donor site complications (Lindner et al 1995).

Although the complication rate of allografting compared to endo-prosthetic reconstruction can be high, one study highlighted that femoral allograft reconstructions could function well for 36 years (Muscolo et al 1992). Of the 6 cases with follow up between 22 and 36 years, 4 femora had fractured during the first 2 years, of which 3 required surgical intervention to position additional allograft resulting in reunion in all cases. The fourth case remained untreated.
and resulted in an established non-union. Indeed, Quinn commented that only infection and the occasional fracture led to catastrophic failure and infection could be treated with an antibiotic impregnated polymethylmethacrylate cement spacer similar to those used in revision of infected massive replacements (Grimer et al 1991). Using this method of control, the likelihood of amputation resulting from the infection can be reduced (Quinn et al 1995). Salvaging other modes of failure using a composite allograft with a total knee replacement can also be successful (Neel et al 1995).

1.3.2. Composites (Implant plus grafting)

To reduce the non-union and fracture rates, allograft prosthesis composites (APC) have been used. They have the added bonus over allografts of durable structural support for the graft, improved stability of the bony junctions permitting faster union thus allowing for faster patient rehabilitation (Mercuri et al 1995). The advantage over endo-prostheses has been the ability to reattach soft tissue structures. Reattachment of the glutei hip abductors in proximal femoral limb salvage improved significantly hip abduction (Langlais et al 1995). A comparative study of 19 APC cases and 20 endo-prosthetic cases of the proximal femur identified that the overall survival of the reconstruction was remarkably similar. There were non-unions of the allograft, but the functional ability of the APC patients was greater (Zehr et al 1991). The disadvantage of APCs was that the specific complications of both forms of limb salvage were present. Graft resorption and non-unions in one series of proximal femoral reconstruction was alarmingly high (Beauchamp et al 1995). Around the knee, Delepine reported a high rate of deep infection that was considered to be soft tissue related and also implant loosening occurred (Delepine et al 1993).

1.3.3. Bone transport

Bone transport using such techniques as the Ilizarov or uni-lateral lengthener has been generally restricted to tumour limb salvage in the diaphyseal region of
long bones. However, the technique has been used for distal femoral tumours where the knee has been fused (Nakatsuka et al 1995). The advantage of this technique has been the low complication rate. Complications included soft tissue inflammations of the wire tract, joint contracture and intermittent pain (Tsuchiya et al 1993). In all cases, the complications did not require the removal of the bone transport devices.

1.3.4. Rotationplasty

This radical procedure is frequently carried out for skeletally immature patients with distal femoral tumours. After excision of the tumour, the remaining distal part of the limb is rotated through 180° and the tibial and femoral stumps attached. The ankle joint then acts as a knee, converting what would have been an 'above-knee' amputation into form of 'below-knee' amputation. This has the added advantage of attaching the exo-prosthesis securely to the foot rather than the thigh. Distal femoral rotationplasty has been reported to provided a comparable alternative to endo-prostheses and better functionality than those with an above-knee amputation (Cammisa et al 1990). Rotationplasty has also been used at the hip with long term success providing excellent function (Winkelmann et al 1995), and for tumours in the proximal tibia (De Bari et al 1990). The disadvantages of rotationplasty has been the unusual appearance of the limb and the higher costs of the exo-prostheses.

1.3.5. Amputation

Amputation although not a limb saving method does have an important role in the treatment of malignant neoplasia of bone. The primary goal is preservation of life and limb reconstruction is secondary. However, studies comparing amputation with methods of limb salvage have shown that disease free survival has not been compromised by using limb sparing treatment methods (Simon et al 1986). Harris reported that amputees were very active and were not worried about damaging their affected limb (Harris et al 1990). The overall
cost of care for a lower limb amputee is significantly higher than that when limb saving methods have been used (Grimer et al 1997, Williams 1994).

1.4. Massive custom-made replacements

The purpose of the massive endo-prosthetic replacement is to preserve the affected limb and restore kinematic function of the joint to provide locomotion.

Bone replacement is known from Egyptian and Inca times. In an Ancient Egyptian mummified corpse, a wooden lower limb replacement was discovered (David 1978). The first modern day custom-made massive endo-prosthetic replacement was inserted in 1940, by Austin Moore and Bohlmann, who replaced the proximal 300 mm of the femur with a CoCrMo alloy replacement that used extra-cortical side plates (Jackson Burrows et al 1975) and was followed shortly after by a further proximal femoral replacement. Shortly after Professor Scales constructed the first of many custom-made massive endo-prosthetic replacements.

1.5. Stanmore custom-made replacements

Professor Scales then Dr Scales, established the Department of Biomedical Engineering designing and fabricating the first massive limb saving replacement in 1950. This proximal humeral replacement, the body of which was fabricated in polyethylene was secured to the bone with two extra-cortical stainless side plates (Jackson Burrows et al 1975). Today, the Division of Biomedical Engineering as it is now known, has world-class recognition for the design, manufacture and research into custom-made endo-prosthetic replacements. Over 3000 special joint and massive replacements have now been designed and fabricated in the Division’s workshops.
1.5.1. The first Stanmore custom-made replacements

The first Stanmore femoral limb saving replacement was inserted in September 1951. This proximal femoral replacement had an acrylic body and 2 cobalt chrome alloy plates that were secured to the medial and lateral aspects of the shaft bone by transverse bolts. In April 1952, the first distal femoral replacement was inserted, the indication was hydatid disease. This replacement had an acrylic body onto which was attached a nylon knee. The replacement was secured to the femur by 2 stainless steel plates. The first all metal distal femoral endo-prosthesis was inserted in November 1954, the body and the extra-cortical plates were fabricated in CoCrMo alloy, that were secured to the femur by 2 transverse screws (Plate 1.1). This replacement was revised after 251 months because an incomplete fracture of the lateral plate identified on radiographs in 1974. In total, 7 lower limb extra-cortical plated Stanmore massive lower limb replacement were inserted, the last being in 1962. The advent of polymethylmethacrylate (PMMA) bone cements in orthopaedic reconstructive surgery dramatically changed the method of fixation from extra-cortical plating to cemented intra-medullary stemmed fixation.

1.5.2. The Stanmore intra-medullary stemmed massive endo-prosthetic replacements

All custom-made intra-medullary stemmed endo-prosthetic replacements that have been designed and manufactured at the Division of Biomedical Engineering's workshops since 1964 have been fabricated in titanium alloy (Ti 4V 6Al, Ti318). There are a number of advantages of using this metal compared to cobalt chrome molybdenum or stainless steel alloys also used in the manufacture of joint replacements. The advantages of titanium alloy include a lower Young's modulus, more biocompatible, increase ease of machining and is lighter. The complications of titanium alloy include notch sensitivity and lower hardness.
Over the decades, the basic designs of the three lower limb implants have evolved (Figure 1.1 and Plate 1.2). The intra-medullary stem has been modified to improve the fixation within the cement mantle and the joining of the stem to the prosthesis body. Initially, intra-medullary stems were parallel, but were later soon replaced by stems with a dimple ground into the stem close to the tip. This design was superseded by the 'D' shaped stem and by 1987, this design was replaced by the present design. The present design comprised of a tapering stem with three milled flutes of differing lengths. Until 1985, intra-medullary stems were either bolted into the prosthesis shaft body or were fabricated as an integral part of the prosthesis shaft. Since then intra-medullary stems have been heat shrunk and riveted into the prosthesis shaft.

1.5.2.1. Proximal femoral

Proximal femoral replacements comprised of 4 components. The prosthesis shaft, intra-medullary stem and trochanteric neck components were fabricated in titanium alloy, onto the trochanteric neck, a CoCrMo femoral head was fitted by heat shrinking. For all but the extensive resections, the femoral intra-medullary stems and to a lesser extent the prosthesis shafts were curved to follow the natural antero-posterior curvature of the femur. The offset of the centre of the femoral head measured perpendicular from the long axis of the femur was reproduced in the replacement by varying the length of the trochanteric neck.

1.5.2.2. Distal femoral

Both distal femoral and proximal tibial replacements comprised of three components, namely the intra-medullary stem, the prosthesis shaft fabricated in titanium alloy and a knee hinge. Until mid 1991, a modified Stanmore fixed hinge total knee replacement (CoCrMo) was used. The Stanmore knee, was virtually superseded by 1994 by the more advanced SMILES (Stanmore Modular Individualised Lower Extremity System) rotating hinge cast in
CoCrMo. This knee hinge, designed at the Division of Biomedical Engineering, was principally designed for use with massive endo-prosthetic replacements. As with the proximal femoral replacements the majority of distal femoral replacement intra-medullary stems were bowed.

1.5.2.3. Proximal tibia

The proximal tibial replacement comprised of a knee hinge, shaft and intra-medullary stem were unlike the distal femoral replacement because it was infrequently curved, due to the straight nature of the tibia. Over the last two decades there were modifications to the patella tendon reattachment. Initially, a transverse hole positioned approximately 30 mm below the axle, approximating to the anatomical position of the tibial tuberosity, allowed for an artificial ligament to be passed through. Later these were replaced by two holes (anterior-posterior), but in 1990 this method of patella tendon reattachment was halted, due to the breakdown of the artificial ligament leading to soft-tissue complications. These complications have partly been remedied by the use of a gastrocnemius flap used since 1990 (Grimer et al 1989, Grimer et al 1991).

1.5.3. Implant design

Concurrently, with the introduction of the individualised modular component system (SMILES) based around the rotating hinge, a knowledge based expert system was programmed. The aim of the knowledge based system was to assist in the design custom-made massive endo-prostheses. Using on-screen prompts the designer digitised key anatomical landmarks, from which the programme designed the replacement. Customised CAD and database packages imported the co-ordinate data and automatically produced scaled engineering drawing and fully annotated surgical planning diagrams. (Crawford et al 1991, Unwin 1992a, Unwin et al 1992b, Unwin and Walker 1993a). The computer-based system has now been in service since 1991 and has
been used successfully to design the majority of Stanmore's lower limb bone tumour replacements.

1.6. Pathology

There are a wide variety of orthopaedic conditions of the lower limb that have required the use of a custom-made massive endo-prosthetic replacement for limb reconstruction. These conditions, fall into 4 broad categories, that are -

- **Bone tumours.** The predominant use of massive endo-prostheses has been for treatment of skeletal neoplasms where the alternative to a custom-made replacement has normally been amputation or an allograft reconstruction.

  Tumours arising in bone are normally graded as either benign or malignant. Rarely do benign tumours require radical surgery unlike malignant bone neoplasia. Malignant tumours arising in bone are rare, however, they account for a significant proportion of neoplasia in children and teenagers. In teenagers, malignant bone tumours are the fifth most commonest neoplasm (Souhami 1987). The average annual incidence of malignant bone tumours in a population of white American children (<14 years) was 6.3 cases per million.

- **Non-neoplastic conditions or diseases of bone.** Degenerative or congenital diseases of bone such as osteoarthritis, Paget's disease, fibrous dysplasia and aneurysmal bone cysts have been treated using massive replacements. In addition, trauma and non-union of fractures have been included in this group. Reconstruction using a massive endo-prosthetic replacements in the lower limb for these conditions is rare.

- **Failed standard joint replacements.** Some failed joint replacements have produced such extensive bone loss that standard revision joint replacements have been inappropriate and massive replacements have needed.
- **Failed massive replacements.** The failure rate of massive endo-prosthetic replacements is relatively high compared to standard joint replacements and therefore there has been a demand for revision massive endo-prosthetic replacements to replace those that have failed.

### 1.6.1. The Stanmore bone tumour replacement registry

Between 1950 when the first bone tumour was treated to the end of 1993, 1686 bone tumour patients had their limb salvaged with a Stanmore custom-made replacement (Figure 1.2). The classification of bone tumours with respect to this research included metastases arising in bone but did not include non-neoplastic conditions such as Paget's disease, aneurysmal bone cyst or fibrous dysplasia.

The majority of custom-made implants were designed for the lower limb (Figure 1.3). In total, 19 different types of implant were used between 1950 and 1993.

The four most commonest bone tumours that occurred in the Stanmore bone tumour massive implant registry, were osteosarcoma (43.4%), chondrosarcoma (15.4%), osteoclastoma (10.0%) and Ewing's sarcoma (8.5%). Prior to 1975, only chondrosarcoma and osteoclastoma patients had been given limb salvage treatment with the exception of one osteosarcoma treated in 1967. From 1975 onwards the number of osteosarcomas being treated with a Stanmore endo-prosthetic replacement rose rapidly and in 1992 and 1993, 78 osteosarcoma cases were treated in each year. In comparison, the number of chondrosarcomas and osteoclastomas being treated rose slowly, with 32 chondrosarcomas in 1993 and 15 osteoclastomas in 1986 being the maximum treated in a year. The first case of Ewing's sarcoma was treated in 1977, with the second in 1979 and by 1991, the number had risen to 21.
Osteosarcoma, is the commonest occurring malignant primary bone tumour with an estimated 2 to 3 cases per million per year of the British population with an annual reporting of between 130 and 150 new cases per year (Souhami 1987). The tumours are normally associated with the metaphysis, destroying the bone as it grows. Osteosarcomas vary in histology and malignancy (Pringle 1987). Skeletal location, age and gender of the patient, size of the tumour and the presence of a pathological fracture are known to have a considerable effect on prognosis. Various chemotherapy regimes have been used, with many treatment centres using multiple drug, multiple cycle adjuvant chemotherapy.

In terms of replacement, osteosarcomas were predominately associated with the lower appendicular skeleton (85.6% in the lower limb), with the tumour occurring most commonly in the distal femur (50.4%), the proximal tibia (26.4%) and the proximal humerus (10.9%). The average age of the patient at the time of the limb salvage surgery was 18.7 years (±0.12 S.E. n=728). The average age of the patients with osteosarcomas that occurred in the proximal tibia were the youngest (17.3 years, n=192) and the patients with proximal femoral osteosarcomas, the oldest (29.3 years, n=33).

Chondrosarcoma, is a cartilage forming malignant tumour and is the second most commonly occurring malignant bone tumour. In the femur, it predominates in the proximal diaphysis (Plate 1.3). Chemotherapeutic drugs are not administered. The long-term prognosis of pelvic and axial skeletal chondrosarcomas is poor, because of the problems encountered achieving complete removal (Pringle 1987).

Of the 4 tumour types described here, patients with chondrosarcoma who underwent limb salvage were the eldest, often in their fifth and sixth decades of life (48.2 years, n=256). The commonest locations were the proximal femur (39.5%), the proximal humerus (18.8%) and the distal femur (17.2%).
**Osteoclastoma**, (Giant Cell Tumour or GCT) is a very low malignancy tumour that contains osteoclast giant cells of a histiocytic origin. Giant cell tumours account for 5% of all bone tumours (benign and malignant), and have a small metastatic potential (Pringle 1987). Chemotherapeutic drugs are not administered. Many GCTs are excised by a wide excision curettage. Lower limb endo-prostheses are used when there has been a pathological fracture or the tumour was extensive with an unobtainable clear margin leaving insufficient cortical bone for weight-bearing.

Patients who underwent limb salvage reconstruction with a massive replacement, predominantly had the tumour around the knee, with 49.3% associated with the distal femur and a further 23.8% in the proximal femur. Ten percent of GCTs were associated with the upper limb. The average age of the 164 osteoclastoma patient at the time of surgery was 36.4 years (±0.31).

**Ewing's sarcoma**, consists of densely packed small round cells of a primitive neuroectodermal origin (Pringle 1987). Ewing's sarcomas are rarer than osteosarcomas and make up approximately 10-14% of all malignant bone tumours in Caucasian populations. In African and Oriental populations Ewing's sarcoma is significantly rarer (Souhami 1987). Radiographically, the appearance of the tumour can appear rather like that of a sectioned onion as a result of fine parallel layers of periosteal lamination. Adjuvant chemotherapy is given to Ewing's sarcoma patients. The prognosis varies greatly depending on the size, location and stage of the tumour and survival of patients without metastases varies from 55% to over 75% at 5 years.

Limb salvage patients with Ewing's sarcoma were on average the youngest (16.9±0.24 years). Eleven percent of the Ewing's sarcoma were restricted to the diaphyseal regions of the humerus, femur and tibia and a further 6.3% occurred in the peri-acetabular region of the pelvis. The most common site for Ewing's sarcoma in this series was the proximal femur (31.5%).
Further study relating the dimensions of 871 femora and tibiae obtained from measurement radiographs to patient age and tumour type are presented in Appendix A.

1.7. Fixation Methods

From the earliest massive endo-prosthetic replacements to the present day, there are principally four types of fixation methods.

1.7.1. Extra-cortical plates

The first method of fixation was the use of extra-cortical side plates and was prior to the introduction of polymethylmethacrylate (PMMA) as 'bone cement'. Austin Moore used side plates on the first massive proximal replacement in 1940 (Jackson Burrows et al 1975). Later, this method of fixation was taken up by Scales and the first side plates were fabricated in stainless steel but on the second case CoCrMo alloy was used. The slotted plates were secured to the bone with transverse bolts. The Stanmore series is the largest and is discussed in greater detail in Chapter 7.

1.7.2. Cemented intra-medullary stems

After the introduction of polymethylmethacrylate (PMMA) into orthopaedic reconstructive surgery in 1958, cemented intra-medullary stemmed fixation superseded extra-cortical plating. Bowed custom-made titanium alloy intra-medullary stems matching the anterior curvature of the femur were grouted in with PMMA. This method has been the predominant form of fixation of the Stanmore custom-made replacements (Scales and Wright 1983, Scales et al 1984). Other major bone tumour centres including the Memorial Sloan Kettering Cancer Center, New York (Horowitz et al 1993), UCLA, Los Angeles (Ward et al 1993) and Paris (Missenard 1991) have also used this fixation method.
1.7.3. Uncemented intra-medullary stems

Uncemented intra-medullary fixation has been generally restricted to skeletally immature cases (Eckardt et al 1993a) and is discussed in greater detail in Chapter 6.

1.7.4. Uncemented intra-medullary stems + extra-cortical plates

One of the most widely distributed massive endo-prosthetic replacement has been the Kotz modular femur and tibia reconstruction endo-prosthesis (KMFTR). This modular replacement has evolved but the basic system of a press-fit madreporic coated intra-medullary stem with two or three side plates has remained (Salzer et al 1989). In recent years, a curved intra-medullary stem has been developed. This replacement with its unique method of fixation has been studied at a number of institutions including the Rizzoli, Bologna (Capanna et al 1994), Vienna (Kotz and Ritschl 1987, Salzer et al 1989, Kotz 1991, Samek et al 1991), and Lieden (Zwart et al 1994).

1.8. Aseptic loosening

Bone, a dynamic living organ, has a biphasic composite structure of inorganic mineral salts and an organic matrix of collagen and ground substance. Bones are formed of cortical and cancellous bone and are considered to be one material whose porosity, density and mechanical properties varies considerably. Bone is an anisotropic viscoelastic material. Mature bone is strongest and stiffest in compression. In compression, cortical bone tends to buckle whilst in tension it fractures transversely, but spiral fractures occur when torsion is applied. Defects such as screw holes significantly effect the strength of the bone (Hipp et al 1990). Bone adapts to the mechanical demands placed upon it. Complex loading patterns are subjected to bones in every day activities. The attachment of muscles and ligaments affect the stress patterns in bone and reduce or neutralise the tensile stresses acting on the bone. The
mechanical behaviour of bone is influenced by its geometry including its length, cross-sectional area and the distribution and distance of bone tissue around the neutral axis. External factors such as activity level, affect the bone mass but also natural factors affect the shape and strength of the bones. With increasing age, the human skeleton loses bone mass (Poss 1992). As a result of femoral bone loss, Smith identified that the outer cortex and medullary canal diameters increased from the age of 45 in females (Smith and Walker 1964).

1.8.1. Definitions of loosening

A generally acceptable definition of aseptic loosening would be the degradation of the implant interface that results in implant instability and pain. With interfacial loosening of the connecting surfaces, the capacity to locally transfer tensile and shear stresses is lost (Huiskes 1986).

Commonly, the terms radiographic loosening and clinical loosening are used. Radiographic loosening describes the observation of the presence of a radiolucent line that partially or totally separates the cement or implant from the adjacent bone. The histology of successful replacements has shown lamellar bone in close contact with cement whilst loosened replacements have a fibrous interlayer between the cement mantle and adjacent bone (Malcolm 1991). The development of radiolucent lines is considered to be a process of aseptic loosening. Progressive loosening is determined from an increase in radiolucent line width and length. As a 'rule of thumb' it is considered that a radiolucency line width of >2 mm is considered to be loose (Sneath pers comm).

Clinical loosening relates to the patient experiencing pain or movement of the replacement and in conjunction with radiographic evidence will be the principal indicators for the determination of revision.
1.8.2. Mechanisms of loosening

There is great debate about the mechanisms and causes of joint replacement aseptic loosening, this process is considered multifactorial (Blunn et al 1991). Aseptic loosening has been described as nearly always a process and rarely an event (Huiskes 1993). The loosening process takes place over time, possibly many years and is an interaction between mechanical and biological processes. Overall, it is considered that the integrity of the interfaces is paramount. The cement/bone interface is essentially a mechanical interlock. The bone adjacent to the joint replacement dynamically adapts to the modified environment and has been investigated using strain adaptive bone remodelling theory (Huiskes et al 1992). This theory in accordance with Wolff's Law briefly states that stress reduction in bone (stress shielding) leads to bone atrophy whilst increased loading leads to bone apposition. Very high compressive stresses in bone leads to necrosis and possible mechanical failure. Imbalance of stresses in the system either in bone or metal can lead to interface debonding. Interfacial stresses reduce in the regions of stress-shielding and increase in those transmitting forces. High stresses in the metallic implant lead to localised mechanical debonding of the interface. Localised debonding leads to increased interfacial stresses in the remainder of the system. Debonding of the cement from the implant has been observed to occur at sharp corners of the implant and regions of a thin mantle of cement (Jasty et al 1991). Jasty concluded that with time, long-term failure was primarily mechanical, and started with the debonding of the interface cement/implant that eventually led to cement mantle fracturing.

Overall, it appears that the process of loosening is long term, however, very high and rapid loading resulting from a stumble or fall may initiate or accelerate the debonding process. Bergmann using data obtained using telemetric methods of instrumented total hip replacements calculated resultant hip joint forces (Bergmann et al 1993). Two patients were monitored undertaking a various of activities. Whilst walking slowly at 1 km h⁻¹ the
median peak force applied to the femoral head was approximately 280% of body weight (BW), increasing the speed to 5 km h\(^{-1}\) the force rose to 480% BW. When a stumble occurred, this caused the peak force to rise to 870% BW. Some components of the gait cycle or certain activities may be more detrimental to the implant interface but little has been undertaken to identify which components are most detrimental. Andriacchi has provided a comprehensive review of the musculoskeletal dynamics and locomotion of the lower limb (Andriacchi and Mikosz 1991). This review highlights the complexity of joint kinematics and of particular relevance the change in lower limb kinematics after joint replacement.

The bonding of the interfaces therefore appears critical for long-term survival but stress distribution is an essential factor. A fully bonded interface prevented the ingress of wear particles and reduced axial and torsional micromotion (Taylor et al 1993). However, Gardiner (Gardiner and Hozack 1994) postulated that an improved bonding of the cement/bone interface may transfer increased stresses and thus causing early interface failure. A compliant interlayer between the implant and supporting bone to improve the stress distribution has been considered, but was identified not to distribute the stresses as hypothesised (Walker et al 1990).

Instability of the implant through interface debonding leads to micromotion and debris production. Some workers suggest that wear debris induces osteolysis whilst others believe that loosening induces wear. Mjöberg reviewed the theories of wear and loosening and concluded that loosening can be explained as a result of early prosthetic instability due to insufficient fixation or early loss of fixation (Mjöberg 1994). Secondary are patient factors such as age, weight. His final conclusion was that wear particles were not the initial cause of loosening. The biological response to the debonding/micromotion and or wear debris is believed to initiate a chain reaction of cellular activity. The role of the macrophage has been considered to be primary in the biological response
to loosening. Macrophage activity responding to the stimuli of phagocytosing PMMA particles produce inflammatory mediators has been postulated (Horowitz et al 1991).

It is recognised that implant design, material stiffness, surgical technique and the application of cement has significant bearing on the interfaces. Second generation cementing techniques and modern stem designs have been reported to improve hip arthroplasty results (Estok and Harris 1994).

1.9. A review of aseptic loosening of massive replacements from other centres.


Centres throughout the world have reported their experiences of massive endoprosthesis. These can be sub-divided into either those who used cemented or uncemented intra-medullary stemmed fixation. Table 1.1. summarises the aseptic loosening results of 23 studies (not including Stanmore). Care is needed when comparing the results from different centres due to the differences in fixation methods, skeletal location, patient age and length of follow-up. Generally with respect to aseptic loosening, uncemented intra-medullary stemmed replacements performed better than cemented stemmed replacements. The only uncemented stemmed series with a number of cases
revised for loosening was reported by Salzer (Salzer et al 1989). The loosening was predominantly restricted to early versions of stem fixation that was later developed into the Kotz design. In nearly all studies of cemented replacements, loosening was a major complication. Cemented stemmed proximal femoral replacements fared better than distal femoral and proximal tibial replacements.

1.10. Statistical methods

Typically for clinical oriented score data, the data gathered was non-Normal (identified using the Shapiro-Wilks test for normality). Non-parametric tests (Siegel and Castellan 1988, Armitage and Berry 1994) were utilised in part due to the non-normality of the data but also 'ranking tests' were required. The Wilcoxon and Mann-Whitney U tests were used to compare 2 non-parametric groups and the Kruskal-Wallis test when three or more populations were compared. Throughout, the mean average has been used and quoted with the standard error. The studies have evaluated many parameters, however, multifactorial analysis has not been used. With the large number of cases reviewed, careful selection of cases reduced the variability of specific comparisons. All statistics except those for survivorship were calculated using JMP (version 2.0.5. SAS Institute Inc.), on an Apple Macintosh LCII computer. The survival analysis was performed using Statworks for the Macintosh (version 4.0.1. Abacus Concept Inc.) with the additional survivorship module.
Figure 1.1. Intra-medullary stemmed endo-prostheses for the replacement of the proximal femur (left), distal femur (centre) and proximal tibia (right).
Figure 12. The number of bone tumour custom-made Stanmore endo-prostheses inserted between 1950 and 1993, highlighting important events.

- The SMILES rotating hinge and uncemented intra-medullary stemmed fixation introduced
- Hydroxyapatite coated collars introduced
- Porous beaded collars introduced

- First chondrosarcoma treated
- First proximal femoral replacement inserted
- First distal femoral replacement inserted & first osteoclastoma treated
- Cemented intra-medullary stemmed fixation introduced
- First ostosarcoma treated
- First proximal tibial replacement inserted
- First Ewing's sarcoma treated
- First proximal femoral replacement inserted
Figure 1.3. The skeletal locations of 1686 Stanmore custom-made bone tumour endo-prostheses inserted between 1950 and 1993.
Plate 1.1. The first all metal distal femoral endo-prosthesis. Extra-cortical plates were used for fixation. This replacement remained in situ for 21 years.
Plate 1.2. Custom-made Stanmore proximal femoral (left), and proximal tibial (centre), distal femoral (right) replacements. These types of replacement were used extensively throughout the 1970s and 1980s. Note that the proximal femoral replacement has a very short stem. Short stems such as this were used infrequently and the typical stem was similar to those on the distal femoral and proximal tibial replacements shown.
Plate 1.3. A chondrosarcoma of the proximal femur. The dimensions on the radiograph were scribed when the engineer was designing the proximal femoral replacement.
Table 1.1. A summary of aseptic loosening in 23 studies from centres throughout the world.

<table>
<thead>
<tr>
<th>Centre</th>
<th>Skeletal replacement</th>
<th>Stem design</th>
<th>Fixation</th>
<th>No. failed or probability of surviving aseptic loosening</th>
<th>Follow-up Mean duration; Range</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bologna</td>
<td>DF=95</td>
<td>Kotz modular</td>
<td>Unc</td>
<td>95 None</td>
<td>51 mths; 2-102 mths</td>
<td>Capanna et al 1994</td>
</tr>
<tr>
<td>New York</td>
<td>DF=61, PF=16, PT=16</td>
<td>Custom-made</td>
<td>C</td>
<td>92 DF=78%, PF=100%, PT=73%</td>
<td>80 mths; 22-120 mths</td>
<td>Horowitz et al 1993</td>
</tr>
<tr>
<td>Bologna</td>
<td>DF=155, PF=45, PT=51</td>
<td>Kotz modular</td>
<td>Unc</td>
<td>257 3 PT femoral stems loosened</td>
<td>No details</td>
<td>Capanna et al 1993</td>
</tr>
<tr>
<td>Leiden</td>
<td>PF=12, DF=17, PT=4</td>
<td>Kotz modular</td>
<td>Unc</td>
<td>33 None</td>
<td>3.1 yrs; 1-8 yrs</td>
<td>Zwart et al 1994</td>
</tr>
<tr>
<td>London</td>
<td>DF=1, TF=2, DF+PT=1, PF=8, PF+HP=1</td>
<td>Kotz modular</td>
<td>Unc</td>
<td>15 None</td>
<td>No details</td>
<td>Jessop et al 1989</td>
</tr>
<tr>
<td>Hannover</td>
<td>PF</td>
<td>Standardised</td>
<td>C</td>
<td>37 1 loosened</td>
<td>114 mths; 31-212 mths</td>
<td>Wipperman et al 1991</td>
</tr>
<tr>
<td>Zagreb</td>
<td>DF=7, PF=4</td>
<td>Kotz modular</td>
<td>Unc</td>
<td>11 None</td>
<td>13 yrs; 10 yrs +</td>
<td>Orlic et al 1991</td>
</tr>
<tr>
<td>Los Angeles</td>
<td>DF</td>
<td>Custom-made, stem and extra-cortical plates</td>
<td>Unc</td>
<td>11 None</td>
<td>10 yrs +</td>
<td>Samek et al 1991</td>
</tr>
<tr>
<td>Sao Paulo, Brazil</td>
<td>PT no femoral components</td>
<td>Custom-made, Late implants - HA coated</td>
<td>Unc</td>
<td>25 2 loosened</td>
<td>8 yrs; 2-15 yrs</td>
<td>Camargo et al 1993</td>
</tr>
<tr>
<td>Goteborg</td>
<td>PF</td>
<td>Long-stemmed Moore THR</td>
<td>C</td>
<td>3 None</td>
<td>16-19 yrs</td>
<td>Stcvt and Gunterberg 1993</td>
</tr>
<tr>
<td>Los Angeles</td>
<td>DF</td>
<td>Custom-made Uncoured</td>
<td>C</td>
<td>36 72%</td>
<td>72 mths; 12-152 mths</td>
<td>Ward et al 1995</td>
</tr>
<tr>
<td>Munich</td>
<td>DF=27, PT=8, TF=1</td>
<td>Custom-made</td>
<td>Unc</td>
<td>22 1 DF cemented</td>
<td>3.8 yrs; 4 mths -11.5 yrs</td>
<td>Gradinger et al 1991</td>
</tr>
<tr>
<td>Osaka</td>
<td>DF</td>
<td>Custom-made</td>
<td>C</td>
<td>23 1 PT uncemented</td>
<td>2.5 yrs</td>
<td>Ueda et al 1991</td>
</tr>
<tr>
<td>Rochester</td>
<td>DF</td>
<td>Custom-made Waldius knee</td>
<td>C</td>
<td>45 13 loosened</td>
<td>4 mths - 16.5 yrs</td>
<td>Shih et al 1991</td>
</tr>
<tr>
<td>Seoul</td>
<td>DF=7, PT=3</td>
<td>Custom-made</td>
<td>Unc</td>
<td>10 None</td>
<td>20 mths; 7-37 mths</td>
<td>Lee et al 1993</td>
</tr>
</tbody>
</table>

**Skeletally immature cases only - Extendible replacements**

<table>
<thead>
<tr>
<th>Centre</th>
<th>Skeletal replacement</th>
<th>Stem design</th>
<th>Fixation</th>
<th>No. failed or probability of surviving aseptic loosening</th>
<th>Follow-up Mean duration; Range</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vienna</td>
<td>Lower limb</td>
<td>Custom-made</td>
<td>C</td>
<td>2 1 DF</td>
<td>6.3 yrs</td>
<td>Schiller et al 1995</td>
</tr>
<tr>
<td>Paris</td>
<td>DF=40, PT=12, M-SF=8, PH=5</td>
<td>Custom-made</td>
<td>C</td>
<td>18 3 DF loosened</td>
<td>5.4 yrs; 4-8 yrs</td>
<td>Messinard 1991</td>
</tr>
<tr>
<td>New York</td>
<td>DF=61, PF=16, PT=16</td>
<td>Custom-made</td>
<td>C</td>
<td>10 DF 3/5 cemented, PT 4/4</td>
<td>5.2 yrs</td>
<td>Kenan et al 1991</td>
</tr>
<tr>
<td>Los Angeles</td>
<td>DF=7, TF=1, PF=1, PT=1, TH=1, PH=1</td>
<td>Custom-made</td>
<td>C</td>
<td>12 None</td>
<td>3.1 yrs</td>
<td>Eckardt et al 1993</td>
</tr>
</tbody>
</table>

**Skeletal replacement:** PF = proximal femoral, DF = distal femoral, TF = total femoral, PT = proximal tibial, M-SF = mid-shaft femoral, PH = proximal humeral, TH = Total humerus, HP = hemi-pelvis.  **Fixation:** C = cemented, Unc = uncemented
Chapter 2

Investigations of aseptic loosening in 1149 bone tumour limb salvage cases
2.1. Introduction

Cemented intra-medullary stemmed massive endo-prostheses are one of the most frequently used devices in limb salvage surgery. Aseptic loosening of cemented intra-medullary stemmed massive endo-prostheses has been identified as the predominant cause of implant related failure (Unwin et al 1991a, Unwin et al 1993b, Unwin et al 1995b, Unwin et al 1995d, Unwin et al 1995e).


2.1.1. Aim

The aim of this retrospective study was to review lower limb replacement cases to establish which parameters had a significant affect on aseptic loosening of cemented intra-medullary stemmed massive endo-prostheses inserted for bone tumour.
2.1.2. Purpose

The purpose was to -

1. establish the extent of aseptic loosening in the three most commonly used lower limb massive endo-prostheses
2. establish which parameters had a significant effect on aseptic loosening
3. produce a learned basis from which to develop new fixation methods
4. use this study as a control group from which to compare new developments
5. disseminate the results of the findings as this may influence decision on the limb salvage methods.

2.1.3. The hypothesis

Seven parameters were to be examined to establish what affect they had on aseptic loosening. The parameters were -

1. skeletal location of the implant
2. the age of the patient at the time of the limb salvage procedure
3. the percentage of bone removed
4. the surgeon
5. the year the implant was inserted
6. chemotherapy
7. knee hinge type

2.2. Materials and Methods

At the Division of Biomedical Engineering, (Royal National Orthopædic Hospital, Stanmore) a patient file containing specific information had been kept for each of the Stanmore massive custom-made endo-prosthetic replacements.
The data included initial presentation details including diagnosis, location of tumour, patient age, referring surgeon and hospital. This was later supplemented by the surgery date and the engineering drawing containing the specific implant details. Since 1990, initial patient details, implant design data, clinical status, clinical and radiographic assessment data have been stored on a customised data-base. This data-base designed by P.Unwin and J.Cobb, permitted rapid access to data and was later programmed by P.Unwin in 1992 and 1993 to calculate clinical and radiographic grades from assessment data.

2.2.1. Selection criteria

The initial criteria for selection was a Stanmore custom-made proximal or distal femoral or proximal tibial replacement inserted prior to 1992, to permit sufficient follow-up period. This produced a total of 1522 cases. To reduce the variability, only those cases with a diagnosis of bone tumour including bone metastases were selected. Conditions such as fibrous dysplasia and Paget's disease were categorised as non-neoplastic and therefore excluded. Neoplastic conditions predominated and accounted for 1167 cases (76.7%) (Table B.1 of Appendix B summaries the diagnostic groups).

An additional 18 cases were excluded from the 1167 bone tumour cases. Nine temporary replacements, that were designed to be in situ for a number of months and later replaced by a definitive endo-prosthesis were excluded as were five replacements which were secured to the bone using extra-cortical fixation. Four cases were excluded as a result of uncemented intra-medullary stem fixation.

2.2.2. The study group

The study group comprised of 1149 cases of which 577 (50.2%) were distal femoral replacements, 290 (25.2%) were proximal femoral replacements and the remaining 282 cases (24.5%) were proximal tibial replacements.
2.2.2.1. Diagnosis

All conditions were bone tumour, of which malignant tumours were predominant. Osteosarcoma was the most frequently occurring tumour (n=521, 45.3%), and was the most common indication in the distal femoral (56.2%) and proximal tibial replacement (59.6%) groups (Table B.2, Appendix B summaries tumour type with respect to implant). In the proximal femoral group, chondrosarcoma (31.0%) was the most common diagnosis followed by bone metastases (17.2%).

2.2.2.2. Age

The average age of the patients at the time of the limb salvage procedure was 29.9 years (±0.55 S.E., range 3 to 84, n=1137). The unimodal distribution had a strong positive skew, (Shapiro-Wilks p<0.01). Proximal tibial patients were on average the youngest (23.5±1.04 years) and proximal femoral patients the eldest (41.5±1.02 years) (Figure 2.1).

With respect to diagnosis, irrespective of skeletal location, those patients with Ewing's sarcoma were the youngest (16.2±0.31 years, n=81) whilst patients with bone metastases were the oldest (55.5±0.43 years, n=72) followed by chondrosarcoma (49.6±0.33 years, n=146). The average age of patients with osteosarcoma was 17 years in both the distal femoral and proximal tibial groups, however, in the proximal femoral group it was 28 years.

Throughout the complete study, the patients have been subdivided into 4 age groups (skeletally immature: ≤ 16 years; young adults: 17 ≤ 25 years, middle aged: 25 < 60 years and old aged: ≥ 60 years).

---

1 12 cases did not have the age of the patient.
2.2.2.3. Gender

The study group comprised of 655 male and 494 females (M:F 1.33:1). In all implant groups males occurred more frequently with the largest difference seen in the proximal tibial group where males accounted for 59.9% of that group, whilst in the proximal femoral group, males accounted for 53.4%. Males in the distal femoral group accounted for 57.4%. The differences in the sex ratio was a result of tumour type. The sex ratio of patients with osteosarcomas was 1.57:1 (M:F), and predominantly occurred around the knee, whilst the sex ratio for chondrosarcomas was 1.39:1 and chondrosarcomas were most commonly associated with the proximal femur. The sex ratio reversed with cases of bone metastases (2 females : 1 male) with the majority occurring in the proximal femur. There were no significant differences between the males and females with respect to patient age or the percentage of bone resected (Table B.3, Appendix B).

2.2.2.4. Resection

Whilst designing custom-made replacements, the percentage of bone resected was calculated by taking measurements from scaled radiographs. The percentage of bone resected was obtained from implant data sheets contained within the case file, unfortunately in the early years no specific record was kept pertaining to the total length of the bone. The average percentage of bone resected was 49.2% and ranged from 19% to 84%. Proximal tibial cases had on average the lowest percentage of bone removed (48.0±0.24%), but also the greatest range (20% to 84%). Proximal femoral had the highest percentage of bone resected (50.5±0.40%) (Figure 2.2). The data distribution was non-parametric (Shapiro-Wilks p<0.01) and uni-modal.

Patients with Ewing’s sarcoma had the greatest percentage of bone resected (59.0±0.39%, n=76) followed by osteosarcoma (51.2±0.16%, n=437), whereas
patients with osteoclastoma had the lowest percentage of bone resected (35.6±0.34%, n=81).

Throughout the complete study, the patients have been subdivided into 3 bone resection groups (< 40%, 40 to 60% and ≥60%). This subdivision produced three equidistant groups. In addition, the subdivision separated those resections which were located in tubular diaphyseal bone (40% to 60%) from those placed entirely or partly in flaring metaphyseal bone.

2.2.2.5. Age and Resection

The youngest age groups (≤ 16 years) of all 3 implant types had a significantly higher percentage of bone resected (Figure 2.3).

2.2.2.6. Knee type

Predominantly, the Stanmore fixed hinge knee replacement was used in conjunction with the distal femoral (88.7%) and proximal tibial replacements (86.5%). The Stanmore knee hinge was first used with massive replacements in 1964. Rotating hinges were used in 103 cases (12%). In 1988, 11 distal femoral replacement cases (1.9%) and 2 proximal tibial replacements (0.7%) with Kinematic rotating hinge knees were inserted. A "Rugged" rotating hinge, a predecessor to the SMILES rotating hinge was used with a distal femoral replacement in 1988. The SMILES rotating knee hinge, designed to supersede the Stanmore hinge as the principal knee for Stanmore massive endo-prosthetic replacements was first used in 1991. The SMILES rotating hinges were used with 53 distal femoral and 36 proximal tibial replacements. The Stanmore hinge however was still being used in 1992, with 41 of the 113 cases in that year utilising this knee.

There was no significant difference between the rotating hinged and the fixed hinged replacements with respect to patient age, percentage of bone resected or sex ratio, in either the distal femoral or proximal tibial groups (Table B.4,
Appendix B). However, in both implant groups, there was a higher percentage of bone resected in those cases that had fixed hinged replacements (DF=49.6±0.61%, PT=48.9±0.9%) compared to those with rotating hinged replacements (DF=46.6±1.5%, PT=47.3±2.2%) (DF p=0.08, PT p=0.49).

The Stanmore knee was first used in 1964, whilst the rotating hinges were not introduced until 1988, as a result of the differing eras the treatment of malignant bone tumours had also changed. Unlike the distal femoral replacements that spanned a greater period the proximal tibial replacements were not inserted in any number until 1983.

2.2.2.7. Year of surgery

Prior to the late 1970s, few patients with osteosarcoma underwent limb salvage surgery, whilst those that did, typically had either chondrosarcoma or osteoclastoma (Chapter 1). Patients with osteosarcoma or M.F.H. had significantly higher percentage of bone resected compared to those with osteoclastoma, parosteal sarcoma and chondrosarcoma (p<0.01).

In all implant groups, there was no significant difference in the age of the patient between 1964 and 1992 with respect to the commonest tumour for each implant type. The slight decrease in age of the distal femoral patients was due to the increased use of extendible replacements for the skeletally immature. In recent years (1984-7 v 1988-92), there has been a significant reduction in the percentage of bone resected in cases of osteosarcoma around the knee but surprisingly not with cases of proximal femoral chondrosarcoma (Table 2.1).

2.2.2.8. Surgeons

Sixty one surgeons, predominately located within Britain, inserted the endoprostheses of the study group. Six surgeons inserted 50 or more, of whom 4 had each inserted more than 100 of replacements.
Surgeons who used open biopsy to determine the level of resection of distal femoral osteosarcomas (57.4±0.8, n=123) and proximal tibial osteosarcomas (55.7±1.2, n=62) resected significantly more than those who did not (DF=46.4±1.1, n=78 and PT=41.8±1.6, n=35). The increasing use of needle biopsy and radiography to determine the level of resection of osteosarcomas over the last two decades has reduced the percentage of bone being resected (Figure 2.4). However, at some centres open biopsy is the preferred technique for the resection level determination. Therefore it is hypothesised that the decrease in the percentage of bone resected between 1964 and 1992 was a result of the technique used to determine the level of resection level.

2.2.2.9. Implant variations

**Acetabular cups**

An acetabular cup was used with all proximal femoral replacement cases. Initially, metal acetabular shells (n=21) were used, but these were gradually superseded by polyethylene acetabular cups (n=269). The first 3 all metal acetabular cups were press-fit, whilst the remainder were cemented into the acetabulum. The majority of the femoral heads used were 32 mm in diameter. Generally the size of the natural femoral head was used to determine the replacement head diameter. Larger heads were chosen to improve joint stability and reduce dislocation. However, the disadvantage of a large femoral head size is the increased wear rate. There has been considerable concern about the effects of wear debris, either linked to loosening (Galante et al 1991, Mjöberg 1994), causing tumours (Heath et al 1971, Bago-Granell et al 1984, Penman and Ring 1984, Swann 1984, Gillespie et al 1988, Lamovec et al 1988, Martin et al 1988, Brien et al 1990, Ward et al 1990, Jacobs et al 1992, Case et al 1994) or other conditions such as inguinal lymphadenopathy (Shinto et al 1993). Polyethylene wear particles have been linked to the formation of osteolysis and granulomas as a result of a foreign body reaction (Mjöberg 1994). Recently,
primarily as a greater variety of acetabular cups have become available for THRs, metal backed cemented and cementless cups and bi-polar cups have been used with proximal femoral replacements. For very young patients, it has been general practise not to use an acetabular cup but to reconstruct as a hemi-arthroplasty.

**Extendible replacements**

Actively extendible replacements for use in the skeletally immature cases, operate by expanding a telescopic mechanism that requires a surgical procedure. The replacement can be lengthened to maintain leg length equality with the growth of the contra-lateral limb. Extendible distal femoral replacements accounted for 16.3% of all distal femoral replacements, 8.5% of proximal tibial replacements and 3.5% of proximal femoral replacements. Three varieties of extending mechanism have been used. The first used a geared mechanism but this was prone to jamming and was superseded by a hollow telescopic piston that was kept distracted by 1/4" ball bearings. Fracturing of the ball-bearing gave rise to the simpler 'C' collar mechanism (Unwin and Walker 1993c, Unwin and Walker 1995f). Since this review there has been the introduction of a new form of mechanism that requires minimal invasive surgery when lengthening the replacement.

**Coatings**

In 1988 and 1989, two ingrowth structures were first used to encourage extracortical bony bridging. The first was a porous beaded structure 25 mm in length which comprised of two layers of titanium alloy beads (0.7 mm Ø), and was located adjacent to the prosthesis plateau. Six distal femoral and 4 proximal femoral replacements had these structures. Hydroxyapatite coatings had been applied to the shaft region adjacent to the prosthesis plateau on 7 distal femoral and 4 proximal femoral replacements. None of the proximal tibial replacements of the study series were hydroxyapatite coated or porous
collared. Porous collared and hydroxyapatite coated replacements are described in detail in Chapter 5.

**Bifurcated or 'rhino horn' stems**

Modified intra-medullary stems have been used with 11 distal femoral replacements when the level of resection was extensive. Ten cases had bifurcated stems and in 1 extreme case, a sharply curved stem that passed through the femoral neck locating the tip of curved stem approximately at the centre of the femoral head was used.

**Telemetry**

In two proximal femoral replacements strain gauges have been attached to the tip of the intra-medullary stem and in the shaft of the replacement to assess the loading of the replacement. The data was telemetered out whilst the patient was performing a number of clinical procedures.

**2.2.3. Assessment**

The latest outcome for each case was determined from medical case notes received or clinical assessment of the patient.

**2.2.3.1. Status and definition of failure**

Each case was categorised into one of the following broad categories -

- amputation
- died
- prosthetic related problems
- no prosthetic related problem
- revised
- no follow-up information

The cause of death, amputation, prosthetic related problem or revision was recorded. Notification of the death of patients was obtained from the referring
hospital or from the National Registry. Patients with no prosthetic related problems may have had tumour recurrence or bone metastases.

The definition of a revision was the undergoing of a surgical procedure that removed the existing endo-prosthesis and replaced it either with the existing endo-prosthesis or a revision endo-prosthesis.

In this study the definition of a 'failed' case, was defined as when a replacement was required to be revised or the limb amputated as a result of aseptic loosening of the custom-made intra-medullary stem. The date of implant failure was the date the revision procedure or amputation took place.

Implant duration was defined as the period of time between the date of operation to insert the replacement to the date of revision, amputation or the last clinical review.

2.2.4. Survivorship statistical methods

Survivorship analysis was first used in orthopaedics to study Stanmore total hip replacements (Dobbs 1980). It has now become a powerful and important tool for the evaluation of implant design. The two methods in general use are the Kaplan-Meier method (Kaplan and Meier 1958) and the Life Tables method (Armitage and Berry 1994). Potential pitfalls of survivorship analysis have been discussed (Murray et al 1993), and include the definition of end-points and classification of cases (Dorey and Amstutz 1986), the number of cases required (Nelissen et al 1992) and the use of confidence intervals (Lettin et al 1991). However, Dorey has concluded that the assumptions that are necessary for the validity of survivorship analysis for use in orthopaedics are upheld (Dorey and Amstutz 1989).

In this study the survivorship statistics were calculated using the Kaplan-Meier method. For the comparison of two or more curves the Logrank (Mantel-Cox) test was performed. The survivorship analyses were performed using the
Statview for the Macintosh and the additional survivorship module (version 4.0.1. Abacus Concept Inc.).

2.3. Results

In total 1040 (90.5%) of the 1149 cases had post-operative follow-up. The proximal and distal femoral implant groups had the longest follow-up (45.9±2.8 months, n=261 and 45.2±2.0, n=524 respectively) and the proximal tibial implant group the shortest (35.9±2.8 months, n=255). The longest follow-up was of a proximal femoral implant that had been in situ for 292 months.

2.3.1. Patient status

Cases with no prosthetic related problems formed the largest group in all three replacement groups (Table 2.2). Amputation in the proximal tibial group was relatively high, whilst in the proximal femoral the percentage of deaths was high. Prosthetic related complications were most commonly pain in the proximal and distal femoral replacements groups and pain or infection in the proximal tibial replacement group. Revision procedures proportionally were most common in the proximal tibial group and rarest in the proximal femoral replacement group. In total 109 cases were lost to follow-up. The majority of these patients were adults, many of whom had returned home abroad.

2.3.1.1. Forms of failure

In total, 255 (22.2%) of the 1149 cases had either the limb amputated or the implant revised. Aseptic loosening of the intra-medullary stem was the most common form of failure in the distal femoral (63.3%) and proximal femoral replacement (40.0%) groups (Table 2.3). However infection was the predominant cause of failure in the proximal tibial group (43.3%). Interestingly, although the revision rate was the lowest in the proximal femoral group the death rate was the highest. The majority of deaths were as a result of disease but the deaths did not appear to have an effect on the failure rate.
2.3.1.2. Aseptic loosening

Aseptic loosening of the custom made intra-medullary stem which necessitated a revision procedure occurred in 94 of the 1149 cases (Plate 2.1). No limb was amputated as a result of a replacement failing from aseptic loosening. The overall mean time to failure was $73.2 \pm 0.7$ months. The shortest implant duration ending in revision was 9 months and the longest was 195 months, both were distal femoral replacements. Revision as a result of aseptic loosening occurred most frequently with distal femoral replacements (10.8%) followed by proximal tibial replacements (7.8%) and least with proximal femoral replacements (3.4%). Extendible replacements were included in this series but it was considered by some that these replacements were temporary (Sneath pers comm).

Of those cases that were revised for aseptic loosening, the Stanmore fixed hinge knee replacement had been utilised in all proximal tibial and all but 2 of the distal femoral. In the 2 distal femoral cases, 1 Kinematic rotating hinge and 1 SMILES rotating hinge had been used. Both of these had short durations to failure (16.7 and 18.4 months).

Overall, proximal femoral replacements had the longest mean time to failure (78.6 months), closely followed by the distal femorals (77.6 months). The two distal femoral cases with rotating hinges were omitted from the analysis as the type of knee hinge configuration was considered to be an important factor in terms of loosening.

Skeletally immature patients ($\leq 16$ years) of both femoral implant groups had the highest proportion of loosened cases, (Table 2.4). In the proximal tibial group, it was the young adults that had the high proportion of loosened cases, (Table 2.4). Young adult patients ($>16 \leq 25$ years old) with tumours around the knee had the shortest mean duration to failure, but in the proximal femoral group it was the skeletally immature patients that had the shortest mean
duration to failure. Males in all implant groups had a higher proportion of cases loosening than females.

The proportion of cases failing in the distal femoral and the proximal tibial group with respect to the percentage of bone resection was higher the greater the percentage of bone resected. In contrast, in the proximal femoral group, the greater the percentage of bone resected the lower the proportion of cases failed. There was no significant difference in the time to failure in any of the three implant groups with respect to the percentage of bone resected, the age or the gender of the patient. No correlation between the percentage of bone resected and patient survival could be identified in any of the implant groups.

2.3.2. Survival analysis

The overall probability of surviving aseptic loosening at 120 months for bone tumour lower limb replacements was $0.696 \pm 0.01$ (n=84). At 120 months, 84 patients were still alive with their original prosthesis in situ. These patients are referred to as being ‘at risk’.

For all further analyses all coated replacements and replacements with rotating hinged knees were omitted. The probabilities of surviving a revision as a result of aseptic loosening at 120 months for the three implant groups were -

- proximal femoral $= 0.879 \pm 0.018$  n=30
- distal femoral $= 0.651 \pm 0.019$  n= 48
- proximal tibial $= 0.515 \pm 0.156$  n=6

There was a significant difference in the probability of survival between the three implant groups (p<0.01). In all groups the probability of aseptic loosening in the first three years was very low, after which the probability of loosening increased substantially (Figure 2.5). In the proximal femoral group after 55 months the rate of descent of the curve decreased. A similar trend was observed in the distal femorals but the rate of descent began to reduce after 130
months. In contrast, in the proximal tibial group the curve increased and plummeted as implant duration increased. The increasing risk with increasing time of the proximal tibial group was more clearly observed in the hazard plot.

2.3.2.1. Patient age (uncoated, fixed hinges)

The age of the patient with either a proximal or distal femoral replacement significantly affected the probability of surviving aseptic loosening (PF p<0.01, DF p<0.01, PT p=0.37) (Figure 2.6).

Skeletally immature patients (<16 year) had the lowest probability of surviving aseptic loosening. In the distal femoral group the curve for patients aged ≤16 years descended at approximately 0.008 per month after approximately 50 months. In comparison, the three curves for those patient aged >16 years fell less dramatically. Due to the small numbers of elderly patients, the two failures may present an exaggerated probability of failure.

With similarity to the above, young patients (≤16 years) with proximal femoral replacements had a poor prognosis represented by relatively steep descending curve, however, there were few failures in a relatively small population. The young and middle aged adult groups had a better prognosis and none of the elderly (≥60 years) failed.

In the proximal tibial replacement group, the skeletally immature and young adult cases had the poorest prognosis throughout much of the duration when omitting elderly patients, of which 2 of the 8 failed.

2.3.2.2. Percentage of bone resected (uncoated, fixed hinges).

The percentage of bone resected had a significant effect on the probability of surviving aseptic loosening. In the distal femoral and proximal tibial groups there was an inverse relationship between the extent of resection and the probability of surviving aseptic loosening (Figure 2.7). In the distal femoral
group the three curves drop steadily after approximately 50 months, but with increasing duration the rate of descent decreased. There was a significant difference in survival between the 3 groups (p=0.01).

In contrast, the shorter the resection for proximal femoral replacements the poorer the prognosis of surviving aseptic loosening. However, the three proximal femoral resection curves were very similar in trend and this was reflecting no significant difference between them (p=0.68).

In the proximal tibial group the greater the percentage of bone resected the poorer the prognosis of surviving aseptic loosening. There was only 1 failure in a total of 52 cases in <40% resection group and there was no significant differences between the three resection groups (p=0.11).

2.5.2.3. Gender (uncoated, fixed hinges)

Male patients with distal femoral replacements had a poorer prognosis of surviving aseptic loosening than females (p=0.14) (Figure 2.8). Whereas in the other two implant groups the probabilities were similar with respect to gender (proximal femoral p=0.56 and proximal tibial p=0.51).

2.5.2.4. Bone resection and patient age (uncoated, fixed hinges, distal femoral cases)

Restricting the selection to uncoated fixed hinged distal femoral replacements due to insufficient numbers in the proximal femoral and proximal tibial replacement groups, the combined effects of age and the level of resection were analysed. The combination of both age and the percentage of bone resected had a profound effect on the probability of survival for young patients (Figure 2.9). Skeletally immature patients (≤16 years) who had greater than 60% resections had the poorest prognosis in terms of aseptic loosening, followed by those who had between 40% - 60% resections. Young adult and middle aged
patients (>16 <60 years) had similar probabilities of survival in all three resection groups.

2.3.2.5. Year of surgery

The year in which the distal femoral limb salvage operations took place were placed into one of three groups, (1964-1983 (n=122), 1984-1987 (n=172) and 1988-1992 (n=122)). For those cases inserted between 1964 and 1983 the probability of survival was 0.95 at 60 months (Figure 2.10). Whereas for those inserted between 1984 and 1987 the probability had fallen to 0.9 and those most recently inserted the probability had fallen further to 0.8 (p<0.01). However, due to the small proportion of cases failing in the 1988-1992 may have resulted in an over exaggeration of failure and therefore should be treated with caution.

2.3.2.6. Chemotherapy

To study if chemotherapy had an effect, patients with distal femoral replacements inserted for either chondrosarcoma (no chemotherapy) or osteosarcoma (chemotherapy) were selected. This identified that patients who were administered chemotherapy (osteosarcoma) had a poorer prognosis. However, there was a marked age difference between the two populations. To reduce variability, only chondrosarcoma or osteosarcoma patients aged between 20 and 60 years with a distal femoral replacement were selected. No significance between the two curves was identified (p=0.82) (Figure 2.11).

2.3.2.7. Surgeon

Selecting only the distal femoral cases of the 2 most prolific surgeons dramatic differences between the curves were observed (Figure 2.12). The curve of Surgeon A descended steadily after approximately 25 months until approximately 100 months when the rate of descent decreased. In contrast, Surgeon B did not have any failure cases until 75 months with 2 failures occurring shortly after. The two late failures in the remaining population had a
marked effect on the curve. There was a significant difference between the two surgeons with respect to surviving aseptic loosening (p=0.03).

From above, it was identified, that both patient age and the percentage of bone resected had significant effects on the outcome. Furthermore, the percentage of bone resected differed between the two surgeons (p<0.01). Surgeon A used open biopsy and resected an average of 57.5±0.9% of the distal femur compared to an average of 46.3±1.5% resected by surgeon B, who used a needle biopsy and radiography to determine the level of resection. Therefore, selecting only patients aged between 20 and 60 years who had resections between 40% and 60%, revealed that there was a significant difference between the 2 surgeons (p=0.04) (Figure 2.12).

2.3.2.8. Rotating hinged versus fixed hinged knee replacements

A small number of rotating hinged knee replacements were in conjunction with both the distal femoral and proximal tibial replacements. In the proximal tibial replacement group (n=38) there were no failures as a result of aseptic loosening. Of the 65 cases with rotating hinged distal femoral replacements, two replacements had failed from aseptic loosening and as a result of the small population the probability of loosening with a rotating hinge appeared to be substantially higher than those with fixed hinged knee replacements (Figure 2.13). Due to the small number of rotating hinge cases and of which only 2 failed the probability of loosening may be exaggerated and therefore should be treated with caution.

2.3.2.9. Survivorship modelling

Recent studies have used additional survivorship methods to those of the Kaplan-Meier probability and the Log-rank comparative tests, for example the Cox proportional hazard (Cox 1972, Carr et al 1993, Armitage and Berry 1994). The potential strength of the Cox model lies in its ability to estimate the effect of
an individual factor while adjusting for the effect of other factors. The approach taken here has been to restrict analysis to homogeneous subgroups where strong associations between influential factors were expected.

2.4. Discussion

Aseptic loosening of cemented intra-medullary stemmed lower limb massive prostheses used for bone tumour limb salvage was the principal cause of revision. Although 8.2% of patients underwent a revision procedure for loosening of the cemented custom-made intra-medullary stem, no limbs were amputated as a result of this mode of failure. It appeared that aseptic loosening was a mid- to long-term problem and therefore studies with short follow-ups had few or no cases of aseptic loosening. Long-term follow-up studies of massive endo-prosthetic replacements have been reported infrequently and no studies have examined factors such as patient age or bone resection with the exception of Unwin (Unwin et al 1991a). This lack is predominantly as a result of the relatively small number of cases reviewed in any single study. The large number reviewed in this study has permitted for the first time subdivision of single implant groups.

A similar composition, but substantially smaller series (n=93) was presented by Horowitz (Horowitz et al 1993). Horowitz reported that the probability of surviving aseptic loosening for 5 years was 78% for distal femoral, 100% for proximal femoral and 73% for proximal tibial replacements. All but 1 of the 93 implants used cemented intra-medullary fixation. The survival results of the distal femorals and proximal tibials were worse than those of this series (89.9% and 86.6% respectively) but proximal femoral results were better (93.9%).

In comparison to total hip (Havelin et al 1994) or total knee replacements (Knutson et al 1994), massive endo-prostheses had substantially higher loosening rates. However, the difference between standard joint replacements and massive endo-prosthetic replacements are considerable and include patient
age, bone quality, soft tissue attachment and the amount of bone resected. These will affect the rate of revision but the mechanism of the cement-bone interface breakdown is suspected to be the same. Studies have examined a variety of risk factors such as gender, patient age, implant type, primary/revision, unilateral/bilateral replacement and implant position (Retpen and Jensen 1993, Havelin et al 1994, Neumann et al 1994, Sullivan et al 1994). Frequently, the former three parameters have been cited as significant in terms of aseptic loosening of joint replacements. It is considered that aseptic loosening of cemented intra-medullary stemmed massive endo-prostheses was dominated by mechanical factors rather than biological. Titanium, PMMA and polyethylene wear debris has been identified in a small number of cases between the cement mantle and cortical bone in retrieved specimens (Blunn pers comm) but this has been attributed to flushing in of the particles. Furthermore, the distal femoral and proximal tibial replacements had the poorest prognosis and the further the resection from the knee (a primary source of wear debris) the greater the probability of loosening.

This study has raised a number of important questions.

- Why do the distal femoral and proximal tibial replacements fare significantly worse than the proximal femoral replacements?

- Why does the percentage of bone resected, the patient’s age, the surgeon and the knee hinge type have significant effects on loosening.

Understanding the answers to these questions may lead to enhanced designs to improve longevity of fixation. The suggested explanations for the difference between implants and the percentage of bone resected are linked.

Firstly, with respect to the femur, the offset distance between the long axis of the femur and a line passing from the centre of the femoral head to the condyles of the knee can be taken as a measure of the medio-lateral bending
moment. The offset distance will be greater in the proximal femur than distally. The more proximal the level of resection the greater the bending moment (Figure 2.14). This greater bending moment with proximal resections will lead to increased cement/bone interface stresses. As a result of the femoral head offset, the shaft bone will be in compression medially and in tension laterally. Although, this model is simplistic it is considered that it represents the predominant loading regime. This model does not take into account muscular forces or the effects of the ilio-tibial tract. Duda constructed a complex model of the femur with 23 muscles with insertions or origins calculate the forces and bending moments (Duda et al 1994). The femoral head offset produced a large bending force at the level of the greater trochanter of 140 Nm, that diminished to approximately zero approximately 30% down the femoral shaft, reaching -20 Nm at the level of the knee.

Laboratory studies using cadaveric femora with distal and proximal femoral replacements inserted performed as predicted, with high compression loads at the shoulder of the prostheses medially and posteriorly and tension anteriorly and laterally (Wright and Meswania 1984). In addition, the radiographic study (Chapter 4) and a long term radiographic study of proximal femoral replacements showed extensive bone remodelling with greater bone mass on the posterior and medial aspects and bone resorption on anterior and lateral sides (Inglis and Walker 1989). The laboratory and radiographic results support the offset theory. Irrespective of the femoral prosthesis type, the more distal the resection level the lower the probability of loosening.

The femoral head offset of total hip replacements has been studied and concluded that an increase in the offset, decreased both the abductor and resultant forces (Davey et al 1993). Strain gauges positioned medially on the proximal, mid and distal region of the stems showed an increase in compressive microstrain and those laterally showed an increase in tension when the femoral head offset was increased from 33 to 55 mm. The offset
distance is considered to be a principal factor in the difference between the 2 femoral implant groups. However, overall the proximal femoral replacement group had a significantly lower probability of failure than the distal femorals replacements and this is believed to be in part related to the location of load transfer with respect to the line of force.

Recent strain gauge data received via telemetry of a proximal femoral replacement showed that with a cemented intra-medullary stem, 70% of the applied load was transferred at the tip of the intra-medullary stem after being in vivo for 65 weeks (Taylor 1993). Initially, the intra-medullary stem tip to shaft ratio was 0.25 and that increased steadily for 30 weeks after the operation. After 65 weeks the tip/shaft ratio remained constant at approximately 0.70. This increase indicated that progressively more of the force was being transmitted through the stem tip. Therefore, if the offset distance at the tip of the stem was taken as the axis of rotation rather than the plateau, then distal femoral replacements would have poorer survival. Comparing a proximal and a distal femoral replacement which both have the same level of resection, the stem tip of the distal femoral replacement will have a larger offset. Using this theory the distal femoral replacements will have a poorer survivorship than the proximal femorals due to the larger offset (Figure 2.15).

Furthermore, the femoral model constructed by Duda (Duda et al 1994), calculated that the compressive force along the longitudinal axis of the femur decreased from approximately -2300 N at the greater trochanter to -953 N at the knee. If this compression force was transmitted in shear between the cortical bone and cement, the more proximal the fixation the greater the interfacial stresses, leading to more rapid decoupling of the interface.

The offset distance, however will not be the only factor, in addition, cement interdigitation will have an effect and this will be determined by the amount of cancellous bone present and the medullary canal shape. Generally, in the
proximal region of the femur there is a large offset and in the trochanteric region, cancellous bone. For extensive distal femoral replacements the stem will be placed into a flaring medullary canal but good cement interdigitation proximally within the cancellous structure can be obtained. For the short proximal femoral replacements, much of the intra-medullary stem is situated within the tapering canal but in this region there is little cancellous bone structure and therefore relatively poor cement interdigitation. For resections in the diaphyseal region of the femur contains little cancellous bone for cement interdigitation and there is an offset for both the distal femoral and proximal femoral replacements and the stems are both located into a flaring canal. In the distal section of the femur there is little or no offset and within the condyles cancellous bone. For the short distal femoral replacements the stem is situated into a tapering medullary canal but for the long proximal femoral replacements it is flaring, however the distal tip of the stem located within cancellous bone providing good cement interdigitation.

The above scenario cannot be used to explain the survivorship of the tibial replacements as the anatomical position of the tibia in the upright stance the tibia is oriented 3° laterally. The cross-section shape of the medullary canal proximally being more triangular rather than ovoid as in the femur would permit improved cement interdigitation, but there is little natural curvature to the bone and therefore rarely was the tibial intra-medullary stem curved. More distally however, the canal shape is more rounded and with little space for cement interdigitation. Smaller straight stems have less torque resistance than larger curved stems commonly used in the femur and therefore increases the risk of stem loosing within the cement rather than the cement within the bone.

Furthermore, in the proximal tibial and distal femoral replacements groups a fully constrained knee was used. The Stanmore knee hinge may indeed result in high torsional forces applied to the cement/bone interface. Patients with proximal femoral replacements retain their knee and therefore the femoral
intra-medullary cement/bone interface may not experience such high torsional forces as much of the torque will be transmitted at the knee. The introduction of rotating knee hinges for both distal femoral and proximal tibial replacements was late in this series (1991) and therefore only a limited follow-up was possible. The philosophy behind the introduction was that rotating hinged replacement had lower torsion stresses at the cement/bone interface of the cemented intra-medullary stems than fully constrained knee hinges (Walker et al 1982). The early results due to the small population size showed a poorer prognosis for the rotating hinged distal femoral replacements compared to the fixed hinged replacements. However, none of the proximal tibial replacements with rotating hinges loosened, but, predominantly, implant duration was under two years. It is unlikely that the result was due to complications encountered with a new design because the cementation and insertion techniques of the femoral intra-medullary stem would remain the same. To establish if rotating hinges do reduce the loosening rate a longer implant duration and a larger study group is required.

The age of the patient had a significant effect on loosening of the prosthesis. Young patients with total hip replacements (Catani 1992, Havelin et al 1994, Johnsson et al 1994) or total knee replacements (Knutson et al 1994) have been recognised to have poorer prognosis. Patients aged over 80 years were reported to have a higher complication rate (Newington et al 1990) but none were revised for aseptic loosening. One study of patients with various pathologies suggested that the pathology had a greater bearing on the outcome than the age (Sarmiento et al 1990). Similarly, cases with massive distal femoral replacements that were inserted for failed primary knee replacements had a significantly poorer prognosis than bone tumour cases (Unwin et al 1993b).

With respect to age, young distal femoral replacement patients had the poorest prognosis in terms of aseptic loosening. In a study of retrieved skeletally immature femora with distal femoral replacements, a neo-cortex had developed
around the cement mantle (Blunn and Wait 1991). Between the neo-cortex and the original cortex there was a region of porotic bone predominantly antero-laterally and an examination of the treated and contra-lateral femora showed a significant increase in the cross-section area of the treated femur. The result of the increase in girth and the formation of the porotic region producing a weaken structure may be a principal factor in the demise of these replacements. Furthermore, the ratio of the femoral head offset and total length of the bone is also greater in skeletally immature patients and this too will further impact on the loosening process (see femoral dimensions, Appendix A). Loosening of cemented intra-medullary stemmed massive replacements in the skeletally immature cases has also been reported (Kenan et al 1991, Missenard 1991, Eckardt et al 1993a, Unwin and Walker 1993c, Unwin and Walker 1995f).

The poorer prognosis for male patients with distal femoral replacements is considered to be multifactorial. Young females had proportionally a smaller femoral head offset moment than males, and therefore young males would be at a greater risk (Appendix A). In addition, males were identified as undertaking more strenuous sports when young and more physically demanding lifestyles when adult and again these are believed to be detrimental (Chapter 3). Males are also heavier than females and patient weight has been cited as a risk factor (Jones et al 1992, Ward et al 1995).

The limited analysis comparing distal femoral osteosarcoma cases with chondrosarcoma cases identified that chemotherapy had no recognisable affect on aseptic loosening. Therefore it would appear that the chemotherapy did not compromise cortical bone remodelling adjacent to the implantation site. However, Young identified that cisplatin significantly restricted extra-cortical bony bridging of porous collared mid-shaft replacement in a animal model (Young et al 1993).
Clearly, there were differences between the two surgeons in terms of revision for aseptic loosening. The variation may be as a result of 1) surgical technique, 2) differing revision criteria, 3) combination of 1 and 2, or 4) none of the above. Analysing the radiographic scores, clinical scores and revision rates excluding aseptic loosening for the 2 surgeons, the similarity was remarkable (Appendix C). Therefore, it is considered the surgical performances of the 2 surgeons were similar and the overriding factor was the decision by the surgeon of when to revise. An important conclusion based upon this hypothesis is that as a result of the significant difference in aseptic loosening rates of the same manufacturers implant, a comparison of loosening rates between different implant types inserted and managed by different surgeons is probably invalid.

Linked to the above, is the method of determining the bone resection level. The majority of malignant tumours arising in bone occur around the knee and it has been identified in both the distal femoral and proximal tibial groups that the greater the resection the higher the probability of loosening. Therefore, the determination of the level of resection will have influence on the survival of the replacement. Clearly, surgeons who used the open biopsy technique resected considerably more distal femur than those who did not use this technique for tumour delimitation.

It would appear that in the long-term, there is very little probability that distal femoral or proximal tibial implants would survive aseptic loosening for two decades or more. However, no proximal femoral implants failed from aseptic loosening after 150 months. It is suggested that those destined failed due to the fixation or biomechanical environment have done so and those which survived for 150 months would continue to survive for many more years. Similarly two long-term studies of cemented THR s reported a decrease in risk of loosening in the later years (Alsema et al 1994, Neumann et al 1994).
Figure 2.1. The age distribution of the patients with respect to implant. There was a significant difference in the age of the patient with respect to skeletal location (p<0.01).

Figure 2.2. The distribution of the percentage of bone resected with respect to implant. There was no significant difference in the percentage of bone resected with respect to skeletal location (p=0.20). (Median, 25% & 75% quartiles, 10% & 90% and circles = outliers >90%).
Figure 2.3. The percentage of bone resected with respect to patient age and implant. (p derived from Kruskal-Wallis test).
Figure 2.4. The percentage of bone resected (mean ± S.E.) with respect to method of biopsy type and implant.
Figure 2.5. The probability of surviving aseptic loosening with proximal, distal femoral or proximal tibial replacements that used cemented intra-medullary stemmed fixation (upper). The probability of surviving (middle) and cumulative hazard (lower) of aseptic loosening with uncoated proximal femoral, distal femoral replacements with a Stanmore knee or uncoated proximal tibial replacements with a Stanmore knee.
Figure 2.6.a. The probability of surviving aseptic loosening (upper) and cumulative hazard (lower) of uncoated distal femoral replacements with respect to age.
Figure 2.6.b. The probability of proximal femoral (upper) and proximal tibial replacements (lower) surviving aseptic loosening with respect to age.
Table 2.7.a. The probability of surviving aseptic loosening (upper) and cumulative hazard (lower) of uncoated distal femoral replacements with respect to the percentage of bone resected.
Table 2.7.b. The probability of proximal femoral (upper) and proximal tibial (lower) surviving aseptic loosening with respect to the percentage of bone resected.
Figure 2.8.a. The probability of surviving aseptic loosening with uncoated proximal femoral replacements (upper) and distal femoral replacements (lower) with respect to gender.
Uncoated proximal tibial replacements with Stanmore hinges

Figure 2.8.b. The probability of surviving aseptic loosening with uncoated proximal tibial replacements with respect to gender.
Figure 2.9. The probability of surviving aseptic loosening for juvenile (upper), young adult (middle) and middle aged (lower) patients with uncoated distal femoral replacements (Stanmore knee hinge) with respect to the percentage of bone resected. The elderly patient group has been omitted due to the small number of patients.
Figure 2.10. The probability of patients with uncoated distal femoral replacements (Stanmore knee hinge), surviving aseptic loosening with respect to year of insertion.
Figure 2.11. The probability of patients with uncoated distal femoral replacements (Stanmore knee hinge), who were administered chemotherapeutic drugs surviving aseptic loosening, compared to those who were not, for all diagnoses (upper) and osteosarcoma patients (lower).
Uncoated distal femoral replacements with Stanmore hinges. Patients aged between 20 - 60 years with 40% - 60% resections.

Figure 2.12. The probability of distal femoral replacements surviving aseptic loosening with respect to surgeon. (Upper - all cases. Lower - patients aged between 20 - 60 years with 40% - 60% resections.)
Uncoated distal femoral replacements

**Figure 2.13.** The probability of uncoated distal femoral replacements surviving aseptic loosening with respect to knee hinge configuration.
Figure 2.14. The offset distance between the line of force and the long axis of the femur.
Figure 2.15. A comparison of offset distance at the tip of the intramedullary stem of a proximal femoral replacement (left) and a distal femoral replacement (right). Both implants replace 50% of the femur.
Plate 2.1. A radiograph of an extendible distal femoral replacement showing aseptic loosening and pivoting of the femoral intra-medullary stem. This replacement had been in situ for four years.
Table 2.1. Patient age and percentage of bone resected with respect to the commonest tumour for each implant group.

<table>
<thead>
<tr>
<th></th>
<th>Patient age (years)</th>
<th>Bone resected (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>mean</td>
</tr>
<tr>
<td><strong>Distal femoral: Osteosarcoma</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1964-83</td>
<td>53</td>
<td>18.5</td>
</tr>
<tr>
<td>1984-87</td>
<td>102</td>
<td>18.1</td>
</tr>
<tr>
<td>1988-92</td>
<td>168</td>
<td>17.5</td>
</tr>
<tr>
<td>p</td>
<td>0.54</td>
<td></td>
</tr>
<tr>
<td><strong>Proximal femoral: Chondrosarcoma</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1964-83</td>
<td>31</td>
<td>50.7</td>
</tr>
<tr>
<td>1984-87</td>
<td>21</td>
<td>48.0</td>
</tr>
<tr>
<td>1988-92</td>
<td>38</td>
<td>50.4</td>
</tr>
<tr>
<td>p</td>
<td>0.77</td>
<td></td>
</tr>
<tr>
<td><strong>Proximal Tibial: Osteosarcoma</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1964-83</td>
<td>28</td>
<td>17.0</td>
</tr>
<tr>
<td>1984-87</td>
<td>52</td>
<td>17.3</td>
</tr>
<tr>
<td>1988-92</td>
<td>87</td>
<td>17.5</td>
</tr>
<tr>
<td>p</td>
<td>0.51</td>
<td></td>
</tr>
</tbody>
</table>

p derived from Kruskal-Wallis test

Note: Because of the unavailability of radiographs for cases pre-1984, resection data has been omitted for 1964-83.
Table 2.2. The status of the 1149 patients, highlighting those who underwent revision.

<table>
<thead>
<tr>
<th>Implant</th>
<th>Distal femoral</th>
<th>Proximal femoral</th>
<th>Proximal tibial</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>%</td>
<td>n</td>
<td>%</td>
</tr>
<tr>
<td>Amputations / rotationplasty</td>
<td>39</td>
<td>6.8</td>
<td>17</td>
<td>5.9</td>
</tr>
<tr>
<td>Died (all causes)</td>
<td>86</td>
<td>14.9</td>
<td>84</td>
<td>29.0</td>
</tr>
<tr>
<td>Prosthetic related complications</td>
<td>36</td>
<td>6.2</td>
<td>19</td>
<td>6.6</td>
</tr>
<tr>
<td>No prosthetic related problems</td>
<td>270</td>
<td>46.8</td>
<td>121</td>
<td>41.7</td>
</tr>
<tr>
<td>Revisions</td>
<td>93</td>
<td>16.1</td>
<td>20</td>
<td>6.9</td>
</tr>
<tr>
<td>No follow-up</td>
<td>53</td>
<td>9.2</td>
<td>29</td>
<td>10.0</td>
</tr>
<tr>
<td>Total</td>
<td>577</td>
<td>100.0</td>
<td>290</td>
<td>100.1</td>
</tr>
</tbody>
</table>
Table 2.3. The form of implant related failure with respect to implant type, highlighting aseptic loosening.

<table>
<thead>
<tr>
<th>Form of failure</th>
<th>Implant femoral</th>
<th></th>
<th>Implant femoral</th>
<th></th>
<th>Implant tibial</th>
<th></th>
<th>Total</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>%</td>
<td>n</td>
<td>%</td>
<td>n</td>
<td>%</td>
<td>n</td>
<td>%</td>
</tr>
<tr>
<td>Amputation: necrosis, circulatory, sterile abscess or pain</td>
<td>2</td>
<td>2.0</td>
<td>0</td>
<td>0.0</td>
<td>3</td>
<td>4.1</td>
<td>5</td>
<td>2.5</td>
</tr>
<tr>
<td>Amputation: infection</td>
<td>4</td>
<td>4.1</td>
<td>5</td>
<td>20.0</td>
<td>19</td>
<td>25.7</td>
<td>28</td>
<td>14.2</td>
</tr>
<tr>
<td>Revision: implant fracture</td>
<td>15</td>
<td>15.3</td>
<td>2</td>
<td>8.0</td>
<td>6</td>
<td>8.1</td>
<td>23</td>
<td>11.7</td>
</tr>
<tr>
<td>Revision: hyper-extension</td>
<td>0</td>
<td>0.0</td>
<td>0</td>
<td>0.0</td>
<td>6</td>
<td>8.1</td>
<td>6</td>
<td>3.0</td>
</tr>
<tr>
<td>Revision: fully extended or jammed extendible implant</td>
<td>5</td>
<td>5.1</td>
<td>2</td>
<td>8.0</td>
<td>1</td>
<td>1.4</td>
<td>8</td>
<td>4.1</td>
</tr>
<tr>
<td>Revision: titanium cyst</td>
<td>0</td>
<td>0.0</td>
<td>0</td>
<td>0.0</td>
<td>2</td>
<td>2.7</td>
<td>2</td>
<td>1.0</td>
</tr>
<tr>
<td>Revision: infection</td>
<td>9</td>
<td>9.2</td>
<td>2</td>
<td>8.0</td>
<td>13</td>
<td>17.6</td>
<td>24</td>
<td>12.2</td>
</tr>
<tr>
<td>Revision: bone fracture</td>
<td>1</td>
<td>1.0</td>
<td>0</td>
<td>0.0</td>
<td>2</td>
<td>2.7</td>
<td>3</td>
<td>1.5</td>
</tr>
<tr>
<td>Revision: acetabular cup aseptic loosening</td>
<td>0</td>
<td>0.0</td>
<td>4</td>
<td>16.0</td>
<td>0</td>
<td>0.0</td>
<td>4</td>
<td>2.0</td>
</tr>
<tr>
<td>Revision: intra-medullary stem aseptic loosening</td>
<td>62</td>
<td>63.3</td>
<td>10</td>
<td>40.0</td>
<td>22</td>
<td>29.7</td>
<td>94</td>
<td>47.7</td>
</tr>
<tr>
<td>Total</td>
<td>98</td>
<td>100.0</td>
<td>25</td>
<td>100.0</td>
<td>74</td>
<td>100.1</td>
<td>197</td>
<td>99.9</td>
</tr>
</tbody>
</table>
Table 2.4. The percentage of cases that failed from aseptic loosening and the mean time to failure with respect to patient age, gender and the percentage of bone resected.

<table>
<thead>
<tr>
<th>Implant</th>
<th>Proximal femoral</th>
<th>Distal femoral</th>
<th>Proximal tibial</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>%</td>
<td>mean duration (mths)</td>
<td>%</td>
</tr>
<tr>
<td>Age (years)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤16</td>
<td>10.5</td>
<td>57.2</td>
<td>15.3</td>
</tr>
<tr>
<td>&gt;16 ≤25</td>
<td>5.0</td>
<td>96.6</td>
<td>10.0</td>
</tr>
<tr>
<td>&gt;25 &lt;60</td>
<td>2.5</td>
<td>90.8</td>
<td>7.7</td>
</tr>
<tr>
<td>≥60</td>
<td>0.0</td>
<td>-</td>
<td>4.0</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>1.4</td>
<td>57.8</td>
<td>3.8</td>
</tr>
<tr>
<td>Male</td>
<td>2.1</td>
<td>92.3</td>
<td>6.6</td>
</tr>
<tr>
<td>Resection (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;40</td>
<td>6.2</td>
<td>77.8</td>
<td>7.3</td>
</tr>
<tr>
<td>≥40-60</td>
<td>2.7</td>
<td>85.0</td>
<td>11.8</td>
</tr>
<tr>
<td>&gt;60</td>
<td>2.0</td>
<td>(57.0)</td>
<td>18.1</td>
</tr>
<tr>
<td>Implant Total</td>
<td>3.5</td>
<td>78.6</td>
<td>11.9</td>
</tr>
<tr>
<td>Number / Range (months)</td>
<td>282</td>
<td>34-108</td>
<td>577</td>
</tr>
</tbody>
</table>

* Group size of 10 patients.

mths = months
Chapter 3

Clinical assessment of patients with cemented intra-medullary endoprostheses of the lower limb
3.1. Introduction

Patient assessment in the clinical environment provides information on the performance of both the patient and implant. Furthermore, clinical assessment can provide data on the acceptance of the procedure.

In 1981, at the first meeting of the International Symposium on Limb Salvage (ISOLS) it was clear to the participants that a standard clinical grading system was required. After a number of trials and modifications, a clinical grading system was devised and was first used at the fourth meeting (1987), (Enneking et al 1993). This clinical grading system has now become standard for the assessment of patients who have undergone a limb salvage procedure.

The ISOLS clinical assessment grading system comprises of six sections, which are -

- Functional activity, that includes walking distance, walking aid, the ability to ascend stairs, and activities of daily living.
- Stability of the replaced joint
- Pain
- Range of replaced joint movement (active only)
- Limb deformity
- Emotional acceptance of the limb salvage procedure.

3.2. Methodology

The clinical assessments of patients with Stanmore custom-made massive replacements were conducted at the Royal Orthopaedic Hospital, Birmingham, the Royal National Orthopaedic Hospital and the Middlesex Hospital. The data collected was used to calculate an ISOLS clinical assessment grade and a BME clinical score.
The questions were asked in a standard format, offering a choice of answers to the patient if an answer was not immediately forthcoming. Assessing the children, effort was made to obtain the answer from the child and then confirming this with the accompanying parent/s. When answering the questions the patients were told to consider the period of time in question was the last 2 months unless there had been a particular episode that was discussed separately in more depth.

All range of movement (ROM) measurements were made using a long arm goniometer. To assess the ROM at the knee, patients with either a distal femoral or proximal tibial replacement were asked to sit on the side of the bed (foot not touching the floor) and raise their affected leg and then flex to its maximum extent unaided. Passive movement of the knee, rotation at the knee about the long axis of the femur and varum/valgum movement at the knee hinge were performed by the assessor. All the ROM at the hip were measured whilst the patient was in a lying in a supine position on the examination bed, with the exception of extension at the hip when the patient lay on their unaffected side and extended their affected limb. Leg length measurements were made by comparing the measurements taken from the anterior superior iliac spine to the medial malleolus of the ankle of the affected and contra-lateral limbs. To assess gait, patients were asked to walk approximately 15 meters along a corridor, turn round and walk back without a walking aid, where permissible.

3.2.1. ISOLS clinical evaluation

The ISOLS (1987) clinical grading system was adopted by the Division of Biomedical Engineering to assess clinically the patients who received a Stanmore custom-made massive endo-prosthesis to comply with ISOLS.

Each of the 6 sub-sections clinical scored as follows, Excellent =4, Good =3, Fair =2, and Poor =1. An overall ISOLS clinical score was calculated by summat
the scores of the 6 sub-sections. The overall ISOLS clinical grade was calculated as follows, Excellent = 24, Good = 21-23, Fair = 18-20, and Poor < 18. To obtain an 'Excellent' grade, the patient must have achieved an 'Excellent' grade in all 6 sub-sections. Tabulated details of the grading system are presented in Appendix D.

3.2.1.1. Modification to the ISOLS system

The ISOLS (1987) clinical grading system was used by a small number of Biomedical Engineering assessors between 1987 and 1990. In 1990, after using the ISOLS (1987) clinical grading system for a number of months, it was considered by a consultant orthopaedic surgeon and me that there were a number of restrictions with the ISOLS system. A more comprehensive system based upon the ISOLS system was then developed. The purpose of the modification was to provide a clearer assessment by asking the patients more specific questions relating to the function of their affected limb. The grading system was constructed to ensure that an ISOLS (1987) clinical assessment grade could be obtained from the data collected.

3.2.2. Biomedical Engineering clinical evaluation

The modifications to the ISOLS system were additional information relating to pain, patient activity level and gait. If the patient reported pain, they were asked about the severity and its location, whether it was a sharp or dull pain and when it occurred. Three time periods were offered were -

- Prior to getting out of bed in the morning
- While going about activities of the day
- While resting in the evening.

The patients were also asked how they considered their lifestyle to be? The options were 'Heavy', 'Medium/Normal' or 'Light'. A 'Heavy' lifestyle was
recorded when the patient was undertaking activities greater than average, for example, carrying heavy objects or having returned to a manual job such as road building. If the patient had returned to their job or was an active housewife or a school pupil, a 'Medium/Normal' lifestyle was recorded. A 'Light' lifestyle was recorded if the patient had given up their job, needed assistance to shop or to and from school.

The overall BME clinical grade was produced by summating scores from 3 subsections, these were -

- Functional activity
- Pain
- Range of movement

Functional activity included walking distance, walking aid, activities of daily living, ability to climb stairs, and joint instability. Emotional acceptance and limb deformity parameters were excluded. Pain was scored as per the ISOLS system. Unlike the ISOLS system both the activity and passive ROM were assessed. Details of grading system are presented in Appendix D.

An overall patient/implant performance score was calculated using the following formula -

$$BFunct = \text{Functional activity}; \quad BPain = \text{Pain score}; \quad BROMact = \text{Range of active joint movement}; \quad BROMpass = \text{Range of passive joint movement}$$
The BME clinical grade was converted into an ordinal score, as follows - 'Excellent' = 12, 'Good' = 11.5-10, 'Fair' = 9.5-7, and 'Poor' <7. An 'Excellent' scored could only be obtained if the patient scored 'Excellent' in all parameters.

3.2.3. Selection criteria.

The selection criteria of the clinical assessments for this study were patients with an uncoated cemented intra-medullary stemmed endo-prosthesis. In addition, with respect to distal femoral and proximal tibial replacement cases, only those with Stanmore fixed knee hinge were selected.

3.3. Results

In total, 352 clinical assessments of uncoated endo-prosthesis were acceptable for study. The mean follow-up duration was 51.3 months (±2.4 S.E.) with the distal femoral replacements having the longest mean follow-up (55.8±3.3 months, n=187) and the proximal tibial replacements the shortest (40.4±4.7 months, n=93) (Figure 3.1). The mean follow-up duration of the proximal femoral replacements was 53.7 months (±5.12 S.E., n=72). The longest implant duration was 275 months, and the patient had a proximal femoral replacement.

3.3.1. Overall Grade

Overall, the majority of patients with a lower limb endo-prosthetic replacement were graded using the ISOLS system as 'Good' (46.6%) or 'Fair' (29.9%). Over ten percent of cases were graded as 'Poor' (10.3%) and 13.2% were graded as 'Excellent'.

Distal femoral replacement proportionally had the greatest percentage of cases scoring an 'Excellent' grade, whereas, the proximal tibial cases had the highest percentage of cases graded as 'Poor' (Figure 3.2). The distal femoral and proximal femoral groups had 66.7% and 66.6% of cases scoring either 'Excellent' or 'Good', compared to only 43.5% of the proximal tibial cases. There was a
significant difference between the three implant groups with the respect to clinical grade (p=0.0005).

The distal femoral cases had on average the highest BME clinical score of 10.3 (n=152), compared to 9.9 (n=52) for the proximal femoral and 9.4 (n=81) for the proximal tibial cases (p<0.01).

**Duration.** With increasing duration the score for the combined group of implant types decreased from 21.2 (ISOLS) at 7.1 months (n=24) to 20.5 at 233 months (n=2) (Figure 3.3). With increasing implant duration the general trend in the three implant groups was a decrease in the ISOLS clinical score that was most pronounced in the proximal tibial group.

3.3.1.1. Patient age

Skeletally immature patients (≤16 years) had the lowest average ISOLS scores (Figure 3.4). However, there was little difference in the BME scores between the age groups of all three implant groups. There was no significant difference between the four age groups with respect to ISOLS or BME score for any of the 3 implant types. In the distal femoral and proximal tibial groups, the ISOLS score rose with slightly increasing age with the elderly patients (≥60 years) having the highest ISOLS score, but in both groups the number of elderly patients was small (DF n=13 and PT n=4). In the adult proximal femoral groups (>16 years) there was slight decrease in ISOLS with increasing age.

With skeletally immature patients (≤16 years) with distal femoral replacements, there was a general decline in the both the ISOLS and BME clinical score with increasing implant duration until 120 months, after which the scores increased marginally. The score of adult patients (>16 years) increased after the first 12 months but dropped slightly after 120 months. In the proximal femoral group, there were few juvenile or elderly patients who had been assessed and therefore no trend could be determined. Similarly no discernible trend could
be identified for young adult or middle aged patients (>16 <60 years) although the number of patients was higher. Similarly, in the proximal tibial group the number of patients assessed in each of age group was small and no trend could be determined.

3.3.1.2. Percentage of bone resected

The level of resection had little effect on either the BME and ISOLS clinical scores in the distal femoral group. Patients with either a proximal femoral or proximal tibial patient with less than 40% of the shaft resected had on average higher scores than those with a greater percentage of bone resected (Figure 3.5).

With respect to duration there was no identifiable trend in the three resection groups of either the proximal or distal femoral groups. In the proximal tibial group there was a decrease in ISOLS clinical score in those patient with either <40% or >60% resections of the tibia.

3.3.2. The sections of the ISOLS and BME clinical grading systems

The distribution of the grades of each of sub-sections of the ISOLS and the BME clinical evaluation systems are presented in Figures 3.6 and 3.7 respectively. Note that the ISOLS grades the Range of movement and Functional activity are more severe than the BME system. Joint instability was included in Functional activity of the BME system but not the ISOLS. The distribution of grades of the activities that together formed the Functional activity grade are illustrated in Figure 3.8

3.3.3. Functional activity

The ISOLS Functional activity assessment included walking distance, walking aid, ability to climb stairs and activities of daily living (Figure 3.8). Overall, the average function grade was 'Good', while the distal femorals having a slightly higher score than the proximal femoral and the proximal tibial replacements
In all replacements groups, the average function score improved with time.

### 3.3.3.1. Patient age

Elderly patients in all implant groups, had lower functional scores. Juvenile and young adult patients with either a distal femoral or proximal tibial replacement had a decreasing score with increasing duration whereas the older patients had an improving score. In all age groups of the proximal femoral group the function score improved with time.

### 3.3.3.2. Percentage of bone resected

With respect to the percentage of bone resected the distribution of grades were similar in all resection groups of the distal femoral replacements, with the majority of cases having an 'Excellent' result. Patients with proximal femoral replacements with either short (<40%) or long (>60%) resections were predominantly 'Excellent' or to a lesser extent 'Good', whereas those with resections between 40%-60% were mainly graded as 'Fair' or 'Good'. A similar distribution of function grades was identified in the 3 proximal tibial group, with the majority of cases classed as 'Good' and to lesser extent 'Excellent', with the 'Fair' and 'Poor' being recorded infrequently.

### 3.3.3.3. Walking distance

Overall, the majority of patients could walk a minimum of 1 mile, with 79.0% of distal femoral patients able to manage this distance, compared to 71.7% of proximal tibial and 65.7% of proximal femoral patients (Figure 3.8). In all three implant groups a larger proportion could walk a mile or further after a duration of 1 year. Few patients could not walk any distance or less than 100 metres and there was no specific period it which this was more prevalent.
The majority of elderly patients were able to walk 1 mile or further, but some elderly patients were unable to walk this far but most could manage a 1/4 mile. However, there was no significant difference between age groups in the distance they could walk. Similarly, there was no significant difference with respect to the percentage of bone resected, although, there was a relatively high frequency of proximal femoral cases with >40% resection who could only manage to walk 1/4 mile or 100 metres.

3.3.3.4. Stairs

In the distal femoral group, 70.7% of patients could ascend stairs normally, with 24.9% able to ascend with one leg at a time, and the remainder unable to ascend stairs (Figure 3.8). Within the first year, 56.7% could ascend normally and this percentage increased to 75.9% between ≥1 <6 years of implant duration, and slightly decreasing in percentage after 6 years. In contrast, fewer patients with a proximal femoral or proximal tibial replacements could ascend stairs normally (PF=53.6%, PT=49.5%). The majority of the remainder had to ascend one leg at a time (PF=37.7%, PT=48.4%). In the proximal femoral group there was a slight increase in the percentage of patients who over time could ascend normally, but, no improvement was evident with proximal tibial patients.

The majority of juvenile and young adult patients (<25 years) could manage to ascend stairs normally, whilst the large majority of the elderly patients either had to ascend one leg at a time or were unable to without assistance. The majority of middle-aged patients with femoral replacements were able to ascend stairs normally, but the majority of proximal tibial patients had to ascend stairs one leg at a time.

With increasing percentage of distal femur resected a higher proportion of patients could ascend stairs normally. A differing trend was identified in the proximal femoral group, the majority of patients with <40% resection and
those with >60% resections were those who could ascended stairs normally and the majority of those with 40-60% resection had to ascend stairs one step at a time. In the proximal tibial group the greater the percentage resected the lower the proportion of patients who could ascend stairs normally.

3.3.3.5. Walking aid

After the first year the large majority of patients (79.3%) used no form of walking aid. Proportionally, patients with distal femoral replacements had fewest of cases using a walking aid and those who did, normally used 1 walking stick (Figure 3.8). The number of patients with a distal femoral replacement not using a walking aid after the first year rose from 63.3% to over 86% at 10 years. Over 64% of patients with proximal femoral replacement used a walking aid in the first year, dropping to 45.9% between 1 and 5 years and further to 22.2% after 5 years. A similar trend of requiring a walking aid, was evident with patients with proximal tibial replacements. Of those proximal tibial cases who did use a walking aid nearly 9% required the use of crutches.

With respect to age, a large majority of young patients (84%) did not require a walking aid. Similarly, the majority of young adult (88%) or middle aged patients (71%) with either a distal femoral or proximal tibial replacement walked without an aid, but a substantial number (39%) of proximal femoral replacements needed 1 walking stick if going out of doors. The majority of elderly patients required the use of a walking stick (58%). The level of resection had little effect on the use of a walking aid with the exception of the proximal femoral replacements cases with 40-60% resections who more frequently required the use of a walking stick.

3.3.3.6. Activity of daily living

All patients with proximal femoral replacements, 98.5% with proximal tibial and 95.1% with a distal femoral replacement were able to achieve all activities
of daily living (Figure 3.8). Of those who were unable to work, were able to bathe and dress themselves. The majority of patients took some form of exercise usually swimming although cycling and golf were popular. Many young patients expressed that they would like to participate in sports particularly football. It was recorded that a small number of patients did participate in active sports such as football, badminton, judo and horse riding.

3.3.3.7. Level of activity

The level of activity was not used in either the ISOLS or the BME assessment systems. The majority of the patients questioned were classed as having an average lifestyle, however 25% of distal femoral and 20% of proximal femoral cases were considered to have heavier than normal lifestyles (Figure 3.9). In addition, 29% of proximal femoral, 15% of distal femoral and 15% of proximal tibial cases had a lighter than normal lifestyle. In particular, it was the elderly patients who had a lighter lifestyles and the younger patients heavier. The percentage of shaft resection had a dominant effect on lifestyle, the lower the percentage of resection the greater the proportion who had a lifestyle heavier than normal.

3.3.4. Instability

Knee instability in patients with either a distal femoral or proximal tibial replacement generally occurred at two specific intervals. Either during the initial rehabilitation after surgery or when polyethylene axle bushes were worn. Knee instability was greatest in the proximal tibial group with 43.9% having some instability, with 13% of patients having an episode of instability at least once a week (Figure 3.8). As implant duration increased the proportion of patients with instability increased as did the frequency of instability. Fewer distal femoral replacement patients had knee instability and had less frequent episodes.
In both implant groups instability was proportionally more common with elderly patients and those with >40% resections. The greater percentage of bone resected in the proximal tibial group the higher the proportion of cases reported no instability.

Patients with proximal femoral replacements infrequently reported instability of the hip, with 79.4% of cases having no periods of instability. Infrequent periods of instability were proportionally more frequent in the young and elderly patients. All patients who had <40% resections and 75% of cases with >40% resections reported no hip instability. Of the small number of proximal femoral replacement patients who reported periods of instability, the large majority patients reported that hip joint instability occurred infrequently. No patient reported hip joint instability episodes that occurred on a daily basis.

3.3.5. Pain

The majority of patients (56.6%) reported having no pain associated with the affected limb (Figure 3.6). Nearly 76% of distal femoral group and 65% of the proximal tibial had no pain in the first year whereas those interviewed with implant duration of between 5 and 10 years, 55.8% of the distal femorals and 47.1% of the proximal tibials had no pain. However, 81% of the distal femoral cases with implant duration greater than 10 years had no pain. In the proximal femoral group, 50% of patients had pain in the first year and with increasing duration this decreased to under 35%. No patient with a proximal femoral replacement reported having severe pain.

3.3.5.1. Patient age

The majority elderly (75%) and young adult (62%) patients with a distal femoral replacements reported no pain, however juvenile and middle aged patient reported pain more frequently (56% & 51% respectively). Similarly, all elderly patients with proximal femoral replacements reported no pain, but only 41% of
the middle aged patients reported no pain. In the proximal tibial group, it was the youngest patients (≤16 years) who reported that they had suffered no pain (63.0%) most frequently. In this group with increasing age of the patient that was an increase in the number of patients reporting pain.

With increasing implant duration, an increasing proportion of young patients with distal femoral replacements and elderly patients with proximal tibial replacements reported having pain with increasing severity.

3.3.5.2. Percentage of bone resected

In all resection groups the majority of patients reported having no episodes of pain. Patients with >60% resections generally had increasing severity of pain with increasing implant duration. In addition, those cases with <40% resection generally had less severe pain with increasing implant duration.

3.3.5.3. Timing and type of pain

Few patients (5%) reported having pain prior to rising in the morning. Furthermore only 2.8% of the patients who reported having pain, had pain only at rest. Of those who did, all but one case had either mild or moderate pain that occurred either a few times per week or every day. This pain was described as a dull throb. The majority of patients who had pain prior to rising reported this within the first year after limb salvage.

Pain was most common on movement. A total of 73.9% of the patients with pain had it associated with movement, and 42.1% of patients with pain had pain only whilst walking.

Of those patients with pain on movement, severe or moderate pain was reported most frequently by patients with distal femoral replacements (13%) or proximal tibial replacements patients (12.1%). However no patient with a proximal femoral replacement had severe pain and only 7.7% had moderate
pain. The majority had episodes of pain occurred either a few times a week or every day. The large majority of patients reported that the pain was sharp. Generally, those who reported sharp pain on movement that occurred a few times a week or every day, only had this pain when taking the first steps either when getting out of bed or after a prolonged period of rest (start-up pain). It was noticed by these patients that after the brief episode of pain it would normally diminish rapidly and would not return again until the following morning.

Pain in the evening was relatively common, with 52.4% of the patients reporting pain having pain at this period of the day. Of those patients with pain, 23.4% had pain only in the evening. Severe pain occurred in only 0.8% distal femoral and 1.5% proximal tibial replacement cases. Of those reporting pain in the evening, the large majority (78.6%) had mild pain which occurred either a few times a week or every day. Generally this pain was reported to be a dull throb. With increasing implant duration the proportion of patients with pain in the evening remained relatively constant.

With respect to the timing of the episode/s of pain, of those patients who reported pain, 12.2% had pain in all three time intervals. The majority of patients had pain occurring either during movement and or after activities. No patients had pain at rest and in the evening and no pain whilst active.

3.3.6. ROM Knee

Both the passive and the active range of movement (ROM) at the knee was marginally greater for patients with distal femoral replacements (passive =96.8°, active =98.6°) compared to those with proximal tibial replacements (passive =72.8°, active =83.0°). For patients with distal femoral replacements (n=187) the average knee flexion =101°, active extension =4.3° and passive knee extension =2.5°. Patients with proximal tibial replacements (n=93) the extensor lag was more pronounced, (knee flexion =91.5°, active extension =18.7°, passive
knee extension =8.4°). Neither patient age or the percentage of bone resected had a significant effect on the ROM in the distal femoral group. However, juvenile patients with a proximal tibial replacement had a significantly poorer active extension (23°) and active ROM (66°) than adult patients (2° and 84° respectively) (extension p=0.03, ROM p=0.03). Patients with proximal tibial resections <40% had a significantly better active extension (4°) and active ROM (96°) than those with resections >40% (21° and 68° respectively) (extension p=0.01, ROM p=0.03).

3.3.6.1. Grade

Of the 334 cases assessed for ROM, 49.4% scored 'Excellent' and a further 29.6% scored 'Good' (Figure 3.6). Distal femoral replacements proportionally had the highest number of cases scoring 'Excellent' (65.4%). The scores in the proximal tibial group were more diverse with a higher proportion being graded as 'Fair' (17.4%) or 'Poor' (16.3%).

3.3.7. ROM Hip

Overall, of the 57 proximal femoral cases assessed the average flexion at the hip was 86.4°, abduction was 30.0° and adduction 19.8°.

3.3.7.1. Grade

The majority of proximal femoral cases were graded as either 'Good' (45.8%) or 'Excellent' (35.6%) and only 3.4% scored 'Poor' (Figure 3.6). Younger patients had better scores than elderly patients and the level of resection had little effect on the ROM of the hip.

3.3.8. Deformity

The most commonly occurring deformity was shortening of the affected limb. Of the 302 cases measured for length, 53.3% had limb length equality (<± 5 mm discrepancy) (Figure 3.10). Shortening of the affected limb by 5 mm or greater
occurred in 32.1% lengthening of 5 mm or more in the remaining 14.6%. Severe limb shortening (≥ 40 mm) was worst with patients who had either a proximal or distal femoral replacement. One distal femoral case had shortening of the affected limb of 100 mm and another 60 mm. Over-lengthening of the affected limb was not so common, but one proximal tibial case had the limb lengthened by 30 mm and another 25 mm.

Leg length discrepancies were not isolated to the skeletally immature cases and were equally found in middle aged patients. Indeed, the middle aged patients had the greatest discrepancy range (-100 mm to +30 mm), compared to young patients (-60 mm to +20 mm). Elderly patients generally had the smallest range of leg length discrepancy. The large majority of skeletally immature patients had extendible replacements and the leg length discrepancy was being corrected periodically.

Few other patients had other forms of deformity, however a small number had fixed flexion deformities (FFD) of the knee. The large majority of cases with fixed flexion deformities were patients with distal femoral replacements or proximal tibial replacements. Most cases with a FFD were skeletally immature and some were linked to a recent lengthening procedure of an extendible endoprosthetic replacement.

3.3.9. Emotional Acceptance

The large of majority of patients who were asked how they accepted their endoprosthesis and limb salvage procedure were either enthusiastic (65.0%) or satisfied (25.3%). Few patients disliked their prosthesis/limb salvage procedure (2.2%). Disliking or accepting their prosthesis/limb salvage procedure was more common with patients with a proximal tibial replacement (14.1%) compared to those with a femoral replacement (8.1%) (Figure 3.6).
Overall, there was an increasing acceptance of the prosthesis/limb salvage procedure with increasing implant duration. Young patients were most likely to dislike their replacement/limb salvage device, and were less enthusiastic about their replacement than elderly patients. The percentage of bone resected had little effect on the emotional acceptance.

3.3.10. Gait

Gait was not a component of either the ISOLS or BME clinical grading systems. A limp was not discernible in 23.1% of cases with a lower limb endo-prosthetic replacement. Gait generally improved with increasing implant duration. Overall, patients with distal femoral replacements had the highest proportion of cases with no limp (21.0%) or a slight limp (44.6%), followed by the proximal tibial group (no limp =28.4%, slight limp =21.1%). In contrast, 65.2% of proximal femoral cases had a pronounced limp (Figure 3.11). Young adult patients had gait closest to normal, whereas, the majority of elderly patients limped. In the distal femoral and proximal tibial groups the level of resection did not have an effect on the proportion of cases with affected gait. In the proximal femoral group, a higher percentage of patients with shorter resections did not limp.

Seventy percent of the distal femoral replacement cases did not walk with a stiff knee or back-kneed (hyper-extension of the knee) but 20% had a mild stiff knee gait and a further 6% had a pronounced stiff knee gait. The remaining 4% of distal femoral cases back kneed compared to over 16% of proximal tibial cases. In addition, a higher proportion of proximal tibial cases (11.8%) had a pronounced stiff knee gait and 19% of proximal tibial replacement cases had a mildly stiff knee gait with the remainder (52.9%) walking without a stiff knee or back-kneed. With increasing implant duration the patients of both implant groups improved.
The majority of patients with a proximal femoral replacement had a moderate or pronounced negative Trendelberg gait (63.8%). Few patients had a mild negative Trendelberg gait (12.5%) and 23.6% had no sign of a Trendelberg. The Trendelberg was more pronounced in the young patients and was mildest in the elderly patients. With respect to the percentage of bone resected, on average the greater the percentage of bone resected the more pronounced the Trendelberg. The Trendelberg became less pronounced with increasing implant duration.

3.3.11. Predictor of aseptic loosening

To assess if aseptic loosening could be predicted by a clinical assessment, a comparison of the those that had failed from aseptic loosening (n=35) with those that had survived (n=295), identified that the majority of clinical parameters were unreliable indicators.

Clinical assessments taken over 12 months prior to revision were excluded from the study. All implant groups were combined to ensure sufficient numbers for statistical reliability.

With the exception of pain and the overall clinical score, there was no significant difference between the clinical assessments of survivors and those that failed (Table 3.1). However, in all clinical parameters those that failed had a lower score, with the exception of the ISOLS deformity parameters where the scores were equal.

The significant difference in the overall clinical grading between the two groups was influenced by the largely by the pain score (Figure 3.12). Moderate or severe pain was recorded in 37.1% of those that failed compared to 9.2% in the survivors group (p<0.01). Furthermore, of the 13 patients that failed, who reported moderate or severe pain all but 1 had the severest pain whilst walking and none had severe pain prior to rising in the morning. The one remaining
case who had pain whilst walking had severe pain after performing daily activities. In comparison, 6 of the 7 patients reporting severe pain, reported it prior to rising in the morning, 3 of who had infected prostheses.

Comparing the ISOLS radiographic grades the majority of those that failed had radiographs that were scored 'Poor' (55.6%), whereas, the majority of the survivors scored either 'Fair' (50.0%) or 'Good' (27.8%) (For radiographic scoring methods see section 4.1.3 'Radiographic scoring systems'). The average radiolucent line score for those patients that failed who reported moderate or severe pain was 3.38 compared to 1.39 for those patients reporting moderate or severe pain who did not fail.

3.4. Discussion

The clinical assessments of 352 bone tumour patients with lower limb massive endo-prostheses has highlighted that aseptic loosening had an affect on the patients. However, assessment parameters with the exception of pain were not able to distinguish those patients that had loosening prostheses.

The collection of reliable data was difficult and required the examinations to be undertaken by a single reviewer. Although a carefully constructed evaluation form was used, data collection was often subjective. In a trial being undertaken at the Birmingham Bone Tumour Treatment Service, four assessors independently reviewed patients using the ISOLS evaluation method. In the majority of cases there was at least one grade difference.

Complicating factors of clinical evaluation included the diverse and widespread nature of the assessments. Many patients during the first year after the limb salvage operation were on chemotherapy treatment and also some patients had unrelated complications that restricted their activities such as asthma or osteoarthritis.
The grading of the parameters was designed to reflect the level of disability, for example, a 'Poor' score in one category equals in terms of disability a 'Poor' score in another category. However, this is arbitrary, for one patient may consider themselves to be severely restricted if they cannot walk more than 100 metres, whereas others may not.

Over time, function ability improved and is considered to be due to a combination of factors including adaptation of gait, ceasing chemotherapy treatment and regaining muscle strength. Younger patients were also more conscious of their image and wanted to join in activities, therefore walking sticks were discarded sooner and boys in particular attempted to play contact sports. With increasing maturity and greater understanding of their disease and limb salvage procedure there was greater acceptance and more responsible attitude. Over-demanding sports or work would affect the loosening of the prosthesis and this may be why males had a poorer prognosis in terms of loosening than females (Figure 2.6). Conversely some patients were reluctant to continue the demanding physiotherapy exercises that resulted in stiffened knees and extensive extensor lags.

Patients with a knee replacement generally had a poorer clinical score than those with a hip replacement and over time the former had a decreasing score whereas the latter improved. Factors such as age and resection had a significant effect on the functional results. Other factors have also been considered to affect clinical results such as extensive excision of the quadriceps that resulted in poorer functional performance (Capanna et al 1991c).

Pain in terms of loosening is one of most important factors but is known to have been difficult to evaluate (Torgerson 1984). Patients with excellent functional results but disabilitated by pain would be considered to have a poorer result than a patient who is unable to walk 100 metres due to extensive muscle resection but otherwise pain-free. Not all pain episodes reported in the
clinical evaluation can be linked to loosening. Pain occurred with infections, neurological damage and unrelated causes such as joint disease in the contralateral limb and was frequently reported as a dull pain. Pain associated to loosening was reported to be sharp and initially predominantly occurred as 'start-up' pain that diminished rapidly. This sharp pain however, became more intense, frequent and prolonged as the prosthesis loosened progressively. The sharp pain would appear to be as a direct result of the cement/implant composite moving axially or rotationally within the medullary cavity.

Emotional acceptance was difficult to assess, as many patients compared this form of limb salvage with amputation rather than about the functionality and cosmetic appearance of the prosthesis. In one study comparing amputees with limb salvage patients, the former had poorer functional scores but there was no difference between the patient's emotional acceptance of the procedure (Rougraff et al 1994). Unlike the large majority of patients who undergo total joint replacement, the bone tumour patients prior to surgery were often young, fit and healthy. After undergoing major limb salvage surgery and treatment for cancer, many patients wished to return to activities such as active participation sports and therefore alternative forms of limb salvaging or amputation ought to be considered. Asking the patients what they want, is believed to improve the outcome evaluation of the treatment (Wright et al 1994).
Figure 3.1. The number of assessments performed with respect to implant duration and implant type.

Figure 3.2. The distribution of the ISOLS clinical grades with respect to implant type.
Figure 3.3. Clinical score (ISOLS) with respect to duration and implant.
Figure 3.4. The ISOLS (upper) and BME (lower) clinical grading scores with respect to patient age and implant.
Figure 3.5. The ISOLS (upper) and BME (lower) clinical grading scores with respect to the percentage of bone resected and implant.
Figure 3.6. The distribution of grades of the six sections that comprise to form the ISOLS clinical evaluation grade.
Figure 3.7 The distribution of grades of the three sections that comprise to form the BME clinical evaluation grade.
Figure 3.8. The individual clinical parameters that together form the Function Activity section of the clinical evaluation systems.
Figure 3.9. The level of activity of the patient with respect to implant type.
Figure 3.10. Leg length discrepancy comparing the length of the limb salvaged leg with the contra-lateral, with respect to implant type.
Figure 3.11. The degree of limp with respect to implant.

Figure 3.12. Pain scores with respect to those classed as survivors or failures.
Table 3.1. A comparison of the clinical grading scores of patients that were revised because of aseptic loosening within 12 months of the clinical assessment and those patients that were not known to have failed from aseptic loosening.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Survivors</th>
<th>Failures</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Biomedical Function</td>
<td>3.2±0.06</td>
<td>3.1±0.17</td>
<td>0.98</td>
</tr>
<tr>
<td>Engineering Pain</td>
<td>3.5±0.05</td>
<td>2.8±0.13</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Grading ROM</td>
<td>3.3±0.05</td>
<td>3.2±0.15</td>
<td>0.29</td>
</tr>
<tr>
<td>System Overall Score</td>
<td>10.1±0.11</td>
<td>9.0±0.34</td>
<td>0.012</td>
</tr>
<tr>
<td>ISOLS Function</td>
<td>3.9±0.02</td>
<td>3.9±0.05</td>
<td>0.18</td>
</tr>
<tr>
<td>Stability</td>
<td>3.5±0.05</td>
<td>3.2±0.18</td>
<td>0.46</td>
</tr>
<tr>
<td>Clinical Pain</td>
<td>3.5±0.04</td>
<td>2.8±0.13</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Grading ROM</td>
<td>3.2±0.06</td>
<td>2.9±0.17</td>
<td>0.26</td>
</tr>
<tr>
<td>System Deformity</td>
<td>3.4±0.06</td>
<td>3.4±0.16</td>
<td>0.72</td>
</tr>
<tr>
<td>Emotion</td>
<td>3.6±0.05</td>
<td>3.4±0.13</td>
<td>0.13</td>
</tr>
<tr>
<td>Overall Score</td>
<td>21.0±0.16</td>
<td>19.7±0.49</td>
<td>0.01</td>
</tr>
</tbody>
</table>

p derived from Wilcoxon Rank test
Chapter 4

Radiographic assessment of cemented intra-medullary stemmed endo-prostheses
4.1. Introduction

Radiographic analysis of endo-prosthetic replacements in conjunction with clinical assessment is essential for assessing the status of endo-prostheses in-situ. Sequential radiographic assessment permits the monitoring of adaptive bony remodelling and indicate to the clinician of when to revise for aseptic loosening.

Few radiographic studies of massive endo-prostheses have been undertaken. Inglis undertook one of the first radiographic studies and reviewed the radiographs of 19 Stanmore proximal femoral replacements that had been in situ for a minimum of 5 years (Inglis and Walker 1989). Franzén, reported the radiographic results of 11 cemented intra-medullary stemmed proximal femoral replacements and noted that 8 cases had pronounced bone atrophy (Franzén et al 1994). Two studies comparing porous collared and uncoated proximal tibial replacements (Ward et al 1993) and distal femoral replacements (Ward et al 1995), both, indicated that there was lower frequency of radiolucent lines associated with porous collared replacements. The radiographic findings of 62 distal femoral uncemented Kotz modular endo-prosthetic cases were reported by Capanna (Capanna et al 1994). No correlation between patient age, chemotherapy, percentage of bone removed or the diameter of the femoral stem and bone remodelling was identified. However, implants secured with six screws had poorer radiographic results than those fixed with 3 screws.

4.1.1. Aim

The aim of the study was to evaluate radiographs of the cemented intra-medullary stemmed endo-prosthetic replacements of the bone tumour study group (described in Chapter 2), using two evaluation methods.
4.1.2. Purpose

The purpose of the study was to -

- assess radiographs of the study group and record the bony adaptation associated with long stemmed cemented intra-medullary fixation of massive endo-prostheses
- correlate the bony adaptation with skeletal implant location, patient age and the percentage of bone resected
- develop a comprehensive radiographic grading system.

4.1.3. Radiographic grading system

The International Society on Limb Salvage (ISOLS) brought together a committee to establish radiographic evaluation methods for the assessment of the common forms of reconstructive limb salvage including endo-prosthetic replacements, allografting, and allograft/endo-prosthesis composites. The current limb salvage radiographic evaluation method was presented at the 1989 meeting (St Malo).

4.1.3.1. The ISOLS implant radiographic evaluation

The form evaluates 6 categories and for each there are four grades ranging from 'Excellent' to 'Poor'.

The 6 categories are -

1. Bone remodelling
2. Interface
3. Anchorage
4. Implant body problems
5. Implant articulation problems
6. Extracortical bone bridging (for implants where extracortical bridging was intended).

The 'Excellent' grade required that there had been no change from the discharge radiograph for all but one of the categories. The exception was the formation of extracortical bony bridging where intended resulted in an 'Excellent' grade.

This wide ranging evaluation form was considered too non-specific by BME staff. In addition, not all items were identifiable solely from the radiograph, for example stem motion (Anchorage). There were also inconsistencies in the measurements, for example, angulation of the stem/shaft of <5° (Interface), gives a 'Fair' result, but, in the both the 'Good' and 'Poor' categories there was no mention of angulation. Furthermore, in the absence of structures to permit bony ingrowth, the ISOLS evaluation system regarded the presence of 'hypertrophy' as a negative feature and thus reduced the grade from 'Excellent' to 'Good'. It was considered that some of the shortfalls could be addressed in a modification to the present ISOLS system.

4.1.3.2. The BME radiographic score

A new system of grading was devised for two principal reasons, to-

1. address the shortfalls, in the ISOLS system
2. provide data for each predetermined parameter in each quadrant, as defined in Figure 4.1.

The criteria identified for the new radiographic scoring system were -

- each bony remodelling parameter present was scored
- all parameters of each quadrant were scored
- only quantitative bony remodelling parameters to be assessed
- raw data was for use by the new BME and ISOLS radiographic evaluation systems
• unambiguous in the identification and extent of the parameter
• all features were identifiable from radiographs in isolation of clinical data
• the system was rapid, for use in the clinical environment
• lengths of the parameters measured to be graded in proportion to the intra-medullary stem length.

This qualitative grading system devised distinguished between adverse and constructive bony remodelling. The bony remodelling parameters are diagrammatically represented in Figure 4.2 and summarised in Appendix E. The parameter scores were calculated and the radiographs graded into 1 of 8 categories ranging from Excellent to Very Poor.

4.1.3.3. Constructive

New bone formation and an increased shaft diameter were classed as constructive features.

4.1.3.4. Adverse

Decreased shaft diameter, radiolucent lines and plateau gaps were classed as adverse remodelling features.

4.1.3.5. Scoring

The constructive and adverse parameters were scored in accordance with system described in Tables 4.1.

Of the 8 grades, 'Excellent' and 'Improved' were only possible when there was no adverse bony remodelling. When no quantifiable difference between the radiograph being assessed and the discharge radiograph a grade of 'No change' was given. There were 5 grades of adverse bony remodelling ranging from 'Very Good' to 'Very Poor'.

146
A computer programme was written for the database that calculated automatically the ISOLS and BME grades from the radiographic data entered. A flow diagram of the BME system is shown in Figure 4.3.

4.2. Methodology

To perform a radiographic assessment the following selection criteria were used -

- only cases of lower limb bone tumour cases that had been selected for study in Chapter 2
- both the frontal and lateral radiograph taken on the same date were present
- minimum implant duration of 6 months
- all the intra-medullary stem and cement mantle were clearly visible in both views
- no cases with porous collars or hydroxyapatite coating
- no distal femoral or proximal tibial replacement case with a rotating hinge
- no bifurcated or 'rhino-horn' shaped intra-medullary stemmed cases

All radiographs were graded using both systems. The ISOLS system was primarily to permit comparison of results with other studies. The more comprehensive BME grading system in addition calculated scores for all qualitative bony remodelling parameters for each quadrant. Summating the quadrant scores a total score for each parameter could be obtained and was used to compare between implant types, patient age groups, resection groups and quadrants.
4.2.1. Data collection

Measurements of each parameter were taken directly from the radiographs using a ruler accounting for radiographic magnification. Each parameter was drawn on the standard diagram in the appropriate location recording the abbreviated code, the length, and breadth where required and finally the zone or zones it had involved. The parameters measured were -

- New bone formation (NBF, pedicle), (length, breadth)
- Pedicle gap (PGap), (width)
- Increased shaft diameter (ISD), (length, width, zone)
- Reduced shaft diameter (RSD), (length, width, zone)
- Radiolucent lines (RLL), (length, width, zone)
- Reduced bone density (RBD), (zone)
- Plateau gap (GAP), (height)
- Plateau cement (CEM), (height)

Parameters are shown in Figure 4.2 and summarised in Appendix E.

4.2.2. Radiographic zones

Pre-defined zones based upon the Gruen zones (Gruen et al 1979) were used to locate the radiographic parameters. Each quadrant was divided into 3 regions (plateau, mid-stem and tip) represented by 10 zones (Figure 4.4).

4.3. Results

4.3.1. Radiographic study group

The study group comprised of 367 cases. The average duration between the limb salvage procedure and radiographic assessment was 49.7±2.2 months (range = 6 to 275 months). The proximal femoral replacement group had the
longest average follow-up (69.9±4.6 months, n=82), followed by distal femoral cases (47.7±3.0 months, n=189) and the proximal tibial replacements the shortest (36.4±4.2, n=96). There was significant difference between the implant types with respect to duration (p<0.01).

4.3.1.1. Grades

**Biomedical Engineering Grading System**

The majority of radiographs were graded 'Very Good', 'Good' or 'Fair', but few were graded 'No Change' or better (Figure 4.5).

**Patient age.** Young patients (≤16 years) with proximal femoral replacements had significantly poorer radiographs than older patients (>16 years) (p<0.01). However, patient age did not significantly effect the radiographic grades of the distal femoral (p=0.17) or the proximal tibial replacements (p=0.22).

**Bone resected.** The percentage of bone resected did not have a significant effect on the proportional distribution of radiographic grades in any of the 3 implant groups (PF p=0.17, DF p=0.67 and PT p=0.67).

**ISOLS**

Overall, 6% of radiographs were graded 'Excellent', whilst, the majority were graded 'Fair' or 'Poor' (Figure 4.6). Radiograph grades of the distal femoral replacements reflected that of the overall distribution, while proximal femoral cases had a higher proportion graded 'Poor' and with proximal tibial cases a higher proportion were graded 'Excellent'.
4.3.2. BME Grading system parameters

4.3.2.1. Constructive

The constructive parameters (NBF and ISD), were most commonly associated with distal femoral replacements and least frequently with the proximal tibial replacements (Figure 4.7). Details of the NBF is presented later (Chapter 7).

Briefly, NBF was present in 87.8% of distal femoral, 70.7% of proximal femoral and 59.4% of proximal tibial replacements. In all 3 replacement types NBF was most commonly observed in the medial quadrant.

4.3.2.2. Increased shaft diameter

Increased shaft diameter, similar to NBF, was most frequently observed on the medial aspect of all three implant locations. (DF=66.1%, PF=48.8% and PT=29.2%). ISD was least likely to occur in the anterior quadrant of distal femorals (37.6%), the lateral quadrant of proximal femorals (14.6%) and the posterior and lateral quadrants of proximal tibial replacements (both 19.8%).

Again, the distal femoral replacement most frequently had ISD in all 4 quadrants (22.8%) but the number of quadrants the ISD occurred in was similar in all 5 categories. When the ISD did occur in the proximal femoral and proximal tibial replacements it was mostly identified in either 1 or 2 quadrants.

Patient age

Increased shaft diameter (ISD) was commonly observed in all age groups of patients with femoral replacements, but ISD was not observed in radiographs of elderly patients (>60 years) with proximal tibial replacements (Figure 4.8). In femoral replacements groups there was little difference between the age groups with respect to ISD score. In the proximal tibial cases with increasing age there was a decrease in the ISD score.
Proximal femoral. With respect to quadrant, ISD was commonest and most extensive in the medial quadrant of young patients. Young patients, commonly had ISD in 1 quadrant (40.0%) or it was not present. A small percentage (4.8%) of middle-aged patients (>25 ≤60 years) had ISD in all quadrants but for the majority of patients it was in either 1 or 2 quadrants.

Distal femoral. In all age groups, ISD was most extensive and frequently observed in the medial quadrant and least extensive and infrequently observed in the anterior quadrant. Juvenile, young adult and middle-aged patients had ISD frequently in 3 or all quadrants, whereas, with elderly patients, few (12.5%) had ISD in 3 or all quadrants.

Proximal tibial. ISD was most common and most extensive in younger patients and was not observed in the radiographs of elderly patients (n=5). ISD in the medial and anterior quadrants occurred most frequently in the younger patients but in the middle-aged patients there was a similar occurrence and extent of the ISD between all quadrants. In all three age groups ISD was observed in all quadrants but was restricted predominantly to 1 or 2 quadrants.

Resection

Overall, the percentage of bone resected had little effect on the presence or extent of ISD with distal femoral replacements, but with increasing bone resected, ISD associated with proximal femoral replacements was less frequent and less extensive. ISD associated with proximal tibial replacements was most common when between 40 and 60% of the bone had been resected but it was not as well developed as those cases with <40% resections (Figure 4.9).

Proximal femoral. Cases with short resections had ISD predominately associated with the medial and posterior quadrants (Figure 4.10). With increasing percentage of bone resected the proportion of cases with ISD in the
medial and posterior decreased whilst in the anterior and lateral quadrants it increased. ISD occurred in the posterior quadrant in 53% of cases with 40-60% of bone resected, but only 13% of those with >60% resections. In all resection groups, the majority of cases had ISD restricted to 1 or 2 quadrants.

**Distal femoral.** In all quadrants there was little difference between resection groups with respect to the presence or extent of ISD. In all groups ISD was commonly observed medially (Figure 4.10). With increasing percentage of bone resected, there was a higher proportion of cases with ISD in all quadrants.

**Proximal tibial.** With cases of short resection (40%), ISD was most commonly observed anteriorly and to a lesser extent laterally (Figure 4.10). Cases with between 40 and 60% resections, predominantly had ISD medially and the anterior and posterior quadrants had the same percentage of cases with ISD. ISD was not observed in cases with >60% shaft resected. When ISD occurred, it was most frequently observed in one or two quadrants irrespective of the percentage of bone resected.

**The location of the ISD**

Increased shaft diameter was predominantly associated with the prosthesis shoulder (Figure 4.11). ISD did occur in the region of the stem tip, but was rarely restricted to mid-section of the stem. Only in proximal femoral cases did the increased region of the shaft extend along the complete length of the stem.

**4.3.2.3. Adverse bony remodelling parameters**

With the exception of plateau gaps, radiolucent lines (RLL) were the most commonly occurring adverse bony remodelling feature associated with distal femoral and proximal tibial replacements (Figure 4.12). However, with proximal femoral replacements a reduction in shaft diameter (RSD) was most frequently observed.
4.3.2.4. Radiolucent lines

Radiolucent lines occurred predominantly between the cement mantle encasing the intra-medullary stem and the shaft bone.

The proximal femoral replacements had the lowest percentage of cases with RLLs (42.8%), but, 8.5% of radiographs had a total score of 17 or greater (mean score =3.4±0.60, maximum =25) (Figure 4.13). Distal femoral replacement cases, had on average the highest RLL scores (3.7±0.40, maximum =24). Proximal tibial cases had the highest percentage of cases with RLLs (60.4%), but, the majority had a total score of less than 5 (mean score =3.2±0.55, maximum =24).

**Distal femoral.** RLLs occurred in all quadrants with the highest incidence laterally (37.0%) and the lowest posteriorly (30.2%). RLLs were most commonly present in either 2 or 4 quadrants (14.8% and 13.8% respectively) compared to 1 or 3 (12.2% and 11.1% respectively). Of those cases that had RLLs present in only 2 quadrants, there was a greater incidence of the RLLs in opposing pairs (A&P or M&L, average =26.8%) compared to non-opposing pairs (A&M, A&L, P&M, or P&L, average =11.6%).

With respect to the quadrant RLL scores the highest were laterally (1.12) and the lowest posteriorly (0.70).

**Proximal femoral.** RLLs were generally evenly distributed between the quadrants with a slightly higher percentage on the anterior quadrant (31.7%), followed by the lateral quadrant (29.3%). If RLLs were present, they were most frequently observed in 3 or all quadrants (14.8% and 13.8% respectively). The posterior quadrant (0.90) followed by the anterior (0.89) had the highest quadrant RLL scores and the medial the lowest score.

**Proximal tibial.** RLLs were most commonly observed on the lateral aspect (39.6%) and least on the anterior (28.1%). Of those cases with RLLs present, they were most commonly present in either 1 quadrant (22.9%) or in all
quadrants (14.6%). With the exception of the anterior quadrant RLL score (0.67), the scores were remarkable similar (lateral =0.84, posterior =0.83 and medial =0.82).

**Patient age**

**Proximal femoral.** The age of the patient had no significant effect on the proportion of RLLs present (p=0.84) or the total RLL score (p=0.83). However, there was a slightly lower proportion of cases with RLLs in the young adult age group (Figure 4.14).

Similarly, there was no significant difference between age groups for any of the quadrants with respect to the proportion of cases with RLLs present, or the total RLL score. Middle aged patients had higher RLL scores in all quadrants compared to younger patients (Figure 4.15). Of the 4 elderly patients, only one had 1 radiolucent line, present in the lateral quadrant.

**Distal femoral.** Patient age had no significant effect on the frequency of RLLs (p=0.33) or the total RLL score (p=0.15) (Figure 4.14). Young patients (≤16 years) had the highest proportion of cases with RLLs present (60.0%) and the most extensive (total RLL score =6.). Elderly patients had the lowest RLL frequency (39%) and the least extensive RLLs (total RLL score =3.2).

The presence and score were dissimilar between the quadrants in all age groups (Figure 4.15). In the younger two age groups, the RLL scores of the anterior and posterior quadrants were lower than those of the medial and lateral quadrants. The middle aged and elderly patients had the lowest RLL scores anteriorly and the highest laterally. There were significantly differences between the four age groups with respect to the RLL score in the anterior and lateral quadrants (anterior p=0.01 and lateral p=0.03).
Proximal tibial. Patient age did not have a significant effect on the severity of RLL (p=0.29) (Figure 4.14). All elderly patients (n=5) had RLLs present and the most extensive RLLs, however the number of cases was small.

Juvenile patients had the highest RLL scores in the posterior and lateral quadrants in comparison to the young adult and middle aged patients. RLLs were most frequently observed in the posterior quadrant (43%) in this age group (≤16 years). Interestingly, the young adult patients had the lowest RLL scores in each quadrant compared to the other age groups (Figure 4.15), the most frequent observed and severest were in the medial (0.77, 42%) and lateral quadrants (0.62, 39%). RLLs were most commonly observed in the lateral quadrant (46%) and were also the most severe (1.0).

Percentage of bone resected

Proximal femoral. The level of resection had a significant effect on the proportion of cases with the frequency and total score of RLLs (Figure 4.16). With an increasing percentage of bone resected, the total RLL score decreased significantly (p<0.01). Patients with short proximal femoral resections (<40%), had frequently, extensive RLLs most commonly on the anterior and posterior quadrants (Figure 4.17). Cases with between 40%-60% or >60% resections had similar proportion of cases with RLLs, but those with >60% resections had significantly less extensive RLLs. In all quadrants there was a significant difference (p<0.05) between the 3 resection groups with respect to the proportion of cases with RLLs and quadrant RLL score.

Distal femoral. There was a decrease in the proportion of cases with RLL present with increasing percentage of bone resected. However, the total RLL score remained remarkably similar for all 3 resection groups (Figure 4.16).

In the <40% resection group, the anterior quadrant had the lowest percentage of RLLs present (35.1%) and the lateral the highest (51.4%), (Figure 4.17). In the
40-60% resection group the distribution between the quadrants was similar, ranging from 27.7% (medial) to 32.8% (lateral), and again in those cases with >60% the lateral quadrant had the highest percentage of RLLs (36.4%) but the posterior the lowest (15.2%). The anterior quadrant had a similar percentage of cases with RLLs present irrespective of the percentage of bone resected (p=0.84), but in the posterior quadrant the higher the percentage of bone resected the lower the percentage of cases with RLLs (p=0.08). The quadrant RLLs scores had a similar distribution pattern to the frequency of RLLs.

**Proximal tibial.** The level of resection had little effect on the overall presence of the RLLs. Similarly, there was no significant difference between the resection groups with respect to the total RLL score, but those with between 40-60% resections had on average lower scores (Figure 4.16).

Between quadrants, there were marked differences between the three resection groups, the most noticeable of which was the lateral (Figure 4.17). Of those cases with short resection, 50% had RLLs in the lateral quadrant compared to 12.5% of cases with >60% resection. Although there was a marked difference in the proportion of cases with RLLs in the lateral quadrant, the severity of the RLLs were relatively similar. Medial and lateral RLL scores were highest in the 40-60% resection group, whereas the anterior RLL scores were on average the lowest compared to the other resection groups. Lateral scores were high and anterior scores low in the 40-60% resection group but vice-versa in the >60% resection group.

**The location of the RLL**

In all 3 implant groups, RLLs were predominantly associated with the prosthesis plateau (Figure 4.18). Nearly 12% of distal femoral cases had RLLs associated with the tip of the IM stem, but in contrast, none of the proximal femoral cases did. In the proximal tibial group, no case had RLLs restricted to the mid section of the IM stem but some did have RLLs present at the stem tip.
With increasing distal femoral resection, there was a decrease in the percentage of cases with RLLs adjacent to the prosthesis plateau, the stem tip or along the complete length of the IM stem (Figure 4.19), but there was an increase in RLLs restricted to the mid-section of the stem. The reverse was observed with proximal femoral cases, with increasing percentage of bone resected there was increase in the percentage of cases with RLLs at the plateau and along the complete length of the IM stem, but there was decrease in those restricted to the mid-section of the stem. With increasing percentage of tibial shaft resected, there was a decrease in the percentage of cases with RLLs associated with the prosthesis plateau, but an increase in RLLs at the stem tip or along the complete length of the IM stem.

In the distal femoral group, the RLLs associated with the plateau were slightly more frequently observed on the medial and lateral quadrants (both 23.3%) compared to the posterior and anterior (20.1% and 19.3% respectively). Similarly in the proximal femoral replacement group in the mid-section of the stem on the lateral quadrant there was a relatively high percentage of cases with RLLs (6.7%) compared to the other quadrants. In the proximal tibial group, there was a little difference between the quadrants with respect to the location of the RLLs.

**Duration**

With increasing implant duration there was a general increase in the total RLL score in both the distal femoral and proximal tibial groups. In contrast, the proximal femoral total RLL score rose to over 9 in the fifth and sixth years of implant duration and declined dramatically over the following years (Figure 4.20). It is interesting to note that in all implant groups, the proportion of cases with RLLs rose rapidly until over 60% of cases had RLLs by the completion of the fourth year of implant duration, but then the proportion of cases with RLLs fell over the following two years before rising again.
Location of RLL along the length of the IM stem

In the first year, all RLLs identified in all quadrants of the three implant types were associated with the plateau, with the exception of 1 proximal femoral case which had a RLL extending continuously along the length of the IM stem/cement mantle in all quadrants. In the second year, the plateau associated RLLs became more numerous and a small proportion of cases had RLLs appearing at other locations (proximal tibial associated with the tip and the distal femoral restricted to the mid section of the intra-medullary stem). In later years, RLLs appeared at other locations. In both the proximal femoral and the proximal tibial groups the number of cases at each time interval were small and the uncommon nature of RLLs in the proximal femoral has added unpredictability of the distribution.

4.3.2.5. Reduced shaft diameter (RSD)

Reduction of the femoral shaft diameter was predominant on the lateral and to a lesser extent the anterior aspects. Of those cases with RSD, it was normal that it was present in 1 quadrant (60.8%), and rarely observed in all quadrants (6.3%). RSD of the tibia was predominantly restricted to the medial and lateral quadrants and predominantly restricted to 1 quadrant (85.7%).

Patient age

RSD occurred most frequently with young adult (80%) and middle aged patients (52%) with proximal femoral replacements, however, no elderly patients had RSD present. In contrast, RSD was more commonly associated with elderly patients with distal femoral replacements (39%) and least frequently in young adult patients (8%). RSD was observed in too few proximal tibial radiographs to determine if patient age had an effect on its presence, but young adult and middle aged patients had the lowest proportion of cases exhibiting RSD (8% and 7% respectively).
Bone resection

With both femoral implants, the more proximal the femoral resection the higher the proportion of cases with RSD in the anterior quadrant and lower the proportion in the posterior quadrant. With respect to proximal femoral cases, with increasing bone resection there was a higher proportion of cases with RSD in the medial and lateral quadrants (<40% =9%, 40-60% =17.6%, >60%=20% and <40% =20%, 40-60% =38.2%, >60%=45.5% respectively). In the distal femoral group the level of resection had little effect on the presence of RSD on the medial or lateral quadrants. RSD was present in too few proximal tibial radiographs to determine if the level of resection had an effect on its presence.

Position along the length of the IM stem

In all quadrants of femoral cases, the majority of RSD was identified adjacent to the prosthesis plateau. However, in distal femorals there were a small number of cases where the RSD in all quadrants was restricted to the mid-section or tip region of the stem. In proximal femoral cases, RSD was present only on the lateral aspect in the mid-section of the IM stem and on the posterior aspect associate with the tip region of the IM stem. Within the proximal tibial group, RSD occurred most frequently in the lateral quadrant adjacent to the plateau.

4.3.2.6. Cavitation

Cavitation was most commonly associated with the proximal tibial replacements (14.6%) and least with distal femoral cases (6.9%). Cavitation was evenly distributed between the quadrants in the distal femoral group and was most commonly restricted to the mid-section of the IM stem. In the proximal femoral group the distribution of the cavitation was again evenly distributed between the quadrants but was generally associated with the plateau. In the proximal tibial group, there were higher frequencies of cavitation on the medial
and lateral quadrants compared to that of the anterior and posterior and was not restricted to any specific location along the IM stem.

Due to the infrequent occurrence of this parameter, no age or resection sub-groupings were made.

4.3.2.7. Reduced bone density (RBD)

Reduced bone density associated with proximal femoral replacement cases was distributed evenly between the quadrants and was most frequently associated with the prosthesis plateau. RBD was least likely to occur in the medial quadrant of distal femoral cases and was distributed evenly between the remaining quadrants. Generally, it was not restricted to any specific region along the length of the IM stem with the exception that it did not occur on the medial aspect at the tip of the IM stem. With respect to the percentage of femur resected, 11.8% of distal femoral cases with between 40-60% resected had RBD and significantly lower percentages in the other two resection groups. In contrast, only 2.9% of proximal femoral cases with 40-60% resections had RBD whereas 13.3% of those with >60% resections had RBD.

Reduced bone density in the proximal tibial group was most commonly observed on the medial and lateral quadrants. In both of these quadrants the RBD was moderately more frequently associated with the plateau region. In no quadrants was RBD present along the complete length of the stem. The level of resection had little effect on the percentage of cases with RBD.

After the first year, in all implant groups there was overall a marginal increase in the percentage of cases with RBD.

4.3.2.8. Plateau gap

Frequently a layer of acrylic bone cement and a radiolucent line were evident between the prosthesis plateau and the resected bone. With respect to the
quadrants, plateau gaps were most frequent and of greatest height in the lateral quadrants of all implant groups. In the distal femoral group, the gaps in the anterior were the least numerous and also the narrowest, however, in the proximal femoral group, posterior gaps were least frequent and those medially the narrowest. The maximum height measured with a distal femoral case was 9 mm (medial quadrant), but with proximal femoral cases the largest gaps were in excess of 20 mm which were present in all but the medial quadrant.

Proximal tibial plateau gaps were most frequently observed and of greatest height laterally, anteriorly the least frequent and posteriorly narrowest (Figure 4.21). The majority of all cases had plateau gaps present in all 4 quadrants (DF=47.1%, PF=35.4%, PT=44.8%).

The percentage of bone resected had an effect on proximal femoral replacements only. The height of the lateral plateau gap decreased with increasing percentage of femoral shaft resected. In all other quadrants, patients with 40-60% of the proximal femur resected had the highest plateau gaps. Furthermore, the majority of patients with <60% resections had plateau gaps in all quadrants compared to patients with >60% who had plateau gaps present in 2 (23%) or 3 (18%) quadrants.

Patient age had little effect on the frequency or height of the plateau gap in any of the implant groups.

**Duration**

After the first year of implant duration there was marginal change in the plateau gap height in any quadrants of the distal femoral and proximal tibial replacements. However, there was a slight increase in plateau gap height in the anterior quadrant of the proximal femoral group after 5 years of implant duration.
4.3.3. Indicators of aseptic loosening

To investigate if any radiographic parameter correlated with aseptic loosening, the 367 cases were divided into two groups, namely -

- failures, those that failed of aseptic loosening (n=62). However, 38 cases failed more than 12 months after the radiographic assessment and were therefore excluded.

- survivors (n=305).

Radiographs of endo-prostheses that failed of aseptic loosening within 12 months of the assessed radiographs, had a similar increase in shaft diameter, similar plateau gap heights and less reduction of shaft diameter, compared to the 'survivors' (Table 4.2). However, radiolucent line scores and pedicle, were significantly more extensive in those that failed.

As expected the majority of failed cases had RLLs (70.8%) leading to a higher percentage of cases graded 'Very Poor' (25.0%) or 'Poor' (16.7%), compared to the survivors (RLLs =52.0%, Very Poor =8.3%, Poor =6.6%) (Figure 4.22).

Five cases that failed did not have any observable radiolucent lines, of which two cases were revised within 3 months of the radiographic assessment. The implant duration of the five cases ranged from 24 months to 105 months.

4.3.4. Correlation between clinical and radiographic assessments

The relationship between clinical and radiographic assessments was investigated. Only cases that had both radiographic and a clinical assessments within 10 months of each other were selected. The majority of cases had both assessments on the same date (66%). The BME radiographic scoring was recategorised using the following criteria - Excellent, Improved and No Change =4, Very Good =3, Good and Fair =2, and Poor and Very Poor =1.
The results highlighted that in all clinical categories there was no correlation with radiographic grade (Table 4.3). Unexpectedly there was no correlation with the pain grading, but, no case with an Excellent radiographic score had a Fair or Poor pain score. However, 17% of cases had either no or mild pain but a Poor radiograph score. As a result of the inhomogeneity often identified between the 3 implant groups, the analysis was repeated with distal femoral replacement cases only (n=66). Although, the numbers were smaller there were more identifiable trends in a number of categories (Emotion, Instability and BME Function). In these cases the trends were similar in that there was a lower clinical score when there was a lower radiographic score, however, in no category was this significant.

4.3.4.1 Radiolucent line and clinical grade correlation

A further examination was performed to identify if there was a correlation between radiolucent line score and clinical grade. (distal femoral cases only). Unfortunately, too few cases had RLL grades, Good (n=5) or Fair (n=7), making the Chi² test invalid. However, the Pain category is worthy of mention. In both the Excellent and Poor graded radiograph groups, the major of cases were categorised as having no or mild pain, furthermore, 6 of the 36 of those radiographs graded Excellent had moderate or severe pain and only 1 case of the 16 radiographic cases graded Poor had moderate pain.

4.4. Discussion

This review of 367 radiographs of lower limb massive uncoated cemented intramedullary stemmed endo-prostheses has been one of the largest studies undertaken and which has provided data with which new design can be compared. In addition, the adaptive bony remodelling data has reflected the adaptation to the new biomechanical environment.
This study of radiographs of implants in-situ between 6 and 275 months, highlighted that bony remodelling occurred more frequently and extensively with distal femoral replacements (Figure 4.5) than proximal femoral or proximal tibial replacements. Generally there was an increase in bone stock (pedicle and increased shaft diameter) around distal femoral replacements and a greater extent of bone loss (decreased shaft diameter) associated with proximal femoral and proximal tibial replacements.

The radiographic parameters examined can be sub-divided into two -

- those resulting from bony adaptation responding to the modified loading environment
- the formation of radiolucent lines that occurred at the cement/bone interface and the prosthesis plateau.

Wright studying the strain in loaded cadaveric femora showed that shaft bone was in compression medially and posteriorly, and in tension laterally and anteriorly (Wright and Meswania 1984). In this radiographic study an increase in the femoral shaft diameter was predominantly medially and posteriorly, and a reduction in femoral shaft diameter occurred anteriorly and laterally. Furthermore, the more proximal the femoral resection the greater the frequency of increased shaft medially and reduction in the shaft laterally. As discussed in the Chapter 2, the offset between the line of force and the longitudinal axis of the femoral replacement/femur would lead to greater compressive stresses medially and tension laterally. In accordance with Wolff's law this would lead to increased shaft diameter and bone density on the medial aspect and reduction in the shaft width and reduced bone density laterally.

Telemetric studies of proximal femoral replacements identified that over 70% of the load was being transmitted in the tip region of the stem after an in-situ period 65 weeks (Taylor 1993). Therefore little load would be transmitted at the
plateau leading to bone resorption adjacent to prosthesis plateau. With the majority of load being transmitted at the IM stem tip, a greater offset and bending moment would exist with a distal femoral compared to proximal femoral replacement (Figure 2.15). The more extensive bony adaptation associated with distal femoral replacements that would be predicted was evident (Figure 4.23).

Using this hypothesis, bony remodelling associated with proximal tibial replacement would be generally evenly distributed between the quadrants and the resection level would have little effect. Indeed, the results confirm this hypothesis.

The forces that resulted in adaptive bone remodelling are linked with radiolucent lines development. Radiolucent lines are an indicator of the process of aseptic loosening, with the formation of RLLs at the bone/cement interface decoupling the mechanical fixation. RLLs were most commonly associated with proximal tibial replacement but these were the least extensive. The most extensive RLLs were associated with distal femoral replacements. RLLs associated with distal femoral replacements were most common and extensive laterally and least common and least extensive posteriorly. This leads to the hypothesis that the bending moment described above, contributes to the formation of the RLLs. Therefore, the more proximal the resection, the greater the femoral head offset leading to higher interfacial stresses. It was identified that short proximal femoral resections had a greater frequency of RLLs. Furthermore, the distribution of cancellous bone also had an effect. If the RLL formation was solely a result of the offset distance then distal femoral replacement cases with extensive resections (<60%) would be predicted to have more RLLs than those with shorter resections. However, there was no difference between the resection groups in terms of the percentage of cases with RLLs or the RLL score. Distal femoral replacement cases with >60% resection would have the proximal region of IM stem secured into cement that was
interdigitated into cancellous bone. The mechanical interlock of the cement into the cancellous bone would be able to resist greater stresses. In contrast, the IM stem of short proximal femoral replacements (<40%) would be located in a region lacking cancellous bone for cement interdigitation, resulting in interface decoupling and the development of RLLs.

The vertical orientation of the proximal tibial replacements not exposed to bending moments would however experience rotation around the longitudinal axis of the implant/tibia. The inability to resist rotation would be greatest in the mid-shaft, corresponding to the lack of cancellous bone and frequent occurrence of RLLs. Fewer RLLs were present where adequate cement interdigitation could be achieved in the cancellous bone proximally and to a lesser extent in the distal tibia.

Predominantly, RLLs formed at the plateau and extended along the length of the cement/bone interface. Ward considered the formation of RLLs to be as a result of the ingress of wear particles causing osteolysis (Ward et al 1993). However, the lack of debris identified in retrieved Stanmore massive replacements would suggest that wear particle induced osteolysis was not a significant factor in the formation of RLLs. In addition, if wear particle induced osteolysis was a principal factor in loosening, then it could be hypothesised that cases with extensive resections, few would have RLLs due to the distance from the replaced joint where the generation of wear debris would occur. These results do not support this hypothesis. Adjacent to the plateau the bending and interfacial shear stresses would be predicted to be the highest and would decrease towards the stem tip and this reflects the observed RLLs.

The plateau gap was evident in the large majority of cases within a year of implantation. This feature did not appear to have a direct effect on loosening. The plateau gaps of the distal femoral were frequently well defined with a distinct demarcation between the bone and fibrous tissue and were rarely
greater than 3 mm in height. In contrast, those associated with proximal femoral and to a lesser extent proximal tibial replacements were greater in height and had a more gradual change from the bone to the fibrous tissue layer. With the proximal femoral and proximal tibial replacements the formation of the plateau gap fitted the stress-shielding hypothesis. In addition, reduction in the shaft diameter and bone density adjacent to the plateau was more common in these two implant groups. The shape and consistency of the plateau gap of distal femoral replacements linked with the rare occurrence of reduction in shaft diameter and bone density would lead to assumption that there was less stress-shielding adjacent to the plateau and there was an additional mechanism of plateau gap formation. Micro-motion and rotation at the interface have not been measured but may factor in the formation of the plateau gap.

Patient age had significant effects on both the adaptive bone remodelling and the development of radiolucent lines in the distal femoral group, but not in either the proximal femoral or tibial groups. Cortical expansion due to bone growth in the skeletally immature cases has been described by Blunn (Blunn and Wait 1991). Centrifugal growth of the cortex away from the cement mantle leading to metaphysealisation and weakened bridging results in the early formation of radiolucent lines. Young patients with distal femoral replacement, had significantly more frequent and extensive radiolucent lines. In addition, they had increased activity levels leading to high and more prolonged interfacial stresses than that expected for elderly patients.

The lack of correlation between clinical assessments parameters have been discussed in Chapter 3. In addition, there was a general lack of correlation between radiographic remodelling features and those that were revised due to aseptic loosening, with the exception of RLLs.
Figure 4.1. A diagrammatic transverse section through a bone, with the quadrants defined.
Figure 4.2. A diagrammatic representation of bony remodelling features identifiable on radiographs.
Figure 4.3. A diagrammatic representation of the BME radiographic evaluation program to score radiographs.
Figure 4.4. The radiographic zones.
Figure 4.5. The BME radiographic grades of 367 cemented intra-medullary stemmed endo-prostheses.

Figure 4.6. The ISOLS radiographic grades with respect to the implant type.
Figure 4.7. The percentage of radiographs showing constructive bony remodelling.
Figure 4.8. The frequency (%) and score of increased shaft diameter with respect to implant type and age of the patient. (p derived from Kruskal-Wallis test).
Figure 4.9. The frequency (%) and score (±S.E.) of increased shaft diameter with respect to implant type and the percentage of bone resected. (p derived from Kruskal-Wallis test)
Figure 4.10. The frequency and score of increased shaft diameter for each quadrant with respect to the percentage of bone resected and implant.
Figure 4.11. The percentage of cases with increased shaft diameter with respect to the location of the radiolucent line.
Figure 4.12. The percentage of radiographs showing adverse bony remodelling features. (RLL = radiolucent lines, RSD = reduced shaft diameter, PGap = plateau gap, RBD = reduced bone density, Cav = cavitation).
Figure 4.13. Distribution of the total RLL scores with respect to implant. There was no significant difference between the 3 implant groups (p=0.19). (The total score = sum of quadrant scores).
Figure 4.14. The frequency (%) and score (±S.E.) of radiolucent lines with respect to age of the patient and implant. (p derived from Kruskal-Wallis test).
Figure 4.15. The frequency (%) and score of radiolucent lines for each quadrant with respect to patient age and implant. (Note the elderly age groups of the proximal femoral and proximal tibial replacements have been omitted due to insufficient numbers).
Figure 4.16. The frequency and score (±S.E.) of radiolucent lines with respect to the percentage of bone resected and implant. (p derived from Kruskal-Wallis test).
Figure 4.17. The frequency (%) and score of radiolucent lines for each quadrant with respect to the percentage of bone resected and implant.
Figure 4.18. The percentage of cases with radiolucent lines with respect to the location of the radiolucent line and implant.
Figure 4.19. The frequency (%) of RLLs along the stem length with respect to the percentage of bone resected and implant.
Figure 4.20. The frequency and score of radiolucent lines with respect to duration and implant.
Figure 4.21. The frequency and height (±S.E.) of the plateau gap with respect to quadrant and implant.
Figure 4.22. Radiolucent line scores with respect to those that failed and those that did not.
Figure 4.23. The frequency of increased and decreased shaft diameter along the stem length for each quadrant with respect to the percentage of bone resected and implant.
Plate 4.1. A typical radiograph of a distal femoral replacement (implant duration = 14 months). Note the extensive medial pedicle, the small lateral pedicle and the shape of the plateau gaps.
Plate 4.2. A radiograph of a loosened distal femoral replacement, showing radiolucent lines between the cement mantle and bone. (Implant duration = 21 months). Note the extensive RLLs on both the medial and lateral aspects. However, the RLLs do not penetrate the proximal cement mass.
Table 4.1. The scoring system for the radiographic parameters

<table>
<thead>
<tr>
<th>Percentage length of IM stem</th>
<th>&lt; 25%</th>
<th>&lt; 50%</th>
<th>&lt; 75%</th>
<th>&lt; 100%</th>
<th>≥ 100%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Score</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Width (mm)</th>
<th>≤ 1</th>
<th>≤ 2</th>
<th>&gt; 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Score</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Plateau gap height (mm)</th>
<th>≤ 1</th>
<th>≤ 2</th>
<th>≤ 5</th>
<th>&gt; 5</th>
</tr>
</thead>
<tbody>
<tr>
<td>Score</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Pedicle area (mm²)</th>
<th>≤ 40</th>
<th>&gt; 40</th>
</tr>
</thead>
<tbody>
<tr>
<td>Score</td>
<td>0</td>
<td>1</td>
</tr>
</tbody>
</table>
Table 4.2. A comparison of the radiographic parameters scores between those cased that failed and those that did not.

<table>
<thead>
<tr>
<th>Radiographic parameter</th>
<th>Failures (n=24)</th>
<th>Survivors (n=305)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pedicle</td>
<td>9.4±1.04</td>
<td>6.1±0.40</td>
<td>0.15</td>
</tr>
<tr>
<td>Increased shaft diameter</td>
<td>3.5±0.76</td>
<td>3.5±0.22</td>
<td>0.92</td>
</tr>
<tr>
<td>Radiolucent lines</td>
<td>5.5±1.05</td>
<td>3.1±0.30</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Reduced shaft diameter</td>
<td>0.2±0.43</td>
<td>0.9±0.12</td>
<td>0.10</td>
</tr>
<tr>
<td>Plateau gap</td>
<td>2.7±0.55</td>
<td>2.1±0.16</td>
<td>0.73</td>
</tr>
<tr>
<td>BME radiographic score</td>
<td>2.8±0.35</td>
<td>4.0±0.10</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>ISOLS radiographic score</td>
<td>1.8±0.18</td>
<td>2.1±0.05</td>
<td>0.03</td>
</tr>
</tbody>
</table>

p derived from Wilcoxon Rank test

Table 4.3. The probability of a correlation between clinical grading parameters and radiographic score.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>All implant types</th>
<th>Distal femoral</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Number</td>
<td>p</td>
<td>Number</td>
</tr>
<tr>
<td>ISOLS Function</td>
<td>129</td>
<td>0.53</td>
<td>65</td>
</tr>
<tr>
<td>ISOLS Instability</td>
<td>115</td>
<td>0.63</td>
<td>57</td>
</tr>
<tr>
<td>ISOLS Pain</td>
<td>125</td>
<td>0.38</td>
<td>64</td>
</tr>
<tr>
<td>ISOLS ROM</td>
<td>123</td>
<td>0.68</td>
<td>64</td>
</tr>
<tr>
<td>ISOLS Emotion</td>
<td>121</td>
<td>0.86</td>
<td>62</td>
</tr>
<tr>
<td>ISOLS Deformity</td>
<td>112</td>
<td>0.64</td>
<td>59</td>
</tr>
<tr>
<td>ISOLS Overall Score</td>
<td>95</td>
<td>0.62</td>
<td>48</td>
</tr>
<tr>
<td>BME Function</td>
<td>116</td>
<td>0.35</td>
<td>58</td>
</tr>
<tr>
<td>BME Pain</td>
<td>125</td>
<td>0.38</td>
<td>64</td>
</tr>
<tr>
<td>BME ROM</td>
<td>123</td>
<td>0.76</td>
<td>64</td>
</tr>
<tr>
<td>BME Overall Score</td>
<td>108</td>
<td>0.74</td>
<td>54</td>
</tr>
</tbody>
</table>

p derived from Spearmans Rank test
Chapter 5

The use of the new bone formation to enhance the fixation of cemented replacements
5.1. Introduction

Aseptic loosening of cemented intra-medullary stemmed massive endoprostheses has been a significant problem, particularly for young patients (Chapter 2) and those who have been revised (Unwin et al 1991b, Unwin et al 1993e), (an updated review of Stanmore massive replacements appears in Appendix F).


In this study, extra-cortical bony bridging formed across the implant/bone junction and has been proposed as a means of improving fixation by reducing the stresses at the cement/bone interface of the intra-medullary canal by the transmission of forces at the prosthesis plateau. Chao has demonstrated the mechanical advantage of having fibrous tissue or preferably bony bridging using finite element analysis (Chao and Sim 1992). This study showed that at the plateau, cement shear stresses would be reduced from 0.18 to 0.08 unit load cm\(^2\), if bony bridging encompassed the proximal prosthesis shaft.
5.2. Purpose

The aims of the study were two fold.

- Firstly, the pedicle associated with uncoated lower limb endo-prostheses replacements was investigated to establish if it is a reliable phenomenon to aid the fixation of massive endo-prostheses.
- Secondly, assess bony ingrowth that occurred in two types of porous surface structures and compare the results with those obtained for uncoated replacements.

5.3. Investigations of the Pedicle Formation

5.3.1. Materials and Method

The data obtained in the detailed radiographic examination (Chapter 4) has been used to investigate the occurrence of the pedicle formation. The cases formed the control for the later comparative analysis with the coated replacements. The control group of uncoated intra-medullary stemmed massive endo-prostheses comprised of 189 distal femoral, 82 proximal femoral and 96 proximal tibial replacements (all distal femoral and proximal tibial replacements used the Stanmore fixed hinge). To assess the presence and dimension of the pedicle, all radiographs were taken 6 months or more after the limb salvage procedure. To identify when pedicle appeared, an addition 74 radiographs of implant durations less than 6 months were assessed.

The length of pedicle was measured from the level of the prosthesis plateau to the tip of the pedicle, parallel to the long axis of the implant. The width of the pedicle and breadth of the gap formed between the pedicle and the prosthesis shaft were measured at the mid-point of the pedicle length perpendicular to the prosthesis shaft. Frequently, pedicle formed the shape of an elongated triangle with the inner edge roughly parallel to the prosthesis shaft (Plate 5.1).
The pedicle was graded depending upon the area (Table 4.1. No pedicle =0, ≤40 mm$^2$ =1, >40 mm$^2$ =2).

5.3.2. Results

5.3.2.1. Pedicle Frequency

Radiographic assessment identified that pedicle was present in 87.8% of distal femoral, 70.7% of proximal femoral and 59.4% of proximal tibial replacements cases that were ≥6 months post implantation.

5.3.2.2. Distribution

Pedicle was most commonly observed on the medial and posterior quadrants of the femoral replacements (Figure 5.1). With proximal tibial replacements, pedicle was most frequently observed on the medial quadrant, but there was a relatively even distribution between the three remaining quadrants.

5.3.2.3. Number of quadrants

The majority of distal femoral cases had pedicle present in all 4 quadrants, whereas the large majority of proximal femoral cases had pedicle in two or less quadrants (Figure 5.2). Of the proximal tibial cases that had pedicle present, the majority had pedicle in one or two quadrants.

5.3.2.4. Dimensions of the pedicle

Generally, the highest pedicle scores reflecting the longer and wider pedicles were present on the posterior and medial aspects of distal femoral replacements and on the medial and anterior aspects of proximal femoral and proximal tibial replacements. Pedicle on the lateral aspect of all implant types had the lowest scores. The longest pedicle observed, measured 220 mm and was present in the posterior quadrant of a distal femoral replacement. (Pedicle dimensions and scores are summarised in Table G.1 of Appendix G).
The aspect ratio of the pedicle (l/w), highlighted that slender pedicles were present in distal femoral posterior quadrants (13.0:1) and in anterior and lateral proximal femoral quadrants (13.9:1 and 13.7:1 respectively). The more robust pedicles were present in medial distal femoral quadrants (7.9:1) and posterior proximal femoral quadrants (7.2:1). With the proximal tibial replacements, pedicles were slender in the anterior (13.0:1), posterior (12.7:1) and the medial (13.7:1) quadrants, but in the lateral quadrant, pedicles were more robust (8.8:1).

**Pedicle gap**

The gap formed between the pedicle formation and the prosthesis shaft was present in all radiographs of uncoated massive endo-prosthetic replacements. The gap was broadest in the proximal femoral group (medial 4.2±0.85) and narrowest in the proximal tibials (lateral 1.5±0.13). (Further details are presented in Table G.2 of Appendix G).

5.3.2.5. **Resection**

Overall, the percentage of bone removed had a significant effect on the presence of pedicle associated with proximal tibial replacements, less so with proximal femoral replacements and least of all with distal femoral replacements (Figure 5.3).

The level of resection had a pronounced effect on the position of the pedicle. In the proximal femoral replacement group the shorter the percentage of bone resected the greater the difference between quadrants with respect to the number of cases with pedicle (Figure 5.4). With decreasing percentage of bone resected there was an increasing percentage of cases with pedicle in the posterior quadrant and a decreasing percentage in the anterior and lateral quadrants. In contrast, with the distal femoral replacements there was
increasing percentage of cases with pedicle with increasing percentage of bone resected in all quadrants.

Pedicle associated with proximal tibial replacements occurred in all quadrants more frequently when between 40% and 60% of the proximal tibial was resected. Pedicle was scarce in all quadrants when <40% of the proximal tibia was resected.

**Number of quadrants**

With respect to the percentage of femur resected, irrespective of implant type, the highest proportion of cases that had pedicle in either 4 or 3 quadrants had between 40% and 60% of the femur resected. Proximal resections generally had pedicle in more quadrants than those cases with distal resections. The level of tibial resection had little effect on the number of quadrants with pedicle present. (Table G.3, Appendix G).

**Dimensions**

The percentage of bone removed had an effect on the size of the pedicle particularly in the femoral replacement groups. In the distal femoral group, the largest pedicles were found in those cases with >60% resections and the smallest in those with <40% resections (Figure 5.4) (Dimensions: Table G.4, Appendix G). Proximal femoral cases with between 40-60% resections had the largest pedicles and those with >60% resection the smallest. The percentage had less of an effect on the proximal tibial replacements and few cases with <40% resections had pedicle. Generally in all aspects with the exception of the medial there were slightly larger pedicles in the 40-60% resection group.

5.3.2.6. **Patient age**

Overall, patient age had a marked affect on the occurrence of pedicle (Figures 5.5 and 5.6). Young patients (≤16 years) with either distal femoral or proximal
tibial replacements had the highest percentage of cases with pedicle and elderly patients (>60 years) the lowest. The age of patients with proximal femoral replacements had little effect on the presence of pedicle.

Quadrant number

Young patients with either distal femoral or proximal tibial replacements had the greater percentage of cases with pedicle in all four quadrants, whereas, many of the old patients had pedicle present in only 1 quadrant (Table G.5, Appendix G).

Dimensions

Young patients with distal femoral or proximal tibial replacements, generally had larger pedicles than elderly patients (Table G.6, Appendix G). In contrast, elderly patients (≥60 years) with proximal femoral replacements had the largest medial and lateral pedicles.

5.3.2.7. Radiolucent lines versus Pedicle formation.

There was no correlation between the presence or absence of radiolucent lines and pedicle associated in any of the quadrants with distal femoral replacements (n=189). Of the quadrants with no pedicle present, 71.1% had no RLLs evident and of those quadrants with pedicle present, 65.4% had no observable RLLs.

5.3.2.8. Duration

New bone formation was evident within 3 months of the limb salvage operation (Figure 5.7). Fifty eight percent of the distal femoral radiographs examined with an implant duration of less than 4 months had pedicle (shortest duration = 2.2 months). After the first year, 85% of all distal femoral radiographs assessed had pedicle in at least one quadrant. Proximal femoral replacement cases developed pedicle a little later, with the first pedicle observed after an implant duration of 4 months. Within the first 3 years the
percentage of cases with pedicle fluctuated, however, between 5 and 10 years of implant duration nearly 95% of the cases assessed had pedicle present. A quarter of the proximal tibial cases had pedicle within 4 months and the percentage rose rapidly but fell again during the second and third years of implant duration. After which there was a further fluctuation in the percentage of cases with pedicle.

5.3.2.9. Discussion of pedicle associated with uncoated replacements

The results of the radiographic study identified that pedicle bone was a predictable phenomenon. Factors affecting the presence of pedicle included, skeletal location of the implant, duration, patient age and the percentage of bone resected. With respect to femoral replacements, pedicle occurred most frequently in the medial and posterior quadrants and the level of resection had a pronounced effect on its frequency and distribution. Similarly, with respect to proximal tibial cases, patient age and the percentage of bone resected affected the frequency of the pedicle but not the distribution. Overall, the proportion of younger patients with pedicle was significantly higher than elderly patients.

5.3.2.10. The formation of the pedicle.

In the published literature only Inglis (Inglis and Walker 1989) has put forward a theory on the development of the pedicle. Inglis suggested that the pedicle has a growth zone located in the shaft bone adjacent to the prosthesis plateau (Inglis and Walker 1989).

In this study, it is hypothesised that the pedicle formation was a result of the bending moment down the femur and offset axial loading producing compressive forces medially and posteriorly and tension laterally and anteriorly. Stimuli due to compression forces is believed to be an important factor in the formation of the pedicle. Cases with a fully bonded cement/bone
interface would transmit forces in shear from the bone to the intra-medullary stem proximally as identified by Taylor (Taylor 1993). Distally, adjacent to the prosthesis plateau, the stress shielded bone would be insufficiently stimulated to form pedicle. But, less bonded implants transmitting higher axial forces distally would stimulate bone adjacent to the prosthesis plateau to form pedicle. Comparing cases with radiolucent lines and with or without pedicle there was no difference in the proportion of cases with radiolucent lines and pedicle and those with no radiolucent lines and no pedicle. However, in the radiographic study, cases that failed had larger pedicles than those that did not (Table 4.2). It is suggested that the forces which contribute to aseptic loosening (i.e. the debonding of the cement/bone interface) also contribute to the generation of pedicle bone.

The level of activity appeared also to be of importance if the assumption that younger patients were more active than the elderly could be made. There have been cases where pedicle has been evident and after a period of inactivity of the patient the pedicle has been seen to resorb and this suggests an activity related bone remodelling response mechanism.

Pedicle associated with mid-shaft replacements has been observed to unite the proximal and distal segments of bone. Therefore it could be considered that the pedicle formation is a product of the "fracture" and is part of the callus formation. Cases that developed pedicle, normally had the pedicle present within 6 months of the limb salvage procedure and those that did not have pedicle within 1 year of the operation rarely developed pedicle.

5.4. Enhancing the fixation

5.4.1. Porous collared replacements

Sintered beaded surfaces were first used on uncemented femoral hip components by Lord (Lord and Bancel 1983). Porous beading has been used
successfully on standard joint replacements (Hungerford et al 1990a, Hungerford et al 1990b) and on the intra-medullary stems of the uncedent Kotz modular massive replacements (Salzer et al 1989, Capanna et al 1991b, Samek et al 1991, Zwart et al 1994). Theoretical and animal studies have suggested that porous beaded surfaces on massive endo-prostheses permitted extra-cortical bony bridging and reduce cement/bone interface stresses (Chao and Sim 1992). In a small study of porous collared proximal tibial replacements, Ward reported a significant reduction of radiolucent lines (Ward et al 1993). Ward considered this to be a result of the fibrous tissue that had developed between the pedicle and porous collar prevented the ingress of wear particles at the cement/bone interface. Chao considered initial implant stability to have a considerable effect on tissue ingrowth (Chao and Sim 1992). Increased implant stability has been demonstrated by Finkelstein, who used a femoral hip component in a canine model (Finkelstein et al 1994). Reduced micromotion resulted with beaded replacements after 6 months being in-situ, compared to press-fit replacements inserted into cadaveric femora.

5.4.1.1. Materials and patients

Fourteen modular collars of a porous beaded structure were obtained from Zimmer Ltd (Warsaw, Indiana). The porous collar was located at the prosthesis shoulder and comprised of two layers of diffusion bonded spherical commercially pure titanium (Ti 125) beads (diameter = 0.7 mm). The region covered a band 25 mm in length, encircling a 28 mm diameter bar of titanium alloy, (TA1), (Plate 5.2). The prosthesis plateau was not coated. The inter-bead pore size was dependent on the configuration of the beads, the maximum dimension for a 3 sided pore were 0.2 mm, 4 sided =0.5 mm and a 5 or more sided pore =1.2 mm.

All 14 porous collared distal (n=10) and proximal femoral (n=4) replacements were included in the study. The first porous collared replacement was used in
September 1988, and the last in June 1989. Bone tumour (n=10) was the predominant indication and the remainder were revisions of aseptic loosened primary distal femoral massive endo-prostheses originally inserted for bone tumour. The average age of the patients with distal femoral replacements was 28 years, whilst those with proximal femoral replacements was 40 years. Eleven patients were male and 3 were female.

5.4.1.2. Results

Thirteen of the 14 cases had follow-up with an average duration of 45.5 months (range 7 to 65 months). The fourteenth patient had returned home abroad, shortly after the limb salvage operation. One patient with a distal femoral replacement had an amputation after 7 months due to recurrence of tumour and another patient with a distal femoral replacement died of disease (24.0 months). One revision distal femoral replacement loosened and was revised after 36 months. This porous collared replacement was replaced with a hydroxyapatite coated cemented intra-medullary stemmed distal femoral replacement. All the remaining patients had no prosthetic related problems.

Radiographic

All thirteen cases with follow-up had radiographic assessments (average duration =40.8 months, range 3 to 63 months). Using the ISOLS radiographic grading, 80% were graded as 'Good' 10% 'Fair' and 10% 'Poor'. No cases were scored 'Excellent' as all cases with pedicle but no other changes, had pedicle that was not integrated into the porous beaded structure and therefore were graded 'Good'.

Pedicle was present in 12 of the 13 cases (92.3%). All 10 distal femoral and 2 of the 3 proximal femoral cases had pedicle it at least one quadrant. Six of the 10 distal femoral cases had pedicle present in 4 quadrants, whereas both of the two proximal femoral cases had pedicle restricted to the medial and posterior
quadrants. Pedicle was most frequently observed in the posterior and medial quadrants (11 cases 84.6%), and least frequently in the anterior and lateral quadrants (7 cases, 53.9%). The longest pedicles were on the posterior (mean =28.1 mm) and the shortest on the lateral (mean =22.9 mm). The one proximal femoral case that did not have pedicle had been in-situ for 59 months at the time the radiographs were obtained.

Pedicle had not ingrown into the porous beaded structure (Plate 5.3). A pedicle gap (radiolucent line) was present along the complete length of the pedicle and the porous beading. The widest gaps were measured on the posterior (mean =1.8 mm) and the narrowest on the anterior (mean =1.0 mm).

A plateau gap was present in 42 (80.8%) of the 52 quadrants. When a plateau gap was present, 71.4% of the quadrants also had pedicle present, and when there was no plateau gap was evident 60% of the quadrants had pedicle. Pedicle was most frequently observed with a plateau gap in the posterior (91.6%) and the medial (77.8%) quadrants. In contrast, in the anterior and lateral quadrants pedicle was less frequently associated with a plateau gap (40.0% and 54.5% respectively).

Radiolucent lines associated with porous collared primary femoral replacements were less frequently observed (28.6%) and were smaller (RLL score =0.9±1.9, maximum =4) than those associated with uncoated proximal and distal femoral replacements (50.8%, RLL score =3.3±0.46, maximum =24) (p=0.21), of the same implant duration range (12 to 46 months).

5.4.2. Discussion - the use of porous collars on massive endo-prostheses

The purpose of the porous collars was to reduce the cement/bone interfacial stresses by the ingrowth of pedicle as predicted by Chao (Chao and Sim 1992). However, no extracortical bony bridging was identified even though all cases examined had pedicle present. The radiographic results obtained were similar
to those of porous coated proximal tibial replacements presented by Ward (Ward et al 1993). In addition, the reduction in the frequency and extent of radiolucent lines compared to uncoated replacements of the UCLA series was also observed. Ward suggested the prevention of the ingress of wear particles to be factor in the reduction of RLLs. However, the lack of debris observed between the cement and bone in retrieved specimens (Blunn pers comm) and the well aligned interdigitated fibrous tissue (Plate 5.4) encompassing the porous collar of the Stanmore retrieval would favour Chao's biomechanical theory (Chao and Sim 1992).

5.4.3. Hydroxyapatite coated replacements

Over the last decade, synthetic hydroxyapatite ceramic has become one of the most important and commonly used osseointegrative surface coating for uncemented total joint replacements because of its osteoconductive properties. The use of hydroxyapatite ceramic coated titanium to provide long term stability of implants by osseointegration was first demonstrated in orthodontic reconstruction (Branemark et al 1977, Adell et al 1981). This invaluable work of osseointegrated dental implants detailing surgical technique and long term results has clearly changed joint replacement.

Hydroxyapatites occur naturally as the mineral phase of bone. Hydroxyapatite belongs to the apatite family who's general chemical formula is

$$M^{2+}X_{3-4}^{6}Z^{-2}.$$ 

The composition of hydroxyapatite is as follows -

$$Ca_{10}(PO_{2})_{6}(OH)_{2}$$
Crystalinity, composition, coating thickness and the design of the underlying substrate surface of the hydroxyapatite ceramic coating are regarded as important issues in bony integration of the coating (Heimke 1990, Frayssinet et al 1994, Thomas 1994).

5.4.3.1. Materials and patients

The first use of a hydroxyapatite coated Stanmore massive endo-prosthetic replacement was in April 1989, when a proximal tibial endo-prosthesis was used to replace a loosened massive endo-prosthesis. Hydroxyapatite ceramic was used infrequently to coat massive endo-prostheses over the following 19 months. In December 1991, a prospective trial was begun to investigate bony ingrowth into hydroxyapatite coated macro-grooves with the aim of comparing the clinical, radiographic and histology findings with the porous collared replacements (described above) and uncoated replacements that were to act as the control group.

Prior to the start of the trial, 6 replacements had been hydroxyapatite coated. Four of the 6 cases, had longitudinal and circumferential grooves machined into the shaft adjacent to the prosthesis plateau. The groove width ranged from 3 to 8 mm wide and were between 30 to 40 mm in length. In the 2 cases, 1 case had longitudinal grooves, 40 mm in length and the other had no grooves but the proximal 60 mm of the shaft was hydroxyapatite coated.

Forty seven cases had a standardised macro-groove structure of 1 mm wide, 1.5 mm deep and approximately 1 mm apart (Plate 5.5). The length of the grooved structure was approximately 25 mm from the top of the prosthesis plateau. The groove width and depth standardised at 1 mm was adopted for ease of machining using a standard 1 mm wide slitting wheel. Orientation was to ease machining and minimise the shear forces on the hydroxyapatite layer and to axial and torsional forces.
Initially, only distal and proximal femoral replacements used for bone tumour or revision of a massive endo-prosthetic replacement were permitted into the trial to allow a direct comparison with the porous collared replacements. However, some of the early radiographic findings appeared promising and so proximal tibial replacements were included in the trial. Furthermore, there was an increasing demand from the surgeons for hydroxyapatite coatings massive endo-prostheses for other skeletal locations.

In all 53 cases, the grooves and plateaux were hydroxyapatite ceramic plasma sprayed. The average percentage crystalinity of the hydroxyapatite coating was 90.7% (±0.36, range 83 to 96%). Morselised bone graft was not used with any of the bone tumour replacements but in a small number of revision cases, pedicle bone, if present was resected, sliced and positioned back upon the hydroxyapatite coated grooved structure.

5.4.4.1. Study group

The study group (n=53) comprised of all of the hydroxyapatite coated, cemented intra-medullary stemmed proximal femoral (n=11), distal femoral (n=27) and proximal tibial (n=15) replacements that had been inserted for either bone tumour or a failed bone tumour massive replacement prior to 1994.

The indications were bone tumour in 29 cases and revisions of failed bone tumour massive endo-prosthetic replacements in 24 cases. Aseptic loosening of the primary replacement accounted for 16 of the 24 revision cases. The average age of the distal femoral replacements was 26.6 years and the sex ratio was 1.7:1 (M:F). The proximal femoral replacements were older, with an average age of 28.5 years and with a sex ratio of 1.75:1. The proximal tibial replacements were the youngest with an average patient age of 26.4 years and the sex ratio was 1.1:1 (M:F). There was no significant difference in patient age between the three replacements groups (p=0.63). The SMILES rotating knee hinge was introduced in 1991 and was used in 18 of the 27 distal femoral and 9 of the 15
proximal tibial cases. Of the 15 replacements that utilised the Stanmore fixed knee hinge, all except 1 were revisions.

5.4.3.2. Results

Fifty (94.3%) of the 53 cases had follow-up with a mean implant duration of 14.4 months (range =1.3 to 52 months). Seven patients had died of disease, one patient with a proximal tibial replacement, fractured his femur and requested an amputation, and 34 were alive with no reported prosthetic related problems. The remaining 8 patients had prosthetic related problems that included infection (n=2), pain associated with the replacement (n=4), complications with the rotating hinged knee joint (n=1) and 1 patient had a loose revision proximal femoral replacement.

Radiographic

Forty six cases (86.8%) had radiographic follow-up, with a mean implant duration of 14.1 months (range =1.1 to 55 months). Pedicle was observed in at least 1 quadrant in 33 cases (71.7%). However, selecting radiographs taken 6 months or more after insertion of the hydroxyapatite coated implant, 81.8% of cases had pedicle.

There was no difference between primary and revision replacements with respect to the presence of pedicle (Fisher's Exact, p=0.30).

Distal femoral replacements had the highest percentage of cases with pedicle present (84.0%), followed by the proximal tibial cases (61.5%), whilst the proximal femoral had the lowest occurrence (50%). In the distal femoral group, pedicle was most frequently observed medially (80%) and least anteriorly (44%). Only 4 cases of the 8 proximal femoral cases with radiographic follow-up had pedicle and therefore too few to make valid statements concerning its distribution. The anterior and lateral quadrants were the most common sites
for pedicle in the proximal tibial group, and pedicle occurred only once on the posterior quadrant.

Predominantly, distal femoral cases had pedicle present in 2 or more quadrants (Figure 5.8). Similarly, all 4 proximal femoral cases had pedicle in 3 or more quadrants. In contrast, the majority of proximal tibial cases that had pedicle, the pedicle was restricted to a single quadrant.

**Implant duration**

The radiograph with shortest implant duration with pedicle present was 4.2 months. Two sets of radiographs of this implant duration had pedicle, one proximal tibial replacement case had a small pedicle (5x1 mm) present in the lateral quadrant and proximal femoral replacement had pedicle present in the anterior, posterior and medial quadrants. Furthermore, the pedicle length in the anterior quadrant was 55 mm and in both the posterior and medial quadrants it measured 40 mm in length. The earliest presence of pedicle with a distal femoral cases was 4.4 months, and this case had pedicle presence in all four quadrants. With increasing implant duration there was an increase in the percentage of cases that had pedicle, and all cases with an implant duration >24 months had pedicle present in at least one quadrant (Figure 5.9).

**Bony ingrowth**

Bony ingrowth is defined as pedicle that has grown into the grooved macrostructure. Bony ingrowth occurred in one or more quadrants in 27 (81.8%) of the 33 cases that had observable pedicle (Plate 5.6). The 6 cases with pedicle but no ingrowth observed, were all distal femoral cases, (primary replacement n=4, revision replacements n=2) (Table 5.1). Furthermore, of the 33 cases with pedicle, 19 had observable bony ingrowth in all quadrants where pedicle was present. There was a significantly higher proportion of ingrowth
of pedicles in both the proximal femoral and proximal tibial groups compared to the distal femoral group (p=0.01).

The lack of pedicle ingrowth, occurred most frequently in the anterior quadrant of the distal femoral group, the posterior and medial quadrants of the proximal femoral group and the lateral quadrant of the proximal tibial group (Table 5.2).

**Pedicle length**

Pedicles were longest in the proximal femoral group and shortest in the proximal tibial group (Figure 5.10). On the average the longest pedicles were observed medially on proximal femorals (23±7.1 mm, n=4) posteriorly on distal femorals (19.9±3.6 mm, n=15) and anteriorly on proximal tibial replacements(10.3±5.6 mm, n=4).

Selecting only the distal femoral cases, there were minor differences (p>0.1) between the lengths of the pedicle that had ingrown and those that had not in both the anterior and posterior quadrants. However, in the medial quadrant, pedicle that had not ingrown were on average longer (19.8±5.3 mm, n=8) than those that had ingrown (16.3±4.4 mm, n=12) (p=0.25). In contrast, ingrown pedicle in the lateral quadrant were on average longer (15.4±5.2 mm, n=7) than those that had not (6.0±6.2 mm, n=5) (p=0.37).

**Plateau gap**

Overall, no relationship between plateau gap and pedicle was evident (p=0.10). However, in both femoral groups, there was a higher proportion of cases with pedicle and plateau gaps present in the same quadrant. Selecting the distal femoral cases, there were an even proportion of cases with and without pedicle when a plateau gap was present with respect to the anterior and lateral quadrants. However, when a plateau gap was present in the medial and posterior quadrants, 75% and 80% of cases respectively had pedicle present, (p>0.1).
The presence of a plateau gap did have a significant effect on the bony ingrowth of the pedicle (p<0.01). Of the 41% of quadrants with no plateau gap, 87% of the pedicles were ingrown, but when there was a plateau gap, 48% of pedicles had ingrowth. In both the posterior and medial quadrants of the distal femoral cases when there was no plateau gap, all pedicles had ingrowth. However, in the anterior and lateral quadrants not all pedicles had ingrown when there was no plateau gap.

**Bone cement**

When a layer of bone cement was present (49% of quadrants) on the plateau, 66% of quadrants had a plateau gap (Figure 5.11). When no cement layer was present 61% of quadrants had no evidence of a plateau gap (p<0.01). This relationship was significant in both femoral groups (DF p=0.01 and PF p=0.04), but not in the proximal tibial group (p=0.77). All distal femoral quadrants were less likely to have plateau gaps when no cement layer was present on the plateau, but in anterior and lateral quadrants there was a significant correlation between those with, and those without, a cement layer.

**Radiolucent lines**

Hydroxyapatite coated primary proximal and distal femoral replacements had on average a lower RLL frequency (27.3%) and RLL score (0.6±1.4, maximum =3) than uncoated primary proximal and distal femoral replacements (41.7%, 2.6±0.3, maximum =24) (p=0.20, Mann-Whitney 'U' test) with the same in-situ time range (1 to 42 months).

**5.4.4. Discussion - bony ingrowth associated with hydroxyapatite collared replacements**

Ingrowth and remodelling of pedicle into the hydroxyapatite of the grooved replacements would confirm that hydroxyapatite is bioactive, encouraging the bonding of bony tissue to the ceramic layer (Heimke 1990).
The dimensions and orientation of the grooves allowed for the structure to be machined into shafts, irrespective of ovality or dimension. Therefore, this grooved structure could be applied to any custom-made massive endoprosthesis, unlike the modular porous beaded components which were circular in cross-section, and produced in one diameter, thus restricting in use.

The groove width and depth standardised at 1 mm was used for ease of machining and it was considered to provide sufficient depth to resist shear. However, Stephenson examined the effect of groove width and depth and showed that deeper and wider grooves had the greatest penetration of bone at 4 and 8 weeks after the insertion of the implant (Stephenson et al 1991).

The length of the pedicle in the medial quadrant of distal femoral replacements was shorter when ingrown, but pedicles in the lateral quadrant were longer than those not ingrown. The coronal plane bending moment created by the offset femoral head would result in tension laterally and compressive medially, which has been demonstrated with cadaveric/implant simulation (Wright and Meswania 1984). The tension applied to the ingrown pedicle of the lateral quadrant is considered to be the stimuli for growth. The sagittal plane bending moment being of small magnitude would not provide the same stimulus and therefore the anterior and posterior pedicle lengths of those ingrown and those not, would be of similar length.

Remodelling of the pedicle was observed in a small number of hydroxyapatite cases with increasing implant duration. Close examination of the pedicle revealed rays of denser bone emanating from the ridges of the grooved structure (Plate 5.7.a and b). This phenomenon has been termed 'trabecularisation'. Heimke predicted the less dense bone would occur within the rectangular shaped grooves. Modification to a triangular shaped grooved structure as described by Heimke (Heimke 1990) to modified the stresses within the bone would reduce the stress-shielded regions.
In two revision cases, resected pedicle was repositioned adjacent to the hydroxyapatite coated grooves hoping for rapid bony incorporation of the ingrowth structure. However, in one case, the pedicle in all four quadrants re-united with the shaft bone but the pedicle did not grow into the grooved structure. In the second case, new bone developed and osseointegrated and later reuniting of the original pedicle occurred. Resected pedicle did not provide a 'rapid start' for extra-cortical fixation. The development of a fibrous tissue interlayer between the hydroxyapatite coated structure and the original pedicle did not remodel.

5.4.4.1. A comparison of hydroxyapatite, porous collared and uncoated femoral replacements.

Extra-cortical bony bridging occurred in 27 of the 50 hydroxyapatite coated cases with radiographic follow-up. In complete contrast, no bony ingrowth was evident in the 13 femoral implants with porous collars.

The proportion of cases exhibiting pedicle in the 2 study groups were similar to that of the control group for all three implant locations (Table 5.3). In all implant groups, a smaller proportion of hydroxyapatite cases had a plateau gap present. Within the distal femoral group, the uncoated (n=189) and the hydroxyapatite cases (n=19) had a remarkably similar proportion of cases with pedicle with respect to the quadrant, but pedicle was present in the medial and posterior quadrants of all of the 8 porous collared cases. The average length of the pedicle was substantially shorter in the hydroxyapatite cases compared to the porous collared or uncoated groups. Seventy five percent of the porous collared cases had pedicle in 3 or all quadrants compared to 59.7% of the uncoated and 52.6% of the hydroxyapatite coated distal femoral replacements.

Both the beaded and hydroxyapatite coating had a major effect in reducing the extent of radiolucent line compared to the uncoated control groups. Comparing the radiolucent line scores of the porous collared and the
hydroxyapatite femoral replacements there was no significant difference between the two groups, either when combining primary and revisions together or separately (combined p=0.83, primaries p=0.82, revision p=0.77). The mean radiolucent scores were higher in the porous collared group for both primaries and revisions (Primary PC =0.86±1.9, Revision PC =6.7±3.07; Primary HA =0.6±1.4, Revision HA =3.0±1.53).

5.5. Discussion - methods of enhancing the fixation.

The pedicle formation could be considered to be a reliable phenomenon and therefore useful in enhancing the fixation of massive endo-prostheses to increase the longevity. Pedicle was most commonly associated with the younger patients and it is this group who have the poorest prognosis in terms of surviving aseptic loosening (Chapter 2).

The mechanical superiority of fibrous or preferably bony bridging has been demonstrated mathematically by Chao (Chao and Sim 1992) to reduce the normal and shear stresses at the cement/bone interface. The well aligned fibrous tissue observed in the histological section of the Stanmore retrieval would indicate that forces were being transmitted between the pedicle and implant. Although of only short follow-up there was a substantial reduction in radiolucent line scores with both porous collared and hydroxyapatite coated replacements compared to uncoated replacements restricted to the same time period. This is in agreement with Ward (Ward et al 1993) who compared porous collared and uncoated proximal tibial replacements.

One revision porous collared replacement did fail from aseptic loosening, and was replaced with a hydroxyapatite coated replacement and although the implant duration of the hydroxyapatite coated replacement had only been short, there was evidence of extra-cortical bony bridging. At the revision procedure, all the original pedicle was resected and not reused.
The development of the fibrous tissue interlayer interdigitating into the porous collared had been described by Cobb (Cobb et al 1991) as a 'biological purse string' that 'seals' the cement bone interface thus reducing the ingress of wear debris and therefore preventing wear-induced osteolysis. However, there is no evidence yet to suggest that it does indeed reduce the ingress of debris. Whichever the mechanism it would be preferable to have bony ingrowth as this would permit mechanical forces to be transmitted and act as a more substantial barrier to wear particles.

Bony ingrowth of the plateau was also considered advantageous either as a barrier to particle migration or mechanical transmitting forces and reducing micro-motion.

5.6. Future work

The early results of the hydroxyapatite coated replacements has been encouraging, it is important that radiographic assessment is continued to establish in the long-term if hydroxyapatite coated replacements have a increased longevity.

A change of the circumferential groove shape from rectangular to triangular as demonstrated by Heimke (Heimke 1990), would improve the stress transfer and reduce the stress-shielding that has been evident (Figure 5.12).
Figure 5.1. The frequency (%) of pedicle with respect to quadrant and implant (uncoated).
Figure 5.2. The number of quadrants with pedicle present with respect to quadrant and implant (uncoated).
Figure 5.3. The frequency of pedicle with respect to implant and percentage of bone resected. (Uncoated implants.)
Figure 5.4. The frequency (%) of pedicle and mean pedicle score (±S.E.) with respect to quadrant, the percentage of bone resected and implant. (Uncoated implants.)
Figure 5.5. The frequency of pedicle with respect to implant, quadrant and the age of the patient. (Uncoated implants.)
Figure 5.6. The frequency (%) of pedicle and pedicle score (±S.E.) with respect to implant, quadrant and the age of the patient at the time of limb salvage. Note, there were too few elderly patients with proximal femoral replacements. (Uncoated implants.)
Figure 5.7. The presence of pedicle with respect to duration and implant. (Uncoated implants.)
Figure 5.8. The number of quadrants with pedicle present with respect to implant. (HA coated implants.)
Figure 5.9. The number of radiographs assessed with and without pedicle, in each time interval. (HA coated implants.)

Figure 5.10. The mean length of the pedicle (±S.E.) with respect to quadrant and implant. (HA coated implants.)
Figure 5.11. The percentage of cases with a plateau gap with respect to the presence or absence of a cement layer on the prosthesis plateau, with respect to quadrant. (HA coated implants.)
Figure 5.12. The rectangular shaped grooves (left) of the present design exhibited bony stress shielding. The triangular shaped grooves (right) as illustrated by Heimke result in a more evenly distributed stresses leading to greater bony contact.
Plate 5.1. Typical pedicle formation on a distal femoral endo-prosthesis. Note the extensive pedicle on the medial aspect of the replacement and the absence of pedicle on the lateral. There is a well defined radiolucent line between the pedicle and implant shaft, the resected bone and the prosthesis plateau and at the cement/bone interface. (Implant duration = 34 months).
Plate 5.2 a & b. A porous collared proximal femoral replacement (upper) and close up of the titanium beaded collar (lower).
Plate 5.3. A radiograph of a porous collared replacement. Note the gap between the pedicle and the porous collar. (Implant duration = 2 years).
Plate 5.4. A transverse section through the retrieved distal femoral implant. (Implant duration = 7 months). The band of aligned fibrous tissue (yellow) is interpositioned between the porous collar (black) and pedicle bone (brown).
Plate 5.5. A hydroxyapatite coated distal femoral replacement.
Plate 5.6. A lateral radiograph showing a well developed posterior pedicle ingrown into the hydroxyapatite coated grooves of a distal femoral replacement. The anterior pedicle does not appear to have fully incorporated into the grooved structure. (Implant duration = 22 months).
Plate 5.7. a and b. Radiographs showing the change in the pedicle structure. Note the fine trabecularisation occurring in the later radiograph. The upper radiograph shows the pedicle formation after an implant duration of 13 months and the lower after 20 months.
Table 5.1. The number of cases with no pedicle, those with pedicle that had no ingrowth, some pedicles with ingrowth and all pedicles with ingrowth with respect to implant.

<table>
<thead>
<tr>
<th>Implant</th>
<th>No pedicle</th>
<th>Cases with pedicle</th>
<th>Quadrants with ingrowth = quadrants with pedicle</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No ingrowth in any quads where pedicle present</td>
<td>Quadrants with ingrowth &lt; quadrants with pedicle</td>
<td></td>
</tr>
<tr>
<td>Proximal femoral</td>
<td>4</td>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td>Distal femoral</td>
<td>4</td>
<td>6</td>
<td>9</td>
</tr>
<tr>
<td>Proximal tibial</td>
<td>5</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>All implants</td>
<td>13</td>
<td>6</td>
<td>8</td>
</tr>
</tbody>
</table>

Table 5.2. The number of cases with pedicle and pedicle ingrowth with respect to implant.

<table>
<thead>
<tr>
<th>Quadrant</th>
<th>Pedicle/ingrowth</th>
<th>Implant</th>
<th>Proximal femoral n=8</th>
<th>Distal femoral n=25</th>
<th>Proximal tibial n=13</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>n</td>
<td>%</td>
<td>n</td>
</tr>
<tr>
<td>Anterior</td>
<td>Pedicle</td>
<td>proximal femoral</td>
<td>4</td>
<td>50.0</td>
<td>11</td>
</tr>
<tr>
<td></td>
<td>Ingrowth</td>
<td>proximal femoral</td>
<td>4</td>
<td>100.0</td>
<td>5</td>
</tr>
<tr>
<td>Posterior</td>
<td>Pedicle</td>
<td>distal femoral</td>
<td>4</td>
<td>50.0</td>
<td>15</td>
</tr>
<tr>
<td></td>
<td>Ingrowth</td>
<td>distal femoral</td>
<td>3</td>
<td>75.0</td>
<td>9</td>
</tr>
<tr>
<td>Medial</td>
<td>Pedicle</td>
<td>proximal tibial</td>
<td>4</td>
<td>50.0</td>
<td>20</td>
</tr>
<tr>
<td></td>
<td>Ingrowth</td>
<td>proximal tibial</td>
<td>3</td>
<td>75.0</td>
<td>12</td>
</tr>
<tr>
<td>Lateral</td>
<td>Pedicle</td>
<td></td>
<td>3</td>
<td>37.5</td>
<td>12</td>
</tr>
<tr>
<td></td>
<td>Ingrowth</td>
<td></td>
<td>3</td>
<td>100.0</td>
<td>7</td>
</tr>
</tbody>
</table>
Table 5.3. A comparison of the uncoated (control), porous collared and hydroxyapatite coated replacements.

<table>
<thead>
<tr>
<th></th>
<th>Uncoated (Control)</th>
<th>Porous collared</th>
<th>Hydroxyapatite coated</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Frequency of pedicle (%) (≥6 months duration)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Proximal femoral</td>
<td>70.7</td>
<td>66.7</td>
<td>60</td>
<td>0.87</td>
</tr>
<tr>
<td>Distal femoral</td>
<td>87.8</td>
<td>100.0</td>
<td>89.5</td>
<td>0.57</td>
</tr>
<tr>
<td>Proximal tibial</td>
<td>59.4</td>
<td>-</td>
<td>55.6</td>
<td>0.99**</td>
</tr>
<tr>
<td><strong>Frequency of plateau gap (%) (≥6 months duration)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Proximal femoral</td>
<td>87.8</td>
<td>100.0</td>
<td>60.0</td>
<td>0.16</td>
</tr>
<tr>
<td>Distal femoral</td>
<td>88.4</td>
<td>100.0</td>
<td>84.2</td>
<td>0.08</td>
</tr>
<tr>
<td>Proximal tibial</td>
<td>87.5</td>
<td>-</td>
<td>62.5</td>
<td>0.09**</td>
</tr>
<tr>
<td><strong>Frequency of pedicle (%) (≥6 months duration)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Distal femoral</td>
<td>Anterior</td>
<td>48.2</td>
<td>75.0</td>
<td>42.1</td>
</tr>
<tr>
<td></td>
<td>Posterior</td>
<td>75.1</td>
<td>100.0</td>
<td>73.7</td>
</tr>
<tr>
<td></td>
<td>Medial</td>
<td>75.7</td>
<td>100.0</td>
<td>84.2</td>
</tr>
<tr>
<td></td>
<td>Lateral</td>
<td>56.6</td>
<td>62.5</td>
<td>52.6</td>
</tr>
<tr>
<td><strong>Pedicle length (≥6 months duration) (Mean length ± SE)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Distal femoral</td>
<td>Anterior</td>
<td>23.7±2.21</td>
<td>20.7±8.60</td>
<td>9.3±7.5</td>
</tr>
<tr>
<td></td>
<td>Posterior</td>
<td>29.7±2.10</td>
<td>22.4±8.7</td>
<td>19.6±6.61</td>
</tr>
<tr>
<td></td>
<td>Medial</td>
<td>23.9±1.72</td>
<td>26.3±7.26</td>
<td>18.3±5.2</td>
</tr>
<tr>
<td></td>
<td>Lateral</td>
<td>24.0±2.16</td>
<td>23.0±10.0</td>
<td>12.5±7.04</td>
</tr>
<tr>
<td><strong>Number of quadrants with pedicle (%)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Distal femoral</td>
<td>0</td>
<td>12.2</td>
<td>0.0</td>
<td>10.5</td>
</tr>
<tr>
<td></td>
<td>1</td>
<td>15.3</td>
<td>0.0</td>
<td>5.3</td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>12.7</td>
<td>25.0</td>
<td>31.6</td>
</tr>
<tr>
<td></td>
<td>3</td>
<td>24.3</td>
<td>12.5</td>
<td>26.3</td>
</tr>
<tr>
<td></td>
<td>4</td>
<td>35.4</td>
<td>62.5</td>
<td>26.3</td>
</tr>
</tbody>
</table>

*p derived from Chi^2 test, ** p derived from Fisher's Exact test, *** p derived from Kruskal-Wallis test
Chapter 6

Uncemented intra-medullary stemmed fixation
6.1. Introduction

Over the last two decades there has been an increasing acceptance of cementless implants and a lowering of age of patients undergoing joint replacement (Catani 1992). These trends have developed in part because of better understanding of bone remodelling and the introduction of porous structures that permit osseointegration, such as sintered beads and hydroxyapatite ceramic. In addition, there was increasing evidence that polymethylmethacrylate (PMMA) caused osteonecrosis due to thermal activity from the polymerisation, monomer toxicity and vascular disruption (Rhinelander et al 1979, Strurup et al 1994). PMMA has low strength, fracture toughness and ageing causes reduction of its mechanical properties, leading to fracturing and break-up of the cement mantle (Black 1988).

There are a number of advantages of cementless intra-medullary fixation compared to cemented fixation.

Stress distribution. The desired affect of uncemented fixation is biological fixation and the stresses within the bone kept as similar to the intact femur as possible. A study conducted by Hua (Hua and Walker 1991), compared the strain patterns (principal maximum strains) between cemented and uncemented massive endo-prostheses in five cadaveric femora using a photoelastic coating technique. The specimens were loaded with 2000N in the sequence intact femur, uncemented and cemented endo-prostheses. On the medial side of the bone for proximal femoral replacements, the strain values for the uncemented stem on the proximal, middle and distal regions were 73±11%, 78±15% and 80±15% of the normal respectively, however, the cemented stems were 53±15%, 57±19% and 60±20%, (p<0.1). On the lateral side the overall strain values for the uncemented stems were higher (closer to the intact bone), than the cemented stems. In the distal femoral replacements a similar pattern of results were obtained.
Load transmission and stress-shielding. Taylor (Taylor 1993) showed by using telemetry of a strain gauged cemented intra-medullary stemmed proximal femoral replacement that in-vivo, 70% of the load was transferred through the tip region of the intra-medullary stem, leading to stress-shielding adjacent to the plateau. Radiographic evaluation of cemented intra-medullary stemmed replacements confirmed these findings (Chapter 4).

Blood supply. Limb salvage has a pronounced and destructive effect on the blood supply (Jackson Burrows et al 1975). Revascularisation of the intra-medullary blood supply is virtually prevented due to the cement blocking the canal (Rhinelander et al 1979). The effect of inserting a THR has little effect on the metaphyseal blood supply, but the diaphyseal blood supply is completely destroyed resulting in bone necrosis. However, the revascularisation of uncemented total hip replacements occurs more rapidly compared to that associated with cemented total hip replacements. It is believed that the spaces around the uncemented femoral component provide sufficient space for the revascularisation to take place.

6.1.1. The use of uncemented massive replacements

Centres throughout the world, have been using uncemented massive endoprosthetic replacements for a number of years and have reported low revision rates in terms of aseptic loosening (Ritschl 1985, Kotz and Ritschl 1987, Salzer et al 1989, Capanna et al 1991b, Kenan et al 1991, Kotz 1991, Samek et al 1991, Capanna et al 1994, Zwart et al 1994). However, many of these centres have reported a higher incidence of mechanical complications, such as stem and screw fractures.

One small (n=5) short-term study of hydroxyapatite coated custom-made distal femoral replacements were similar in design to the Stanmore uncemented endo-prostheses reported below. Kay reported no major complications and that radiographically all implants were secure (Kay et al 1994). Interestingly,
they suggested that the indication for hydroxyapatite coated uncemented replacements were aggressive benign lesions, low-grade sarcomas and revisions of failed cemented endo-prostheses.

6.1.2. Aim

The principal aim of the project was to evaluate a new method of fixation of massive endo-prostheses, due to the unacceptable rate of loosening with cemented endo-prostheses. The principal target groups were skeletally immature patients and those who required a revision of an existing massive endo-prosthesis.

The purpose of the uncemented implant was to provide long-term functional fixation, based upon the hypothesis that uncemented intra-medullary stemmed fixation produces a smaller change in the stresses in the remaining femur, resulting in less adaptive remodelling.

6.2. Methodology

The project was sub-divided into two tasks -

1. Pre-clinical trials:

The aim of this task was to propose and evaluate an uncemented intra-medullary stemmed replacement. The components of this task were -

- design of the implant and associated instrumentation
- manufacture of trial implants and instrumentation
- insertion of the implants by orthopaedic surgeons using and evaluating the custom-made tooling and procedure
- fatigue testing of trial implants in cadaveric femora.
2. Clinical evaluation:

Once a suitable design was agreed upon, then with ethical approval the next phase was to undertake a clinical trial. The evaluation involved -

- insertion of uncemented replacements into suitably selected patients
- radiographic assessments
- clinical assessments.

The long-term retrospective cross-sectional study of the cemented massive lower limb replacements (Chapters 2-4) acted as basis from which to compare the proposed designs.

6.3. Design Rationale

The design rationale of the uncemented intra-medullary stem were -

- to ensure that the stresses in the surrounding femoral bone were as close as possible to that of intact femora
- a method of initial fixation to provide a basis for long-term fixation.
- no additional shaft bone to be resected
- surgical procedure to be straight forward and not to extend surgery time over that of a cemented replacement
- production costs kept to a minimum to ensure a viable marketable product.

The proposed designs

The proposed design of the intra-medullary stem was circular in cross-section that was tight fitting in the lower section, 'loose' fitting centrally, and the upper stem restrained by a polyethylene sleeve (Figure 6.1). This design permitted the transmission of axial forces at the prosthesis plateau and therefore reduce
the effect of stress-shielding that was evident in the tip loading of cemented intra-medullary stemmed replacements. The lower section of the intra-medullary stem was to be hydroxyapatite ceramic coated, to encourage osseointegration for long term fixation. The polyethylene sleeve was designed to resist toggling of the stem within the canal but allowed both axial and rotation movement. Axial rotation was restricted by two lugs on the prosthesis plateau. The stem and prosthesis shaft were fabricated in titanium alloy, taking advantage of the lower Young's modulus with better biocompatibility compared to cobalt chromium alloys. Titanium alloy was easier to machine and had been used routinely by the technicians since the early 1960s. The knowledge of the material and the ability to machine titanium more rapidly than alloys such as cobalt chrome molybdenum, ensured production costs were kept to a minimum.

The orthopaedic surgeons of the Birmingham Bone Tumour Treatment Service collaborated in the design process.

6.3.1. Pre-clinical trials

Five trial implants with accompanying custom-made tooling were individually designed and manufactured to fit cadaveric femora in an iterative design process. Frontal and lateral measurement radiographs were obtained of all cadaveric femora and each implant design was individualised to fit the recipient bone. Accurate measurements were taken of the medullary canal and width of the bone at the level of resection and at incremental distances along the bone. Each implant was inserted into cadaveric femora by orthopaedic surgeons and Biomedical Engineering staff.

To evaluate the ovality of the femoral medullary canal, 10 pairs of measurement radiographs (frontal and lateral) of femora were dimensioned using a computer based digitiser. At 10% increments of the total femoral length, the widths of the outer cortex and medullary canal were measured
perpendicular to the long axis of the femur. The medullary canal ovality ranged from 1.79:1 (frontal:lateral) at 10% level proximal to the knee to 0.85:1 at 50% level of the total femoral length (Figure 6.2).

The first replacement (PF) was designed to the criteria proposed with the exception of a hydroxyapatite coating (Plate 6.1). The intra-medullary stem length was 140 mm and the length from the plateau to the tip of the plastic sleeve was designed to be 155 mm. To ensure precise location of the implant in the bone, individualised tools and jigs were required. The tools and jigs required were -

- precision reamer
- sleeve introducer
- lug slot cutting jig
- pilot for end-miller to fit the existing Harris-Galante end-miller.

Each tool was individualised to ensure a precise fit of the implant within the canal.

The procedure to insert the trial proximal femoral uncemented replacement into a cadaveric distal femur was as follows -

- resected bone perpendicular to the long axis of the bone at the correct location with an oscillatory bone saw
- ream the canal to a depth of 160 mm with a rigid reamer
- end-miller used with the long pilot to ensure the resected surface was perpendicular to the femoral long axis (Plate 6.2)
- slots for the lugs cut (anterior - posterior) with the lug slot cutting jig positioned and a 6 mm diameter drill bit passed through and trimmed with osteotome whilst jig in-situ (Plate 6.3)
- cement restrictor inserted to a depth of 155 mm
bone cement was mixed and applied using a 14 mm diameter cement gun nozzle. The end of nozzle was inserted until the cement restrictor was contacted and then the cement pumped in whilst slowly being withdrawn for 50 mm. The pumping of the cement was ceased and the cement gun withdrawn.

the polyethylene sleeve was inserted using the sleeve introducer to the correct depth and retained until the cement had cured and then withdrawn.

the implant inserted by slight tapping of a soft mallet until the prosthesis plateau was in contact with the resected bone surface and ensuring the apex of the lugs did not contact the base of the slots.

test the implant was secure in torsion and axial movement.

The second implant (DF) was similar in design, but the stem was curved using a hydraulic press, to match the natural curvature of the cadaveric femur. (The designs of the 5 trial implants are summarised in Table H.1 of Appendix H.) The procedure for insertion as described for trial 1 was used. Whilst inserting the implant (trial 2) the femur fractured longitudinally emanating from the anti-rotational lug slots.

As a result of the fracturing, two conclusions were made -

1. the slots cut for the lugs reduced the strength of the bone and fracturing was a likely event

2. the curvature of a stem could not be accurately machined or the bone reamed to match the curvature

As a direct result of the bone fractures, the next three trial implants all used a single transverse screw (A-P) to control rotation and the stems were straight.

To resist longitudinal fracturing of the femur, a convex prosthesis plateau on trial implant 3 (PF) was designed (Figure 6.3). The flange of the plateau was
fenestrated to permit revascularisation of the shaft bone within the concavity. A custom-made end-miller was required to produce the convex shape on the resected bone surface. In addition, a precision reamer and a custom-made self-tapping cortical bone screw were designed and manufactured in titanium alloy.

The polyethylene sleeve was modified and an integral proximal flange was fabricated to prevent cement from migrating proximally and fouling the stem. The procedure to insert the implant was similar to that described above except the cutting of the slots was not performed. On inserting the implant (trial 3), the stem became jammed on tapping the prosthesis the remaining 10 mm the bone was heard to fracture. After fracturing, the prosthesis was easier to position. To place the transverse screw a jig was fastened to the prosthesis shaft and both the anterior and posterior cortices were drilled with a 2.8 mm diameter drill bit. A 5 mm diameter drill bit was used to enlarge the hole in the anterior cortex. The screw was placed with considerable effort as the teeth would not initially bite into the cortical bone posteriorly. Once positioned, there was no discernible movement of the replacement and the shaped plateau retained the longitudinal fracture that had emanated from the resected bone surface. The conclusion of the shaped plateau was that it did contain the fracture, but was complex to manufacture and it was considered that bone death would occur. The in-situ implant, later underwent fatigue testing.

With trial implant 4 (DF), the shaped plateau was omitted. The procedure went according to plan, with no bone fracturing, but again the insertion of the transverse screw caused problems. Stability of the implant in the bone was achieved and later underwent fatigue testing.

Trial implant 5 (PF), was of similar design to trial 4, but had a stem length of 110 mm. No complications were encountered and again the implant was secure within the bone.

Improvements for the tooling and procedure were suggested, these were -
• to obtain or manufacture an effective end-miller
• reposition the anti-rotation screw jig on the sleeve introducer
• use commercially available bone taps to assist in the insertion of the transverse screw.

6.3.1.1. Fatigue testing

The last three implants inserted into cadaveric femora were fatigue tested using a dynamic hydraulic testing apparatus and loaded with a sinusoidal wave form. The proximal end of the proximal femoral implants (trials 3 and 5), had been designed to bolt on a transverse plate on which a metallic femoral head was secured. The femoral head was positioned 40 mm medial to the longitudinal axis of the implant to simulate the natural femoral head offset. Distally, the condyles of the femora were secured into a chamber with cement. The distal femoral replacement (trial 4) was bolted to the test jig and an acetabular cup with a large internal diameter was positioned on the cadaveric femoral head (Plate 6.4).

Each implant/femur was angled 9° laterally and 9° posteriorly to represent anatomical positioning of an upright stance. The femoral bone was kept wet by Ringer's solution. The solution was kept in polyethylene tube secured around the implant shaft and also around the base plate in tests 1 and 3 (trial 3 and 5), and around the femoral neck in test 2 (trial 4).

Trial implant 3, was initially loaded at 1.5 kN at 2 Hz for 100,000 cycles after which the frequency was increased to 3 Hz. After 1 million cycles the load was increased to 2 kN and after a further 1 million cycles the loading was increased to 2.5 kN. After a total of 2.5 million cycles a transverse fracture was detected at the level of the distal tip of the sleeve and the femoral shaft fractured completely after an additional 200,000 cycles.
The same loading regime was used to fatigue trial implant 4, but after 1.7 million cycles the femoral neck fractured and the testing was terminated.

The final fatigue test of trial implant 5 completed 10 million cycles loading at 2.3 kN (4 Hz). No complications were observed whilst testing.

6.3.1.2. Sectioning of fatigued implants

Trials implants 3, 4 and 5 that had been fatigued tested were sectioned to examine the fit and fill of the femoral cavity by the stem and also the position of the cemented distal sleeve. Using an Exact diamond saw, each bone was sectioned into 5 mm slices. The sections were placed in sequentially order and radiographed. In all cases, the sections in the region of the precision fitting showed a very high percentage of femoral cavity filled (range 91% - 99%).

The sections of trial 3, showed that the cement had interdigitated into the cancellous bone but had not penetrated in the posterior of the femoral canal. The sleeve was positioned anteriorly as a result of the curvature of the femur. The proximal flange of the sleeve of trial 4 were vertical and cement was absent from the sleeve tip with much of the cement having ingressed proximally and was present 70 mm along the stem from the tip. Sectioning of trial 5 identified that the transverse screw had fractured at the site of the posterior aperture of the stem. It was unknown when the fracture had occurred.

In conclusion the trial insertions, fatigue testing and sectioning identified that -

- transverse screws could fracture
- cutting slots into the resected bone surface may cause longitudinal fractures
- the ratio of the stem diameter to drill or precision reamer was critical to produce implant stability without fracturing of the bone
- the positioning of the sleeve would permit sinkage of 5 mm
• retaining the cement with the proximal flange on the polyethylene sleeve was not always possible and the cement could foul the positioning of the intra-medullary stem

• the antero-posterior curvature of the femur caused difficulties with long stemmed replacements, shorter stems were therefore required.

6.3.2. Experimental Studies

An initial photo-elastic coating study comparing uncemented and cemented massive endo-prostheses in cadaveric femora had been undertaken by Hua of the Department of Biomedical Engineering. Addition photo-elastic coating studies were using artificial femora bones (SEAB) were completed by Mr A. Jones. This intercalated BSc Honours in Orthopaedic Science project was supervised by P. Unwin and Dr G. Blunn.

6.3.3. Clinical studies

6.3.3.1. Patients

After the completion of the pre-clinical trials, it was considered that ethically approved clinical trials could begin. The first insertion of a uncemented massive endo-prosthesis took place in May 1991 in Birmingham. In total, 20 uncemented replacements were inserted prior to October 1994. The group comprised of 9 distal femoral, 3 proximal femoral, 3 proximal tibial, 3 proximal humeral, 1 distal humeral and 1 mid-shaft tibial replacement. The indication of 18 cases was bone tumour and the 2 remaining cases were revisions of loosened distal femoral replacements. The details of the 20 cases are presented in Table H.2. of Appendix H.

6.3.3.2. Implant design

Over the 40 months, the design of the uncemented intra-medullary stemmed endo-prostheses evolved as a direct result of complications either inserting the
replacement or subsequently. (A summary of the design features of each of the 20 replacements is presented in Table H.3 of Appendix H). The first two endoprostheses, used an anti-rotation screw and were not coated with hydroxyapatite ceramic (Plate 6.5). As a result of a femoral fracture emanating from the anti-rotation screw that also fractured (Case 2), the anti-rotation screw method of creating rotational stability was abandoned and integral anti-rotation lugs were reintroduced. All remaining 18 cases used anti-rotation lugs.

Hydroxyapatite was considered to be essential for long-term fixation and was applied to the remaining 18 uncemented replacements. The hydroxyapatite was applied to the intra-medullary stem, prosthesis plateau and proximal shaft. Longitudinal and circumferential grooves milled into the proximal shaft were based on the design used with the cemented intra-medullary stemmed replacements (Chapter 5). The first 4 replacements had the hydroxyapatite coating restricted to the precision region of the IM stem. However, after the abandonment of the anti-toggle sleeve, the complete length of the intra-medullary stem was coated in hydroxyapatite from case 7 onwards. All subsequent cases had the IM stem fully coated with the exception of case 8 where 9 mm of the IM stem adjacent to the plateau was left uncoated by the plasma spraying company who considered the pre-treatment and coating processes may compromise the fatigue strength of the stem.

The polyethylene sleeves designed to resist toggling of the stem were found to technically difficult to insert. With the first three cases, the diameter of the medullary canal was sufficiently large to permit the use of an anti-toggle sleeve. However, when designing the implant for case 4, a 10 year boy who required a distal femoral replacement, the medullary canal diameter was 10 mm. It was not possible to design a sleeve with sufficient wall thickness and a stem with sufficient strength to fit within the sleeve. The sleeve was omitted and the stem design consisted of a distal press fit section and a smaller diameter proximal
section that did not contact the endosteal surface (Plate 6.6). This 2 section stem design was used subsequently in all remaining cases.

Two replacements, a revision distal femoral (case 6) and a primary proximal femoral (case 11) had conical plateaux. The conical plateau of the revision distal femoral replacement was designed to fill an endosteal defect and to assist in rotational stability in the porotic cortical bone of the remaining femoral shaft. The conical plateau of the proximal femoral replacement was designed to aid rotational stability, but due to the complexity of design and manufacture of the components this design feature was abandoned after this case.

The precision fitting section of the stem was parallel in all but three cases (cases 17, 19 and 20). These three cases had tapering stems because the level of the resection was prior to the isthmus of the canal and therefore the convergence of the medullary canal necessitated the need for a tapering stem.

In one case, at the request of the surgeon, two extra-cortical plates to augment the uncemented stem were designed and manufactured. The design of the plates were similar to that being tested in the animal study (Chapter 7).

6.3.3.3. Technical problems inserting the replacements

As a result of the uncemented prostheses being used as primary and revision prostheses in various skeletal locations and over a wide range of patient ages, the determination of the press-fit section of the intra-medullary stem and the precision reamer was complex. The factors involved were the -

- diameter of the precision reamer
- difference in size between the reamer and the diameter of the precision region of the intra-medullary stem
- skeletal location
- age of the patient
• primary or revision replacement.

Initially, to determine the diameter of the press-fit section the larger of the two canal diameters (proximal (A&C) and distal (B&D)) on the frontal (A) and lateral (C) radiograph were selected (Figure 6.4), then the smaller of these two selected diameters (C) was used for the dimension of the press-fit stem. Due to instability of the implant in case 4, the largest of all 4 diameters was used for the stem dimension (A). (Stem and reamer diameters are presented in Table H.4. Appendix H).

Furthermore, the difference between the stem and reamer diameters was increased to produce a larger interference fit. However, the combination of the changing of the selected canal width and increasing the interference fit, resulted in the occasional problem whilst inserting the implant. In three cases the implant jammed before the prosthesis plateau was abutted against the resected bone surface leaving a gap of 2 or 3 mm. Whilst trying to close this gap, small longitudinally fractures of the shaft bone occurred in five cases (3 proximal tibial cases and both revision cases).

Determining the medullary canal diameters of tibiae was difficult from radiographs because of the cross-section shape of the medullary cavity. Cadaveric tibiae were used to verify the shape of the medullary canal at the level of resection. In small diameter bones such as the humerus the diametric difference between the press-fit stem and the precision reamer was reduced to prevent bone fracture.

The bones of young patients were known to have greater elasticity than elderly patients (Poss 1992). Therefore, the diametric difference between the press-fit stem and the precision reamer was reduced in the elderly to prevent bone fracture. The radiographs of revision cases required close examination to determine the extent of the fibrous tissue interface and bone cement mantle.
6.3.4. Results

6.3.4.1. Clinical follow-up

Fourteen patients had follow-up and the status of each patient is summarised in Table 6.1. The average implant duration was 15.5 months (±3.35 S.E. n=13) and the longest 40 months. Six of the 14 patients had no prosthetic related problems, whilst one patient had some instability of the knee and another had pain associated with the loosening of the cemented proximal IM stem of a mid-shaft tibial replacement (case 16). Two patients died of their disease (cases 1 and 2) and a further 2 had their affected limbs amputated, both as a result of infection (cases 7 and 13).

The first patient who had an uncoated proximal humeral died of her disease after 25 months. Radiographically this prosthesis appeared loose. The limb was not retrieved after the patient's death. The second patient who had a distal femoral replacement with a transverse anti-rotation screw, fractured his femur after 3.5 months. However, due to progression of disease, the replacement was not revised and the patient died 18 months after the limb salvage procedure. The helical fracture of the femur was associated with the transverse screw that had also fractured.

The first hydroxyapatite coated distal femoral replacement with anti-rotation lugs, failed as a result of aseptic loosening after 6 months. The patient at the time of the limb salvage surgery weighed approximately 110 kg's and it was considered that this was a contributing factor. No further replacements were inserted in Birmingham and the trial was later continued at the Middlesex hospital. The first skeletally immature patient (case 4) who had a distal femoral replacement fractured his affected femur whilst playing basketball two months after insertion of the replacement. After 6 weeks in plaster, the helical fracture emanating from the anterior anti-rotation lug had united, but extensive radiolucent lines were present between the stem and cortex. However, the
patient was pain free and returned to participate in sports with no further complication or pain, although the radiographs were graded 'Poor' (Table 6.2). Interestingly, case 5 was very similar to case 4, but the replacement was tighter fitting. This patient has been less active and has suffered intermittently with a stiff knee that has been linked to the extending of the extendible replacement. Remarkably, the patients who were revised with uncemented replacements have reported no pain or complication and have noted that quality of life has improved since the procedure. The remainder of the cases have been followed-up an insufficient period of time.

6.3.4.2. Radiographic follow-up

Eleven cases had radiographic follow-up and 5 cases had more than one radiographic assessment. The follow-up was relatively short with a mean duration of 8.7 months, ranging from 2.8 to 27.4 months. Three 3 cases were graded 'Very Good' or better, 3 cases were graded 'Poor' or worse and the remainder were either 'Good' or 'Fair' (Table 6.2).

Radiolucent lines (RLL) were observed in 5 cases, of which two were revision cases that had extensive cavitation and radiolucent lines prior to revision. In both revision cases (6 and 18), with increasing implant duration, there was a discernible increase in density of bone adjacent to the press-fit section of the stem and there was reduction in the extent of cavitation and radiolucent lines (Plates 6.7a and 6.7b).

Reduction in the girth of the shaft (RSD) was observed in 5 cases. In all cases the reduction was associated with the bone adjacent to the press-fit region. However, the waisting was restricted to the mid-section of the press-fit region and did not extend to the plateau, with the exception of case 8. Case 8 had extensive bony remodelling after 11.9 months, with reduction in shaft girth. Adjacent to the transition of the press-fit and sliding regions of the stem there was a pronounce increase in shaft girth in all quadrants. This increased
measured approximately 25 mm in length and an increase of between 2 -3 mm on the radii. No RLLs were evident and the patient was not experience pain or having any other related problems.

Cases 4 and 5 were similar, both were males aged 10 years with osteosarcoma of the distal femur, but, radiographically the two cases were distinctly different. Case 4, after 27 months had extensive radiolucent lines along the length of the IM stem resulting from the helical fracture (described above), and there was an increase in the shaft diameter and pedicle was present in all quadrants (Plate 6.8). The pedicle was observed to be in close proximity to the HA coated grooved structure at the distal tips but bony ingrowth was not positively identified. A plateau gap had developed which was continuous with pedicle gap. An increase in bone density was observed along the length of the stem in the posterior quadrant, forming a mantle around the proximal tip of the IM stem. Case 5, after nearly 1 year of implant duration showed little radiographic change from the discharge radiographs with the exception of a reduction in the shaft diameter adjacent to the mid-section of the press-fit region of the IM stem (Plate 6.9). No plateau gap, RLLs or pedicle were observed. Radiographs at 17.5 months post-op showed a slight increase in the extent of the shaft reduction. Pedicle was identified within the HA coated circumferential grooves on the proximal shaft (lateral film), but due to the orientation of the frontal film in relation to the implant, the grooves could not be clearly seen.

A matched comparison (patient age, skeletal location and implant duration) of the uncemented with cemented intra-medullary stemmed replacements, highlighted that patients with uncemented replacements generally had better radiographic grades (Table 6.3).

6.3.5. Discussion - the use of uncemented intra-medullary fixation

The early results of the uncemented replacements could be described as mixed. Evolution of the design has taken place with corresponding improvement of
results. However, the follow-up for the majority of replacements has been less than two years and no retrieved specimens were obtained. Previously, it was noted that the large majority of replacements revised for aseptic loosening occurred after 6 years duration and therefore it has not been possible to determine if uncemented fixation will provide long-term fixation. This discussion, therefore confines itself predominantly to the design of the uncemented system.

The rationale of the design was to ensure the changes in femoral strain were kept to a minimum, transfer load at the prosthesis plateau and provide sufficient initial implant stability to permit osseointegration for long-term implant fixation. Hua studied the strain in cadaveric femora with cementless and cemented massive femoral replacement and concluded that the strain was closer to intact femora with uncemented replacements (Hua and Walker 1991). Similar results were also found with uncemented THRs (Walker et al 1990, Zhou et al 1990, Hua and Walker 1995). Strain in the proximal femur was found to be dependent upon the tightness of the fit in the anterior-posterior and medial-lateral directions (Hua and Walker 1995). However, in studies such as these no biological fixation was simulated. Modelling osseointegrated uncemented THRs using proximal cemented fixation, Zhou identified that there were localised patches of high strain possibly reflecting endosteal contact points (Zhou et al 1990).

All massive replacements of this study were inserted into diaphyseal bone that has a more uniform geometry than the proximal femur and therefore the strain distribution was considered to be more evenly distributed than with THRs. The early radiographic findings agree with Hua with respect to the tightness of fit. The stem of case 5, was tight fitting and examination of the reamed cavity at the operation, showed a near circular cavity predicting a high degree of fit and fill and producing a low and even stress distribution. The near lack of radiographic change in this case would indicate that the change of femoral
strain has been kept to a minimum. In addition, the tight-fit of the stem would have helped initial implant stability.

Initial stability of the replacement is of paramount importance (Walker et al 1990) and initial stability will be dependent upon stem shape, surface finish, the degree of fit and fill of the cavity and load applied to the replacement. Burke noted that the micromotion of cementless THRs was marginally less than cemented THRs when simulating a single limb stance but was much more unstable when simulating activities such as stair climbing that applied torsional loads (Burke et al 1991). Similarly, Phillips found that uncemented THRs were unable to resist torsional loads between 62 and 171% of body weight and were unstable within 800 cycles. Phillips concluded that patients with uncemented replacements should be protected from torsional loading until bony ingrowth has occurred (Phillips et al 1991). Unlike anatomical or custom-made THRs, symmetric stems are known to be inherently less stable (Hua and Walker 1995), and therefore with circular stems additional mechanical fixation is required. Initial mechanical implant stability achieved by tight-fitting stems and anti-rotation lugs is believed to have been successful as indicated by the radiographic results. When initial implant stability was lost as demonstrated by case 4, the result was the development a fibrous tissue interface. Although machining a close tolerance transverse slot in the cortical bone to locate the anti-rotation lug reduced torsional strength of cortical bone, it is considered that integral anti-rotation lugs provided greater implant stability than transverse anti-rotation screws and did not compromise the strength of the IM stem. Anti-rotational screws were used in the later cadaveric trials and early clinical cases, but as a result of screw and bone fracture with both trial and patient replacements, screws were abandoned. Furthermore, studies have shown that a transverse hole with a diameter 1/5th of the shaft bone diameter reduced the intact bone strength by 40% (Hipp et al 1990).
The primary indication for uncemented replacements in this study, were skeletally immature patients, who would require small diameter stems and therefore a transverse hole through the IM stem would seriously compromise stem strength. In the design used by Kay (Kay et al 1994), a transverse anti-rotational screw has been used and no complications were reported, however, all patients treated were skeletally mature.

Similar to Kay's series, hydroxyapatite coating has been used for osseointegration for long-term fixation. The first two Stanmore uncemented replacements were not coated and did not have satisfactory radiographs. Hydroxyapatite coating or a porous ingrowth structure such as madreporic surface used successfully with the Kotz modular uncemented endo-prostheses (Capanna et al 1994) would appear to be an important factor in the design of uncemented replacements.

Unlike Kay's series that had contoured stems matching the natural bow of the femur, all the Stanmore replacements had straight stems in the press-fit region. The decision to have a straight stem was based upon the ability to ream a hole of precise diameter within the femoral cavity. Custom-made rigid reamers were straightforward to machine and the cadaveric studies showed that they performed well with the minimum of bone damage.

Surgical preparation, the design and use of associated tooling were deemed to be important to insert the replacement in its correct anatomical position. Preparation of the medullary cavity results in mechanical and thermal damage of the endosteal bone surface. Careful preparation of the host bone was advocated by Branemark when inserting dental implants (Branemark et al 1977). Furthermore, unlike skeletal implants, dental implant remained unloaded for 3 months to ensure osseointegration (Adell et al 1981). Bone necrosis due to high speed drilling significantly reduced bone ingrowth in the short-term in a animal study conducted by Ohashi (Ohashi et al 1994). For
success of massive endo-prostheses, early bone ingrowth was considered to be paramount to the eventual long-term successful of the fixation. Specialist tooling was designed to ensure that minimal mechanical and thermal damage was done to the bone. Irrigation whilst reaming and milling was performed to reduce heat build-up. Irrigation of saw blades to cool and lubricate the cut bone surface has been shown to significantly improve bony fixation of cementless tibial components (Toksvig-Larsen et al 1994).

The effects of the vascularisation of the reamed femur were also considered to have an effect (Hughes et al 1993). In the early cases (1-4) less extensive reaming was performed and in the femur, a posterior cavity remained to allow for revascularisation. But, due to implant instability, a higher fit and fill of the cavity was required to increase stability. The long term effects on the revascularisation are unknown and a redesign of the stem may be required.

Concurrently, at the time of the introduction of the uncemented system for clinical use, the SMILES rotating hinge was beginning its clinical trials. The rotating hinge by the nature of its design reduces torsional forces at the implant/bone interface (Walker et al 1982) and therefore, rotating hinges were utilised where possible. In contrast to the control group (Chapter 2) the majority of distal femoral and proximal tibial uncemented replacements utilised rotating knee hinges.

The radiographic results were encouraging, particularly with the skeletally immature and revision cases where preservation of bone stock had occurred. The increased shaft diameter at the transition from the precision to the sliding fit regions of the stem would suggest that load is being transferred at this location. The reduction in shaft diameter in the middle of the precision fit region of the stem (case 5) would indicate that stress shielding was occurring. In other cases when abutment of the plateau has not been achieved, the 1-2 mm
gap had within months in-filled with bone and therefore it was considered that load was being transmitted to the stem adjacent to the prosthesis plateau.

The design of custom-made uncemented replacements with its additional customised tooling took longer to produce than custom-made cemented replacements and was therefore more expensive. Although uncemented replacements may initially appear to be more expensive, with increased implant longevity they may be more cost-effective (Gillespie et al 1995). In addition, the majority of patients undergoing limb salvage for bone tumour are in their second or third decades of life and with increasing disease-free survival due to improved adjuvant chemotherapeutic regimes, many of the patients will require their endo-prosthesis to function for many decades. Unlike Kay’s series where the criteria for consideration of an uncemented replacement was a patient with an expected long-term prognosis, young patients with highly malignant tumours were being treated in this study. The target groups for the Stanmore replacements were the young and those that required revision irrespective of life expectancy.

6.3.6. The future of uncemented intra-medullary fixation

This study is part of a long-term commitment to improving the fixation of massive endo-prostheses and continuing evolution of the design is important. The early results have provided encouraging results and highlighted the weakness of the design. Future designs require to address these weakness and rotational stability is considered to be one of the most important. Initial mechanical stability of the replacement is probably essential to permit osseointegration for long-term biological fixation. Three developments are suggested -

- Anatomically shaped intra-medullary stems that would require less bone to be removed and provided rotational stability.
- Longitudinal cutting teeth to assist in the rotational stability.
• Longitudinal grooves, that reduce the stem stiffness and provide channels for revascularisation to occur. The high degree of fit and fill of the stem prevents revascularisation of the endosteal bone surface.

Using computer-aid design and computer aided machining (CAD-CAM) all three modifications could be incorporated in one design thus providing improved initial stability and space for endosteal revascularisation.
Figure 6.1. The design of the original proposed uncemented intra-medullary stemmed replacement.
Figure 6.2. The ovality of the intra-medullary canal at 10% increments along the length of 10 femora. Bars = standard error.
Figure 6.3. The design of the shaped plateau. The concave design was designed to reduce the possibility of longitudinal fracture of the bone.
Figure 6.4 The cross-section of femur illustrating the canal widths as described in the text.
Plate 6.1. A trial uncemented replacement and associated custom-made tools. (Left to right: transverse screw drill guide, the trial implant, sleeve introducer, end miller with pilot (upper), polyethylene sleeve (lower), the precision reamer secured to the universal drill attachment, cannulated rigid drill).
Plate 6.2. A custom-made miller with a precisely fitting pilot to prevent toggle whilst operating the device was used to produce a flat resected bone surface perpendicular to the long axis of the bone shaft.
Plate 6.3. Anti-rotation lugs were used on the uncemented replacements in the later clinical cases. Specialised tooling was required to produce a recess. A close fit was considered essential to obtain initial implant stability.
Plate 6.4. A proximal femoral replacement inserted into a cadaveric femur, undergoing fatigue testing to ensure that the intra-medullary will not fracture under normal use.
Plate 6.5. The first uncoated uncemented endo-prosthesis. This proximal humeral replacement had a screw passed through the aperture in the intra-medullary stem to prevent rotation. The intra-medullary stem was not hydroxyapatite coated.
Plate 6.6. An uncemented extendible distal femoral replacement with hydroxyapatite coating. Note the two sectioned stem, anti-rotation lugs and that the proximal section of the stem has been curved posteriorly to prevent contacting of the anterior endosteal surface of the femur.
Plate 6.7 a & b. Radiographs of a revision distal femoral replacement 1 day (upper) and 9 months (lower) following insertion of the implant. The later radiograph shows extensively bone remodelling with in-filling distally and an increase in bone girth adjacent to the junction of the proximal and distal stem sections.
Plate 6.8. The frontal radiograph of case 4, showing the helical fracture and some bony remodelling. (Implant duration = 2 months). There has been remodelling around the anti-rotation lug, the tip of the intra-medullary stem and a small medial pedicle has developed but has not ingrown.
Plate 6.9. The radiograph of case 5, showing the general lack of remodelling after an implant duration of 14 months. There has been a small reduction in bone girth distally and a slight increase in girth adjacent to the junction of the proximal and distal stem sections.
Table 6.1. The status of the 20 patient with uncemented massive replacements

<table>
<thead>
<tr>
<th>No.</th>
<th>Implant</th>
<th>Status</th>
<th>Duration (months)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>humerus proximal</td>
<td>Died of disease</td>
<td>25.4</td>
</tr>
<tr>
<td>2</td>
<td>femur distal</td>
<td>Died of disease</td>
<td>18.2</td>
</tr>
<tr>
<td>3</td>
<td>femur distal</td>
<td>Revised: aseptic loosening</td>
<td>6.0</td>
</tr>
<tr>
<td>4</td>
<td>femur distal</td>
<td>No prosthetic related problems</td>
<td>40.0</td>
</tr>
<tr>
<td>5</td>
<td>femur distal</td>
<td>No prosthetic related problems</td>
<td>37.0</td>
</tr>
<tr>
<td>6</td>
<td>femur distal</td>
<td>Knee instability</td>
<td>14.8</td>
</tr>
<tr>
<td>7</td>
<td>tibia proximal</td>
<td>Amputation: infection</td>
<td>16.9</td>
</tr>
<tr>
<td>9</td>
<td>humerus proximal</td>
<td>No prosthetic related problems</td>
<td>10.7</td>
</tr>
<tr>
<td>10</td>
<td>humerus distal</td>
<td>No prosthetic related problems</td>
<td>7.7</td>
</tr>
<tr>
<td>12</td>
<td>femur distal</td>
<td>Returned home abroad</td>
<td></td>
</tr>
<tr>
<td>13</td>
<td>humerus proximal</td>
<td>No prosthetic related problems</td>
<td>9.3</td>
</tr>
<tr>
<td>14</td>
<td>femur proximal</td>
<td>Amputation: infection</td>
<td>0.4</td>
</tr>
<tr>
<td>16</td>
<td>tibia mid-shaft</td>
<td>Pain associated with a loose</td>
<td>9.6</td>
</tr>
<tr>
<td></td>
<td></td>
<td>cemented proximal stem</td>
<td></td>
</tr>
<tr>
<td>18</td>
<td>femur distal</td>
<td>No prosthetic related problems</td>
<td>5.4</td>
</tr>
</tbody>
</table>
Table 6.2. The overall radiographic and individual parameter scores of the un cemented intra-medullary stemmed replacements.

<table>
<thead>
<tr>
<th>No.</th>
<th>Implant</th>
<th>Duration (months)</th>
<th>NBF</th>
<th>ISD</th>
<th>RLL</th>
<th>GAP</th>
<th>RSD</th>
<th>Grade (BME)</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>3</td>
<td>DF</td>
<td>3.9</td>
<td>2</td>
<td>3</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>Fair</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>DF</td>
<td>5.3</td>
<td>2</td>
<td>4</td>
<td>5</td>
<td>0</td>
<td>0</td>
<td>Very Poor</td>
<td>Revised 3 weeks later</td>
</tr>
<tr>
<td>4</td>
<td>DF</td>
<td>27.4</td>
<td>1</td>
<td>4</td>
<td>4</td>
<td>0</td>
<td>0</td>
<td>Poor</td>
<td>Fractured femur @ 8 wks</td>
</tr>
<tr>
<td>5</td>
<td>DF</td>
<td>3.7</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>Very Good</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>DF</td>
<td>11.2</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>Very Good</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>DF</td>
<td>17.5</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>2</td>
<td>Good</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>DF</td>
<td>2.8</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>0</td>
<td>0</td>
<td>Good</td>
<td>Increased bone density</td>
</tr>
<tr>
<td>6</td>
<td>DF</td>
<td>14.8</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>0</td>
<td>0</td>
<td>Good</td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>PT</td>
<td>17.2</td>
<td>2</td>
<td>2</td>
<td>0</td>
<td>0</td>
<td>3</td>
<td>Fair</td>
<td>Infected</td>
</tr>
<tr>
<td>8</td>
<td>PT</td>
<td>11.9</td>
<td>0</td>
<td>2</td>
<td>0</td>
<td>2</td>
<td>3</td>
<td>Fair</td>
<td></td>
</tr>
<tr>
<td>10</td>
<td>DH</td>
<td>11.6</td>
<td>1</td>
<td>2</td>
<td>4</td>
<td>0</td>
<td>1</td>
<td>Poor</td>
<td></td>
</tr>
<tr>
<td>11</td>
<td>PF</td>
<td>1.2</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>No Change</td>
<td></td>
</tr>
<tr>
<td>11</td>
<td>PF</td>
<td>9.7</td>
<td>2</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>Excellent</td>
<td>Pedicle not attached</td>
</tr>
<tr>
<td>13</td>
<td>PH</td>
<td>6.2</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>Very Good</td>
<td></td>
</tr>
<tr>
<td>16</td>
<td>M-S T</td>
<td>6.7</td>
<td>1</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>Improved</td>
<td>2mm plateau gap in-filled</td>
</tr>
<tr>
<td>18</td>
<td>DF</td>
<td>2.9</td>
<td>0</td>
<td>0</td>
<td>4</td>
<td>2</td>
<td>0</td>
<td>Fair</td>
<td>Porotic (medial)</td>
</tr>
<tr>
<td>18</td>
<td>DF</td>
<td>5.4</td>
<td>0</td>
<td>0</td>
<td>3</td>
<td>2</td>
<td>1</td>
<td>Good</td>
<td>Increased bone density</td>
</tr>
</tbody>
</table>

NBF = new bone formation or pedicle, ISD = increased shaft diameter, RLL = radiolucent lines, GAP = plateau gap, RSD = reduced shaft diameter, Grade = Biomedical Engineering radiographic assessment grade. wks = weeks.

DF = distal femoral, PF proximal femoral, PT = proximal tibial, M-S T = mid-shaft tibial, PH = proximal humeral, DH = distal humeral.
Table 6.3. A matched comparison of radiographs of un cemented and cemented replacements. (Lower limb primary replacements only).

<table>
<thead>
<tr>
<th>Number</th>
<th>Replacement</th>
<th>Age</th>
<th>Resect</th>
<th>Sex</th>
<th>Knee type</th>
<th>Coat</th>
<th>Duration</th>
<th>CON</th>
<th>ADV</th>
<th>NBF</th>
<th>ISD</th>
<th>RLL</th>
<th>GAP</th>
<th>RSD</th>
<th>BME X-ray grade</th>
</tr>
</thead>
<tbody>
<tr>
<td>4</td>
<td>Distal femoral</td>
<td>10</td>
<td>M</td>
<td>Smiles</td>
<td>HA</td>
<td>27.4</td>
<td>4</td>
<td>4</td>
<td>1</td>
<td>4</td>
<td>4</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>POOR</td>
</tr>
<tr>
<td>11</td>
<td>Distal femoral</td>
<td>53</td>
<td>F</td>
<td>Stanmore</td>
<td>Unc</td>
<td>29.7</td>
<td>4</td>
<td>5</td>
<td>4</td>
<td>0</td>
<td>5</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>VERY POOR</td>
</tr>
<tr>
<td>12</td>
<td>Distal femoral</td>
<td>61</td>
<td>M</td>
<td>Stanmore</td>
<td>Unc</td>
<td>34.6</td>
<td>5</td>
<td>2</td>
<td>5</td>
<td>3</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>0</td>
<td>GOOD</td>
</tr>
<tr>
<td>11</td>
<td>Distal femoral</td>
<td>54</td>
<td>M</td>
<td>Stanmore</td>
<td>Unc</td>
<td>13.3</td>
<td>4</td>
<td>3</td>
<td>2</td>
<td>4</td>
<td>3</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>FAIR</td>
</tr>
<tr>
<td>5</td>
<td>Distal femoral</td>
<td>10</td>
<td>M</td>
<td>Smiles</td>
<td>HA</td>
<td>17.5</td>
<td>1</td>
<td>2</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>2</td>
<td>GOOD</td>
</tr>
<tr>
<td>10</td>
<td>Distal femoral</td>
<td>79</td>
<td>F</td>
<td>Stanmore</td>
<td>Unc</td>
<td>12.0</td>
<td>2</td>
<td>4</td>
<td>2</td>
<td>1</td>
<td>4</td>
<td>2</td>
<td>0</td>
<td>0</td>
<td>POOR</td>
</tr>
<tr>
<td>11</td>
<td>Distal femoral</td>
<td>54</td>
<td>M</td>
<td>Stanmore</td>
<td>Unc</td>
<td>13.3</td>
<td>4</td>
<td>3</td>
<td>2</td>
<td>4</td>
<td>3</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>FAIR</td>
</tr>
<tr>
<td>11</td>
<td>Distal femoral</td>
<td>50</td>
<td>M</td>
<td>Stanmore</td>
<td>Unc</td>
<td>9.1</td>
<td>9</td>
<td>3</td>
<td>9</td>
<td>2</td>
<td>0</td>
<td>2</td>
<td>3</td>
<td>0</td>
<td>FAIR</td>
</tr>
<tr>
<td>8</td>
<td>Proximal tibial</td>
<td>17</td>
<td>F</td>
<td>Smiles</td>
<td>HA</td>
<td>11.9</td>
<td>2</td>
<td>3</td>
<td>0</td>
<td>2</td>
<td>0</td>
<td>2</td>
<td>3</td>
<td>0</td>
<td>GOOD</td>
</tr>
<tr>
<td>17</td>
<td>Proximal tibial</td>
<td>49</td>
<td>F</td>
<td>Stanmore</td>
<td>Unc</td>
<td>19.3</td>
<td>2</td>
<td>0</td>
<td>2</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>IMPROVED</td>
</tr>
<tr>
<td>18</td>
<td>Proximal tibial</td>
<td>50</td>
<td>M</td>
<td>Stanmore</td>
<td>Unc</td>
<td>11.3</td>
<td>6</td>
<td>2</td>
<td>0</td>
<td>6</td>
<td>0</td>
<td>2</td>
<td>0</td>
<td>0</td>
<td>GOOD</td>
</tr>
<tr>
<td>18</td>
<td>Proximal tibial</td>
<td>46</td>
<td>M</td>
<td>Stanmore</td>
<td>Unc</td>
<td>14.7</td>
<td>4</td>
<td>3</td>
<td>4</td>
<td>2</td>
<td>2</td>
<td>3</td>
<td>0</td>
<td>0</td>
<td>FAIR</td>
</tr>
<tr>
<td>11</td>
<td>Proximal femoral</td>
<td>16</td>
<td>M</td>
<td>HA</td>
<td>9.7</td>
<td>2</td>
<td>0</td>
<td>2</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>EXCELLENT</td>
<td></td>
</tr>
<tr>
<td>18</td>
<td>Proximal femoral</td>
<td>46</td>
<td>M</td>
<td>Unc</td>
<td>7.8</td>
<td>4</td>
<td>2</td>
<td>4</td>
<td>1</td>
<td>0</td>
<td>2</td>
<td>1</td>
<td>0</td>
<td>GOOD</td>
<td></td>
</tr>
<tr>
<td>16</td>
<td>Midshaft tibial</td>
<td>14</td>
<td>F</td>
<td>HA</td>
<td>6.7</td>
<td>1</td>
<td>0</td>
<td>1</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>IMPROVED</td>
<td></td>
</tr>
<tr>
<td>14</td>
<td>Midshaft tibial</td>
<td>52</td>
<td>M</td>
<td>Stanmore</td>
<td>Unc</td>
<td>6.4</td>
<td>5</td>
<td>2</td>
<td>5</td>
<td>0</td>
<td>0</td>
<td>2</td>
<td>0</td>
<td>0</td>
<td>GOOD</td>
</tr>
<tr>
<td>13</td>
<td>Midshaft tibial</td>
<td>52</td>
<td>F</td>
<td>Stanmore</td>
<td>Unc</td>
<td>7.5</td>
<td>0</td>
<td>2</td>
<td>0</td>
<td>0</td>
<td>2</td>
<td>2</td>
<td>0</td>
<td>0</td>
<td>GOOD</td>
</tr>
<tr>
<td>13</td>
<td>Midshaft tibial</td>
<td>58</td>
<td>M</td>
<td>Stanmore</td>
<td>Unc</td>
<td>10.3</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>0</td>
<td>0</td>
<td>GOOD</td>
</tr>
<tr>
<td>3</td>
<td>Distal femoral</td>
<td>19</td>
<td>M</td>
<td>Smiles</td>
<td>HA</td>
<td>5.3</td>
<td>2</td>
<td>5</td>
<td>2</td>
<td>4</td>
<td>5</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>VERY POOR</td>
</tr>
<tr>
<td>19</td>
<td>Distal femoral</td>
<td>36</td>
<td>M</td>
<td>Stanmore</td>
<td>Unc</td>
<td>6.5</td>
<td>5</td>
<td>3</td>
<td>5</td>
<td>5</td>
<td>3</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>FAIR</td>
</tr>
<tr>
<td>20</td>
<td>Distal femoral</td>
<td>58</td>
<td>M</td>
<td>Stanmore</td>
<td>Unc</td>
<td>8.5</td>
<td>5</td>
<td>1</td>
<td>5</td>
<td>4</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>VERY GOOD</td>
</tr>
<tr>
<td>16</td>
<td>Distal femoral</td>
<td>52</td>
<td>F</td>
<td>Stanmore</td>
<td>Unc</td>
<td>7.8</td>
<td>5</td>
<td>4</td>
<td>5</td>
<td>2</td>
<td>0</td>
<td>2</td>
<td>0</td>
<td>0</td>
<td>GOOD</td>
</tr>
<tr>
<td>7</td>
<td>Proximal tibial</td>
<td>10</td>
<td>F</td>
<td>Smiles</td>
<td>HA</td>
<td>17.2</td>
<td>2</td>
<td>3</td>
<td>2</td>
<td>2</td>
<td>0</td>
<td>0</td>
<td>3</td>
<td>0</td>
<td>FAIR</td>
</tr>
<tr>
<td>11</td>
<td>Proximal tibial</td>
<td>48</td>
<td>F</td>
<td>Stanmore</td>
<td>Unc</td>
<td>17.3</td>
<td>2</td>
<td>2</td>
<td>0</td>
<td>2</td>
<td>2</td>
<td>0</td>
<td>2</td>
<td>0</td>
<td>GOOD</td>
</tr>
<tr>
<td>11</td>
<td>Proximal tibial</td>
<td>62</td>
<td>F</td>
<td>Stanmore</td>
<td>Unc</td>
<td>10.8</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>0</td>
<td>GOOD</td>
</tr>
<tr>
<td>12</td>
<td>Proximal tibial</td>
<td>62</td>
<td>F</td>
<td>Stanmore</td>
<td>Unc</td>
<td>19.7</td>
<td>12</td>
<td>3</td>
<td>2</td>
<td>0</td>
<td>3</td>
<td>0</td>
<td>3</td>
<td>0</td>
<td>FAIR</td>
</tr>
</tbody>
</table>
Chapter 7

Extra-cortical plated massive endo-prosthetic replacements
7.1. Introduction

The first Stanmore custom-made massive endo-prosthetic replacements used extra-cortical fixation. One distal femoral replacement with two extra-cortical plates was inserted in 1954 and was revised 21 years later. Furthermore, the young lady led a full and an active life and after revision of the extra-cortical plated replacement continued to so. This remarkable case, was the inspiration to investigate the extra-cortical fixation to provide an alternative method of fixation, taking advantage of improved materials, manufacturing techniques and bioactive coatings.

7.1.1. Extra-cortical fixation of the first Stanmore massive replacements.

Seven extra-cortical plated femoral replacements were designed, fabricated and inserted at the Royal National Orthopædic Hospital at Stanmore between September 1951 and December 1962. The pathology of the 4 proximal femoral and 1 of the 3 distal femoral replacements was neoplasia, the pathology of the two remaining distal femoral cases were hydatid disease and rheumatoid arthritis.

The first proximal femoral replacement shaft had an acrylic shaft with two cobalt chrome plates positioned on the medial and lateral aspects of the femoral shaft. All of the remaining proximal femoral shaft bodies were fabricated in CoCrMo and each had 2 plates, one medial and one laterally, which were secured with three transverse screws. In one case the plates were fenestrated. The first distal femoral replacement had an acrylic body, a knee hinge fabricated in nylon and two extra-cortical plates fabricated in stainless steel. The second and third distal femoral replacements were fabricated entirely in CoCrMo. All plates were secured with transverse screws that passed through both plates, positioned on the medial and lateral aspects of the femur.
The results of these femoral replacements were mixed. Two patients died (6 and 71 months) and all remaining cases failed. Two patients (1 PF and 1 DF) had their limbs amputated because of infection (12 and 15 months). In a further case, the replacement was removed after the remaining femur collapsed and the prosthesis had ruptured the skin. However, this prosthesis had been used satisfactory for over 10 years. In the two remaining cases, the prostheses were revised with cemented intra-medullary stemmed replacements after the extra-cortical plates had fractured, they were revised after 65 months and 251 months. The radiographic appearance of the long-term surviving distal femoral replacement (Plate 7.1), showed bone overgrowth at the tip of the lateral plate and some bone resorption adjacent to the prosthesis plateau. At the time of revision, bone was not osseointegrated with the plates and a fibrous tissue interlayer was present.

The first review of the Stanmore was conducted in 1968 by Jackson Burrows (Jackson Burrows 1968), and this was followed by a more extensive review of proximal femoral and humeral replacements in 1975 (Jackson Burrows et al 1975). This important paper, reviewed 24 bone tumour limb salvage cases, including both the extra-cortical plated prostheses and the first 16 implants that used intra-medullary stem fixation. They identified that the extra-cortical plated cases loosened as a result of bone resorption under the plates, of which 3 were humeral and 1 femoral. It was suggested that the bone resorption was a result of dividing the endosteal blood supply and the plates restricted the periosteal blood supply. When the blood supplies could be preserved resorption did not occur.

7.1.2. Aim

The initial aim of this long-term study was to -

- propose a number of designs and select the most favourable
- evaluate the selected designs using an animal model
7.1.3. Purpose

The purpose of the study was to demonstrate an alternative method of massive endo-prosthetic replacement fixation that would have increased longevity.

7.1.4. Intra-medullary versus Extra-cortical

There are a number of advantages of using extra-cortical fixation, over intra-medullary stemmed fixation either cemented or press-fit.

Blood supply and mechanical damage. Limb salvage has a pronounced and destructive effect on the blood supply (Jackson Burrows et al 1975). The normal blood supply to the long bones is via three sources (Rhinelander and Wilson 1982). Metaphyseal vessels supply blood to the cancellous bone of the metaphysis, whilst the cortical bone blood supply comes from the nutrient artery and the periosteum. At the origins and insertions of muscles, it is believed that the outer one-third of the cortex is supplied by periosteal vessels. The major cortical blood supply comes from the nutrient artery that enters the medullary canal in the region of the mid-shaft and branches. The branching blood vessels anastomose with the periosteal blood supply, resulting in a centrifugal flow from the endosteal surface to the periosteal surface. Resecting the long bone and filling the cavity with a cemented intra-medullary stem severely curtailed the blood supply (Blunn et al 1991). Revascularisation of the intra-medullary blood supply was virtually prevented due to the cement blocking the canal after the insertion of a THR (Rhinelander et al 1979). The effect of inserting a THR has little effect on the metaphyseal blood supply, but the diaphyseal blood supply was completely destroyed resulting in bone necrosis.

Using extra-cortical plates for fixation, it was considered there would be less damage to the cortical bone blood supply. In addition, the endosteal bone will not have been damaged by the exothermic reaction of the curing acrylic cement,
or by the mechanical and thermal damage caused by reaming that resulting in bone necrosis.

The location of the transmission of forces. The transmission of forces from the bone to the implant can be optimised by positioning of the plates around the shaft. With intra-medullary stemmed fixation the positioning of the stem within the canal is limited.

Revisability. Extraction of intra-medullary stems and bone cement from deep within medullary canal can be problematic and time consuming. Revising a prosthesis with extra-cortical plates may present the surgeon with fewer problems partly as a result of access. As there will be no damage to the intra-medullary canal then conventional intra-medullary methods of fixation can be employed if required.

Bone shape. One of the major disadvantages of the press-fit intra-medullary stems is the inability to obtain a secure fit when the canal diverges out in the metaphyseal regions of the bone. Using extra-cortical plates these can be designed and manufactured to take into account the geometry of the bone.

Disadvantages. The possible disadvantages of extra-cortical plates would include the more extensive exposure of the bone required to fit the plates. The periosteum and its associated blood supply would be disrupted when peeled back and the underlying bone would be devascularised causing bone resorption (Jackson Burrows et al 1975).

7.2. Design Rationale

Two major designs were put forward, these were -

- plated models
- 'basket' models.
7.2.1. Plated design

A number of parameters were considered and included -

- number of plates
- position of the plates
- plate design (taper, internal/external radii)
- material
- initial and long-term fixation.

Initially, the number of plates suggested varied from one large plate to many thin elongated plates. Designs with 2 and 3 plates were considered to be the most favourable. A design with one plate, had the disadvantages of instability and the large continuous coverage of bone leading to periosteal necrosis, stress-shielding and complexities in manufacture. A design using many narrow plates was unacceptable, due to increased possibility of plate fracture and/or screw fracture. The two and three plated designs provided a similar coverage of bone to that of the one plated design, but divided would permit revascularisation across a smaller area. The position of the plates depended upon the location of the resection and the number of plates. The surface shape of the femur permitted fixation of the plates on all aspects, with the exception of the posterior due to the prominence of the linear aspera. The factors taken into account were -

- was the plate in tension or compression?
- would it be subjected to a large bending moment?
- would there be access to secure the plate?

On both the two and the three plated designs, one plate would be positioned on the anterior surface restraining movement in the sagittal plane and the second located on the postero-lateral surface restraining movement in the coronal and
sagittal planes. If a third plate was required this would be positioned on the postero-medial surface providing additional support. The position of the plates on the original replacements were medial and lateral, this was considered disadvantageous in terms of implant stability and screw fracture. Anterior-posterior movement of the replacement would only be restrained by screws that would be in shear (Figure 7.1).

The proposed extra-cortical plates were designed to be of unequal lengths, the breadth tapered and each plate would have 2 longitudinal grooves to assist revascularisation (Figure 7.2). The original proposed design had plates that were recessed and bolted into the shaft body of the prosthesis, to permit revision in the event of a plate fracture. Furthermore using this method there would not be a radius at the plate/plateau junction. However, due to strength considerations, machining complications and the possibility of cold welding, integral plates were chosen. The material selected was titanium alloy as a result of its biocompatibility, its modulus, its compatibility with other materials and its ease of machining. Cobalt chrome alloys were considered too stiff and hard to machine, stainless steel alloys, although improved, were rejected as a result of the galvanic reaction with dissimilar metals. Polymeric materials were rejected due to the poor strength.

Osseointegration for long-term fixation was considered to be paramount and therefore initial stable fixation of the plates was required. Anti-rotation lugs were considered to provide insufficient stability. Lugs had been used successfully to prevent rotation on the tight fitting un cemented IM stems. The 'loose' fit nature of the plates required more substantial initial fixation and therefore the alternative to lugs was uni-cortical screws. Uni-cortical titanium cortical screws allowed for greater versatility than transverse screws as used the early replacements. Transverse screws would restrict non-homogenous movement within the structure of the femur and in addition, plates would need to be parallel to each other, restricting the location of the plates. Some concern
over the shear fracturing of the screws was expressed, however, initially patients would not be permitted to fully weight bear providing time for osseointegration to occur. In addition, it considered that after complete osseointegration of the plates, transmitted load via the plates would reduce the likelihood of screw fracture. The plates were hydroxyapatite coating to encourage osseointegration.

7.2.1.1. Basket design

The 'basket' design, was a tubular construction that encircled the bone. The initial design was circular in cross-section, that was longitudinally slotted in the mid-section of the tube, keeping the upper rim intact to maintain its structural strength (Figure 7.3). The first proposed design had a flat rim and the length of the tubular section was 60 mm with a wall thickness of 3 mm tapering to 2 mm. This design was later modified with a rim that angled down from the lateral to the medial. Uni-cortical screws were required for initial stability to permit long-term stability through osseointegration of the hydroxyapatite coating, applied to all basket surfaces. The disadvantages of a circular cross-section was that it was unable to resist rotation and it did not conform to the cross-sectional shape of the femur resulting in a small contact area. In addition, the linear aspera required either removal or to be encompassed within the basket.

Anatomical basket

With the increasing use and wider availability of computerised tomography (CT), an anatomically shaped basket produced using computer controlled milling machines was developed. The anatomically shaped cross-section basket could be produced with either parallel or flaring side walls (Figure 7.3). Anatomically shaped baskets had a number of advantages over the circular baskets. The close proximity to the shaft of the individualised anatomically shaped basket would osseointegrate rapidly. Torsional resistance due to the basket shape would be enhanced. Disadvantages, would be availability of CT
scans, the greater complexity in designing and machining, and restrictions to the tube depth that could be.milled with conventional tooling. Furthermore, the basket design would have extensive coverage of the shaft bone leading to stress shielding and possible devascularisation due to periosteal disturbance.

7.3. Experimental Studies

7.3.1. Laboratory

Photo-elastic coating, frozen stress modelling and fatigue tests were carried out by BSc students under the supervision of P.Unwin and Dr G.Blunn of the Department of Biomedical Engineering.

7.3.2. Animal model

The rationale for -

- an animal model

The primary reason for the animal was to evaluate the proposed designs in a model that was similar in size to that of a human and so the bone/implant could be retrieved for histological examination. There are a number of advantages in using an large animal model, such as a goat or a sheep. The orientation of the tibiae are generally vertical, the body weight is applied to the limbs in a biphasic manner similar to that in humans (Bergmann et al 1985). Further considerations, were the surgical access and rehabilitation.

- goats over other mammals

Goats are similar in body weight (40-70 kg depending upon the breed) to that of a small human and the tibia is a similar diameter. In addition, goats have no fibula. Goats are relatively intelligent and it was considered that this would be important while rehabilitating. Goats are
high browsers and regularly stand on their rear legs to reach vegetation and therefore loading the implant in a similar manner to a biped.

7.3.2.1. Methodology. The goat study.

To assess the various proposed models in-vivo, a goat model was used. A mid-shaft replacement had the advantages of allowing an experimental fixation device at one end and a cemented intra-medullary stem acting as a control at the other. Furthermore, the replacement did not require a joint replacement that would have been complex to design and manufacture and would lead to more complex surgery and rehabilitation. Each of the goats would have their right mid-shaft tibia replaced and after a period of six months culled. Both tibiae were to removed for histological examination. Bone marking by injection twice within the six months would provide data on the bone remodelling in response to the plates. At the time of culling the blood supply to the tibiae would be labelled with barium sulphate to assess the vascular network.

The implants

The mid-shaft tibial implants were individually designed from lateral measurement radiographs and fabricated in the Departmental workshops. Only lateral radiographs were required, as prior to the design of the first goat replacement, cadaveric tibiae had been obtained for examination of the size and shape of the medullary canal and outer cortex. These specimens were used as a basis for the design taking into scaling and radiographic magnification. In addition, the section of bone resected from the mid-shaft of the tibial at each operation were retained for future reference of the cross-section shape and bone density.

All extra-cortical plated replacements inserted, were either 2 or 3 plated (Table 7.1). All plates were 12 mm wide with a concave inner surface and secured with two uni-cortical screws. Plate length of 2 plated designs were 60 mm and
50 mm, while those with 3 plates were 60 mm, 50 mm and 50 mm. Initially, plates were grooved but later, these changed to slots to permit osseointegration, reduce the longitudinal stiffness and reduce the bone area coverage (Plate 7.2). Each slotted plate had two parallel slots 2 mm wide. The lengths of the slots were dependent upon the location of the screw holes. Dimensions of the plates are detailed in Table J.1 of Appendix J.

One anatomical basket replacement was designed and manufactured but was not inserted due to death of the animal during surgery. This implant was designed using computer aided techniques. Cross-section profiles obtained from contact radiograph thin sections of a cadaveric goat tibia were scaled to fit the measurements obtained from the measurement radiographs of the chosen goat. Using CAD and a tool-path generation software package (Quicksurf), the tool-path was calculated to produce a tapered anatomically shaped basket. The machining tool-path comprised of three components, these were an outer path that removed the bulk of the material external to the basket and two inner paths that removed material from the inner. The complete tool-path file was downloaded to a 4 axis Fadal computer numeric controlled (CNC) milling machine and a prototype basket component was machined in polyethylene. Encouraged by the results of the prototype (Plate 7.3), a second component was machined in titanium alloy (Ti 318). The walls were slotted and later entirely coated in hydroxyapatite (plate 7.4). After the death of the goat, the tibia was transected at the appropriate location and the component fitted. The anatomically shaped basket component fitted snugly without being tight and was rotationally stable.

7.3.2.2. Surgical procedure

The operative procedure describing the insertion of a goat mid-shaft tibial replacement is described in Appendix J.
7.3.2.3. In-vivo

Radiographic

After 2 months and again after 4 months post-operatively the goat were placed under heavy sedation (xylazine) and the right hind limb X-rayed.

Bone marking

Agents to lay down coloured annuli in bone identifiable in histological sections to quantify bony remodelling, were administered twice, once at 2 months and with a different agent after 4 months. The agents used were Oxytetracycline, Calcein and Dedomycin. All agents were administered by subcutaneous injection, daily for a period of three days.

7.3.2.4. Retrieval study and blood supply labelling

After six months, the animal was culled, using an intra-venous overdose of pentobarbitone sodium (Euthatal, Rhone Merviaux, 0.25 ml/kg). Once the animal had been certified dead by the three independent methods, the abdominal wall adjacent to the inguinal groove on the affected side was opened and the femoral artery and vein identified. On isolation of the two blood vessels, a soft cannulae was inserted into the artery, barium sulphate/heparin solution was then administered at a pressure of 105 mg/Hg. The femoral vein was severed and once the barium sulphate appeared as a steady flow and undiluted by blood, both vessels were tied off. The contra-lateral limb was then processed in the same way, which allowed a direct comparison of the blood systems. Both limbs were removed, roughly defleshed, radiographed and then fixed in formalin in preparation for histological examination.

7.3.2.5. Histology

The retrieved tibiae were sectioned into 6 mm sections using an Exact saw. Contact radiographs of the sections were obtained. The specimens were then
processed for calcified and decalcified histological examination (Sections and contact radiographs prepared by histology staff).

To calculate the percentage of coverage the plates were sub-divided into 3 zones. These were - a) the internal concave surface, b) the plate edges and c) the external convex plate surface (Figure 7.4). The lengths of the plate surface and bone contact were measured and the percentage of contact, calculated. Slots and screws were not included in the contact length.

7.3.3. Results

Ten goats with extra-cortical plated mid-shaft replacements were culled (Plate 7.5), 3 of which were premature due rotational instability of the cemented distal intra-medullary stem. The average duration of those that reached full duration was 182 days (range 152 to 214 days).

7.3.3.1. Contact radiographs

Seven complete sets of contact radiographs were available for review (Plate 7.6). Extensive bone remodelling had occurred and many sections through the extra-cortical plates showed the plates encompassed by cortical bone (Table 7.2). There was integration of bone with the plates that appeared to increase from the plateau to the plate tip, although on some plates the bony attachment was localised.

Observed in the majority of the distal sections was cavitation along the internal surfaces of the plates and extensive cortical extension. This cortical extension manifested in a similar appearance to that of a bony cyst. It had a well defined rim and with internal cavity that was segregated from the medullary canal. Osteopaenia and cortical bone loss was present distally in the majority of cases.
The majority of the plate tips were integrated into the cortical bone. Mid-stem sections were transitional between the plateau and the plate tip sections. The slotted plates had bone within the slots of all plates.

The external, internal and plate edges at the plate tips had a higher percentage of plate in direct contact with bone than sections adjacent to the plateau (Table 7.3). On the plate edges there was a higher percent of bone coverage at all levels along the length of the plates. However, between different plates of the same transverse section, the percentage of bony contact length could vary considerably. In addition, between cases the range of coverage was extensive. The case with the stiffest plates (G7) had overall, more bony contact adjacent to the plateau and less at the plate tips. The more moderately flexible plates, that were slotted, generally, had the plate tips incorporated into the tibial cortex. Case G29, had extensive bone overgrowth, but had minimal bone apposition and was considered to be loose distally although the tips of the plates appeared incorporated into the tibial cortex.

There was no difference between the 2 plated and 3 plated replacements, in terms of percentage of bone apposition.

7.4. Clinical Application

During the animal model study, a case of a girl with an extensive bone tumour of the distal femur was presented for limb salvage reconstruction. The extensive nature of the tumour indicated that 73% of the distal femur required resecting. Possible reconstructive methods were -

1. A 'rhino-horn' medullary stem
2. A total femoral replacement
3. An extra-cortical plated replacement.
Due to age of the patient, the damage caused to the growth plates in the remaining proximal femur caused by mechanical and thermal damage whilst securing the 'rhino-horn' shaped intra-medullary stem was considered to be unsatisfactory. A total femoral replacement would negate the need for fixation, but acetabular reconstruction would be required. The prognosis of the girl was reasonable and therefore if she did survive her disease then she could expect to survive 7 or more decades and therefore to replaced a healthy acetabulum at such an early age again was considered unsatisfactory. Using extra-cortical fixation it was considered that the growth plates and associated blood supply would be undamaged and the hip joint would remain intact. If failure of the extra-cortical plated implant did occur then conversion to a total femoral replacement was still an option.

Encouraged by the early results of the animal study, a proposed design of a three plated prosthesis was submitted for discussion (Figure 7.5). The plates positioned on the lateral, posterior and slightly lateral to anterior. In addition, a small basket 3 mm deep would be produced to restrict any movement of the remaining femur distally.

Due to the extensive tumour, the resection level was 94 mm distal from the top of the femoral head, leaving a short segment of bone onto which the plates had to be secured. The plates were slotted and 2 screws holes in each. Hydroxyapatite coating was applied to all surfaces of the plates and to the grooved proximal shaft.

The limb salvage operation was performed in late 1994, and the girl was the first patient for 32 years to receive an extra-cortical plated Stanmore massive endo-prosthetic replacement. The resection of the distal femur was performed according to plan and the implant was then positioned in the correct anatomical location. The plate tips fitted tightly against the cortex and once secured by the screws, the implant was stable under provocation.
Rehabilitation of the patient was slow due in part to the chemotherapy treatment but also as a precautionary measure. During the months following the limb salvage procedure, the limb strengthened and the patient had been weight-bearing on the limb. Examination of radiographs taken after 6 months did not show the extensive bone remodelling observed in the animal model (Plate 7.7). The most marked change from the discharge radiographs was the small degree of bone resorption observed in the lateral cortex adjacent to the prosthesis plateau. No bone remodelling at the plate tips was identified.

7.5. Discussion

This initial phase of this long-term study has shown that the concept of extra-cortical fixation is achievable and is worthy of further investigation. However, the first custom-made massive Stanmore endo-prostheses, had used this method of fixation and had showed that the concept was achievable with extraordinary long-term success of one distal femoral replacement. Modification to these early designs, included a change to hydroxyapatite coated titanium alloy plates, repositioning of the plates and uni-cortical screws. The early results of this study, would indicate that these changes have been advantageous. Osseointegration of the plates in the animal model has been achieved and no plate fracture has occurred. The plates of the original replacements were mechanically secure but were known to fracture and they were not biologically attached (Wilson pers comm). The early results of the recent distal femoral replacement case were satisfactory and there had been no indication that the fixation was unstable and it is unknown if osseointegration of the plates has occurred.

The goat model was considered to be a successful model to demonstrate the fixation of extra-cortical plates. Remarkably, the goats stood within hours of the limb salvage procedure and within the week were partially weight-bearing. Normally within one month of the operation the goats had returned to near
pre-operative activity and mobility levels. The ability to stand upon their hind legs adequately demonstrated that a substantial load was being transmitted via the replacement. The only major complication was the cemented intra-medullary stemmed fixation. Rotational instability of the cemented component resulting from the lack of interdigitation in the near circular medullary canal led to the early termination of three goats.

Extensive bony remodelling observed in the goat model may be considered to un-representative of remodelling that may be expected to occur in humans. The cyst-like cortical extensions observed in a number of cases between plates adjacent to the plateau are not understood. They may have formed as reaction to the peeling back of the periosteum that may or may not be linked with revascularisation, or are a product of bony remodelling.

In this small series the number of plates or plate stiffness did not appear to have an effect on ingrowth or remodelling. The flexural stiffness of the plates was related to the material modulus and the direction of force applied to the cross-sectional area of the plate (second moment of area). For example the anterior plate will be most flexible when a force is applied in the antero-posterior direction and stiffest when applied in the medio-lateral direction.

The screws required to secure the implant for initial fixation did have a minimal effect causing some cavitation along the internal surface of the plate. Slotting of the plates increased the contact area and was considered to increase the stability of the replacement. Cortical osteopaenia or complete bone loss adjacent to the plate inner surface did occur and was most extensive and frequent in sections adjacent to the prosthesis plateau. Stress shielding and devascularisation of the outer cortex are suggested to be the primary causes of this adverse bony remodelling. In contrast, at the tips of the plates dense cortical bone was identified in close contact suggesting that load bearing was transmitted in the proximal region of the plates.
At present, there is insufficient data to suggest the optimum number of plates required for long-term fixation. The three plated design provided greater stability when tested at the time of insertion but may result in greater osteopaenia due to stress-shielding or ischaemia due to damage of the periosteal blood supply.

The use of temporary fracture fixation plates has been well documented. One recent study using dual-energy x-ray absorptiometry has identified that the bone mineral content (BMC) of cortical bone which had been plated and the plate removed within 14 days of scanning showed a higher BMC than in controls (Janes et al 1993). This indicates that demineralisation resulting from stress-shielding did not occur. This has important implications for this study indicating that ischaemia may be an important factor initially that will have long-term implications. Extensive work using the animal model developed in this initial phase of the work programme will be required to establish the cause of the extensive bone remodelling that has occurred adjacent to the internal surface of the extra-cortical plates.

7.6. Future work

This study is continuing with extensive histological examination of the transverse sections are being carried out using scanning electron and light microscopy. Further modifications to the goat implants are to include a reduction in the plate width and breadth.
Figure 7.1. The cross-section of a femur with a lateral and medial extracortical plate demonstrating that with an antero-posterior force the fixation screws are subjected to a shear force.
Figure 7.2. The design of the extra-cortical plated replacement for use in the animal model.
Figure 7.3. The designs of the cylindrical (left) and anatomic shaped extra-cortical basket (right) components.
Figure 7.4. A cross-section of an extra-cortical plate showing the bone apposition zones.
Figure 7.5. The 3 plated design used for reconstruction of the right distal femur of a 10 year old girl with osteosarcoma.
Plate 7.1. A radiograph of an extra-cortical plated distal femoral replacement (Implant duration 18 years). The femoral and tibial plates were secured with transverse bolts. Bone had encased the proximal tip of the medial femoral plate. (Plate 1.1 provides shows this in greater detail).
Plate 7.2. A extra-cortical plated mid-shaft tibial replacement with 3 proximal plates and a distal intra-medullary stem. The hydroxyapatite coating covered all plate surfaces, the plateau and the proximal shaft.
Plate 7.3. An anatomically shaped basket viewed looking into the basket. This trial was fabricated in polyethylene and machined by computer controlled milling machine. (Top = proximal, right = medial).
Plate 7.4. A disassembled anatomically shaped basket fabricated in titanium alloy and coated in hydroxyapatite ceramic.
Plate 7.5. A radiograph of a extra-cortical plated mid-shaft tibial replacement in a goat model. This three plated design was secured to the proximal tibia with uni-cortical screws. Bone has begun to developed over the posterior plate and around the implant shaft. (Implant duration = 3 months).
Plate 7.6. A contact radiograph of a transverse section through a retrieved extra-cortical plated mid-shaft tibial replacement. The goat was culled 6 months following implantation. Note the bony attachment of the antero-medial plate (upper right), and the vascularisation of the cortex adjacent to the inner surfaces of the posterior and lateral plates.
Plate 7.7. A radiograph of the extra-cortical plated distal femoral replacement that was the first of its kind to be used for over 3 decades (implant duration = 4 months). There was some periosteal activity with some bone forming around but not into the anterior plate.
Table 7.1. A summary of the extra-cortical plated replacements.

<table>
<thead>
<tr>
<th>Implant</th>
<th>Number of plates</th>
<th>Maximum plate thickness (mm)</th>
<th>Minimum plate thickness (mm)</th>
<th>Slotted</th>
</tr>
</thead>
<tbody>
<tr>
<td>G73</td>
<td>3</td>
<td>2.0</td>
<td>1.25</td>
<td>No</td>
</tr>
<tr>
<td>G77</td>
<td>2</td>
<td>2.0</td>
<td>1.25</td>
<td>No</td>
</tr>
<tr>
<td>G40</td>
<td>2</td>
<td>2.0</td>
<td>1.25</td>
<td>No</td>
</tr>
<tr>
<td>G7</td>
<td>3</td>
<td>3.0</td>
<td>2.0</td>
<td>No</td>
</tr>
<tr>
<td>G62</td>
<td>2</td>
<td>2.5</td>
<td>1.5</td>
<td>Yes</td>
</tr>
<tr>
<td>G64</td>
<td>3</td>
<td>2.5</td>
<td>1.5</td>
<td>Yes</td>
</tr>
<tr>
<td>G29</td>
<td>2</td>
<td>2.5</td>
<td>1.5</td>
<td>Yes</td>
</tr>
<tr>
<td>G78</td>
<td>3</td>
<td>2.5</td>
<td>1.5</td>
<td>Yes</td>
</tr>
<tr>
<td>G59</td>
<td>2</td>
<td>2.5</td>
<td>1.5</td>
<td>Yes</td>
</tr>
<tr>
<td>G74</td>
<td>2</td>
<td>2.5</td>
<td>1.5</td>
<td>Yes</td>
</tr>
</tbody>
</table>
Table 7.2. A summary of the bone remodelling at the plateau, mid-section and tip regions of the extra-cortical plates.

<table>
<thead>
<tr>
<th>No. days*</th>
<th>Plate stiffness</th>
<th>Plateau</th>
<th>Mid-section</th>
<th>Plate tip</th>
</tr>
</thead>
<tbody>
<tr>
<td>G73 152 d</td>
<td>flexible</td>
<td>Bony ingrowth</td>
<td>Bony ingrowth</td>
<td>Dense bone</td>
</tr>
<tr>
<td>G40 178 d</td>
<td>flexible</td>
<td>Little bony ingrowth</td>
<td>Bony ingrowth</td>
<td>Plate tip incorporated into cortex</td>
</tr>
<tr>
<td>G7 182 d</td>
<td>stiff</td>
<td>Cortical bone loss</td>
<td>Bony ingrowth</td>
<td>Bony ingrowth</td>
</tr>
<tr>
<td>G64 189 d</td>
<td>moderate</td>
<td>Bony ingrowth</td>
<td>Bony ingrowth</td>
<td>Plate tip incorporated into cortex</td>
</tr>
<tr>
<td>G29 51 d</td>
<td>moderate</td>
<td>Minimal bony ingrowth</td>
<td>Minimal bony ingrowth</td>
<td>Bony ingrowth</td>
</tr>
<tr>
<td>G78 214 d</td>
<td>moderate</td>
<td>Bony ingrowth</td>
<td>Bony ingrowth</td>
<td>Bony ingrowth</td>
</tr>
<tr>
<td>G74 163 d</td>
<td>moderate</td>
<td>Extensive cortical extension</td>
<td>Bony ingrowth</td>
<td>Plate tip incorporated into cortex</td>
</tr>
<tr>
<td>G59 195 d</td>
<td>moderate</td>
<td>Extensive cortical extension</td>
<td>Bony ingrowth</td>
<td>Plate tip incorporated into cortex</td>
</tr>
</tbody>
</table>

* days of implant duration, d = days
Table 7.3. Bony apposition around the extra-cortical plates using the zones illustrated in Figure 7.4.

<table>
<thead>
<tr>
<th>No.</th>
<th>No.</th>
<th>Plate</th>
<th>Plateau</th>
<th>Mid-section</th>
<th>Tip</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Int'</td>
<td>Edges</td>
<td>Ext'</td>
</tr>
<tr>
<td>G73</td>
<td>3</td>
<td>flex'</td>
<td>80</td>
<td>30</td>
<td>50</td>
</tr>
<tr>
<td>G40</td>
<td>2</td>
<td>flex'</td>
<td>15</td>
<td>0</td>
<td>40</td>
</tr>
<tr>
<td>G7</td>
<td>3</td>
<td>stiff</td>
<td>55</td>
<td>50</td>
<td>55</td>
</tr>
<tr>
<td>G64</td>
<td>3</td>
<td>mod'</td>
<td>10</td>
<td>60</td>
<td>0</td>
</tr>
<tr>
<td>G29*</td>
<td>2</td>
<td>mod'</td>
<td>15</td>
<td>15</td>
<td>0</td>
</tr>
<tr>
<td>G78</td>
<td>3</td>
<td>mod'</td>
<td>55</td>
<td>95</td>
<td>0</td>
</tr>
<tr>
<td>G74</td>
<td>2</td>
<td>mod'</td>
<td>15</td>
<td>80</td>
<td>75</td>
</tr>
<tr>
<td>G59</td>
<td>2</td>
<td>mod'</td>
<td>15</td>
<td>80</td>
<td>70</td>
</tr>
<tr>
<td>Mean</td>
<td></td>
<td></td>
<td>35</td>
<td>47</td>
<td>31</td>
</tr>
<tr>
<td>Range</td>
<td></td>
<td></td>
<td>10-80</td>
<td>0-95</td>
<td>0-75</td>
</tr>
</tbody>
</table>

* implant loose

Stiff = stiffness, flex' = flexible, mod' = moderate. Int' = internal, Ext' = external.
Chapter 8

Summary and Conclusions
Aseptic loosening has been identified as being the predominant cause of failure with cemented intra-medullary stemmed massive endo-prostheses of the lower limb (Chapter 2). Massive endo-prostheses have been predominantly used in the limb reconstruction following excision of bone tumour. The majority of patients, who underwent bone tumour limb salvage surgery were in their second or third decade of life (Chapter 2). In extensive implant survival analysis (Chapter 2), radiographic assessment (Chapter 4) and clinical evaluation studies (Chapter 3), have identified that the skeletal location, the percentage of bone resected and patient age are contributory factors to aseptic loosening of the cemented intra-medullary stemmed massive endo-prosthetic replacement. In addition, the surgeon influenced implant duration by determining when to revise. The process of loosening was considered to be predominantly mechanical and not biological. The findings of the survival analysis and radiographic assessments were consistent with this theory (Chapters 2 and 4). The mechanical decoupling of the cement and bone resulting from bending predominantly in the coronal plane and torsion in the femur and torsion in the tibia. The interface was also dependant upon interdigitation of the cement into the cancellous bone. Young patients additionally had centrifugal bone growth with a developing medullary canal between the cement mantle and the endosteal bone surface, resulting in the loss of fixation at the bone/cement interface.

The radiographic evaluation (Chapter 4) identified the process developed over 5-10 years depending on bone resection and patient age. The deterioration of the mechanical integrity of the cement/bone structure was identifiable by radiolucent line development and to a lesser extent the level and type of pain. Early studies, did not identify aseptic loosening as a problems because of the short implant duration. Aseptic loosening should therefore be considered to be a mid to long term complication.
Three methods of enhancing the fixation were examined (Chapters 5-7). The concept of extra-cortical bony bridging to reduce the cement/bone interface stresses as described by Chao and his co-workers was only feasible if pedicle formation was predictable. The radiographic evaluation established that the pedicle was a predictable phenomenon. However, the pedicle growth mechanism is unknown and is assumed to relate to the strain in the bone adjacent to the prosthesis plateau. The reduction in radiolucent lines and the extent of bone ingrowth has been encouraging and in part led to the development of the Stanmore uncemented intra-medullary stemmed replacements. The success of the hydroxyapatite coated uncemented intra-medullary fixation relied upon initial implant stability to obtain osseointegration for long-term implant fixation. The short-term clinical and radiographic results of the uncemented intra-medullary fixation have been encouraging. In particular the early results of the target groups, namely the skeletally immature patients and those who have undergone revision have been promising.

The new methods of fixation have been based upon an understanding of the lower limb anatomy and biomechanics in conjunction with the radiographic and survival data of the cemented intra-medullary replacements. However, the addition cost of coatings, special design features and tooling need to be balanced against addition longevity of the replacement.

8.1. Future

Unquestionably, extra-cortical fixation has already been proved that it is a successful method by the results of the first Stanmore massive replacements. However, at present it cannot be determined if this mode of fixation will provide an alternative to intra-medullary fixation.

The acceptance by bone tumour surgeons in the UK and abroad of the hydroxyapatite coated Stanmore cemented stemmed replacements reinforces
the value of this work. In addition, there is growing use of uncemented intra-
medullary stemmed replacements particularly for the young patients and those
who require revision of a massive endo-prosthesis because of the encouraging
radiographic results.

8.2. Conclusions

Chapter 2.

• Aseptic loosening of the cemented intra-medullary stemmed femoral and
proximal tibial custom-made Stanmore massive endo-prostheses was the
principal mode of implant related failure.

• Factors related to aseptic loosening included - skeletal location, patient
age, percentage of bone resected, the period the limb salvage procedure
took place and the performing surgeon.

Chapter 3.

• The overall clinical assessment grade was a poor predictor of aseptic
loosening.

• Patients were not compromised by loosening prostheses

• The presence of pain correlated with radiographic evaluations of
loosened cemented intra-medullary replacements.

• With increasing implant duration patients with proximal femoral
replacements improved their gait and had fewer episodes of pain. For
patients with distal femoral or proximal tibial replacements there was
increased likelihood that with increasing implant duration these patients
would have decreasing function and increased pain.

Chapter 4.

• The presence of radiolucent lines was the only parameter linked directly
with aseptic loosening.
• Increased and decreased shaft diameters reflected the mechanics of the lower limb highlighting compression (medially) and stress-shielding (laterally) respectively.

• The percentage of bone resected and patient age had a considerable effect on the radiographic features recorded.

Chapter 5.

• Pedicle was predictable phenomenon but was affected by skeletal location of the implant, patient age, the percentage of bone resected and the quadrant.

• Extra-cortical bony bridging did not occur with uncoated or porous collared replacements.

• Bony ingrowth was evident with hydroxyapatite coated replacements.

Chapter 6.

• Hydroxyapatite coating and anti-rotation lugs were important design features of uncemented intra-medullary replacements.

• The early radiographic results of the hydroxyapatite coated uncemented intra-medullary stemmed replacements were encouraging, particularly for the skeletally immature and revision cases.

Chapter 7.

• Results of the animal model would suggest that extra-cortical plates have potential.

• Plate stiffness would appear to affect bone apposition and extensive bone loss under the plate was common.


326


Publications
Refereed Papers (Senior author).


Extendible massive endo-prosthetic replacements for the skeletally immature. A survivorship study of 144 cases. Accepted by the Journal of Clinical Orthopaedics and Related Research.

Oral Presentations (Senior author).


**Poster Presentations (Senior author).**


**Invited Articles (Senior author).**

Appendices
Appendix A.

Additional information on the dimension of the femur and tibia.

A.1. Bone geometry

The lower appendicular skeleton comprises of 60 bones. However, with respect to bone tumour limb-salvage of the lower limb, only 2 bones are of importance, namely the femur and the tibia.

A.1.1. Femora

The femur is the largest bone in the human skeleton. The proximal diarthodial joint of the hip has the femoral head articulating with the pelvic acetabulum. The distal diarthodial joint of the knee has the femoral condyles articulating with proximal expansion of the tibia.

The average total length of 655 femora, measured parallel to the long axis of the femur from the base of the condyles to the top of the femoral head whilst designing the custom-made endo-prosthetic replacement was 439±1.8 mm (S.E.), ranging from 190 mm to 554 mm. With respect to gender, the 368 male femora were significantly longer than 287 female femora (450±2.3 mm and 425±2.6 mm respectively) (Wilcoxon Rank p<0.01). The femora of young male patients (≤16 years) grew in length by an average of 11.6 mm per year, whilst the female femora grew 8.3 mm per year.

The femoral offset measured perpendicular from the long axis of the femur to the centre of the femora head, averaged 39.9±0.42 mm (n=182, range 16 - 55 mm). Correcting for femoral head anteversion assuming the angle of anteversion was 15°, the calculated offset averaged 41.3 mm (range 16.6 mm to
The average male femoral head offset measured 42.3 mm compared to 40.0 mm for females (Wilcoxon Rank p<0.01).

The femoral head offset lever arm was calculated (total femoral length/femoral head offset), where a small ratio indicated a large offset and a short femoral length. The average ratio was 10.95± 0.1, (n=184, range 7.7 - 16.6). In skeletally mature cases (≥20 years) the female ratio was 10.9±0.17 and males 10.8±0.14 (p=0.63). The femora length of young male patients (<20 years) grew by 9.6 mm for every 1 mm offset increase, while female femora grew in length by 3.3 mm. The bone length/offset ratio for females decreased by 0.27 per year from 13.4 at the age of 9 to 10.9 at 19 years old, while the male ratio remained relatively constant as growth continued to skeletal maturity.

Osteosarcoma and Ewing's sarcoma patients (≥19 years) had on average longer femora (459 mm and 465 mm respectively) than those patients with M.F.H. (447 mm) femoral bone metastases (445 mm), osteoclastoma (450 mm) or chondrosarcoma (452 mm) (p>0.1).

A.1.2. Tibiae

The tibia is the larger of the two bones in the leg. The proximal tibial expansion articulates with the femur and distally with the talus of the ankle. The fibula head articulates with inferior lateral surface of the proximal tibia and distally the fibula articulates with the lateral aspect of the talus.

The mean length of 216 tibiae was 358±2.7 mm (range 220 to 470 mm). Male tibiae averaged 365±3.4 mm in length, compared to 349±4.2 mm in females (Wilcoxon Rank p<0.01). Young male patients (≤16 years) had an average annual tibial growth of 11.3 mm and females 6.6 mm.

The 3 commonest tibial tumour were osteosarcoma, chondrosarcoma and Ewing's sarcoma. Patients with the chondrosarcoma had the longest tibiae (372±11.7 mm, n=14) while those with Ewing's sarcoma the shortest (352±9.5
mm, n=21). However, the majority of the Ewing's sarcoma and osteosarcoma patients were skeletally immature compared to those with chondrosarcoma or other bone tumour types (p<0.01). However, there was little difference in the lengths of the tibia of skeletally mature patients (≥20 years) with respect to the 3 commonest tumour types, (osteosarcoma 375±6.5 mm, n=20; chondrosarcoma 373±7.7 mm, n=14; Ewing's sarcoma 384±9.6 mm, n=9, p=0.86).
Appendix B.

Additional data on the Stanmore massive lower limb custom-made endo-prostheses.

Table B.1. The diagnostic grouping of 1522 massive endo-prosthetic cases.

<table>
<thead>
<tr>
<th>Diagnostic group</th>
<th>Distal femoral n</th>
<th>%</th>
<th>Proximal femoral n</th>
<th>%</th>
<th>Proximal tibial n</th>
<th>%</th>
<th>Total n</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bone tumour</td>
<td>588</td>
<td>77.1</td>
<td>294</td>
<td>68.7</td>
<td>285</td>
<td>86.1</td>
<td>1167</td>
<td>76.7</td>
</tr>
<tr>
<td>Replacement of temporary bone tumour replacements</td>
<td>4</td>
<td>0.5</td>
<td>0</td>
<td>0.0</td>
<td>3</td>
<td>0.9</td>
<td>7</td>
<td>0.5</td>
</tr>
<tr>
<td>Failed massive replacements</td>
<td>75</td>
<td>9.8</td>
<td>23</td>
<td>5.4</td>
<td>38</td>
<td>11.5</td>
<td>136</td>
<td>8.9</td>
</tr>
<tr>
<td>Failed standard joint replacements</td>
<td>80</td>
<td>10.5</td>
<td>67</td>
<td>15.7</td>
<td>3</td>
<td>0.9</td>
<td>150</td>
<td>9.9</td>
</tr>
<tr>
<td>Other bony conditions and trauma</td>
<td>16</td>
<td>2.1</td>
<td>44</td>
<td>10.3</td>
<td>2</td>
<td>0.6</td>
<td>62</td>
<td>4.1</td>
</tr>
<tr>
<td>Total (Implant %)</td>
<td>759</td>
<td>50.1</td>
<td>428</td>
<td>28.1</td>
<td>328</td>
<td>21.8</td>
<td>1522</td>
<td>100.0</td>
</tr>
</tbody>
</table>

Table B.2. Diagnosis with respect to implant type

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Distal femoral n</th>
<th>%</th>
<th>Proximal femoral n</th>
<th>%</th>
<th>Proximal tibial n</th>
<th>%</th>
<th>Total n</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Osteosarcoma</td>
<td>324</td>
<td>56.2</td>
<td>29</td>
<td>10.0</td>
<td>168</td>
<td>59.6</td>
<td>521</td>
<td>45.3</td>
</tr>
<tr>
<td>Chondrosarcoma</td>
<td>36</td>
<td>6.2</td>
<td>90</td>
<td>31.0</td>
<td>20</td>
<td>7.1</td>
<td>146</td>
<td>12.7</td>
</tr>
<tr>
<td>Ewing's sarcoma</td>
<td>18</td>
<td>3.1</td>
<td>40</td>
<td>13.8</td>
<td>23</td>
<td>8.2</td>
<td>81</td>
<td>7.0</td>
</tr>
<tr>
<td>Osteoclastoma</td>
<td>74</td>
<td>12.8</td>
<td>26</td>
<td>9.0</td>
<td>36</td>
<td>12.8</td>
<td>136</td>
<td>11.8</td>
</tr>
<tr>
<td>Bone metastases</td>
<td>18</td>
<td>3.1</td>
<td>50</td>
<td>17.2</td>
<td>4</td>
<td>1.4</td>
<td>72</td>
<td>6.3</td>
</tr>
<tr>
<td>Other bone tumours</td>
<td>107</td>
<td>18.5</td>
<td>55</td>
<td>19.0</td>
<td>31</td>
<td>11.0</td>
<td>193</td>
<td>16.8</td>
</tr>
<tr>
<td>Total</td>
<td>577</td>
<td>100.0</td>
<td>290</td>
<td>100.0</td>
<td>282</td>
<td>100.0</td>
<td>1149</td>
<td>100.0</td>
</tr>
</tbody>
</table>

344
Table B.3. A comparison between the sexes of patient age and percentage of bone resected with respect to implant.

<table>
<thead>
<tr>
<th>Implant</th>
<th>Female</th>
<th>Male</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>mean±SE</td>
<td>n</td>
</tr>
<tr>
<td>Distal femoral</td>
<td>218</td>
<td>26.9±1.12</td>
<td>281</td>
</tr>
<tr>
<td>Proximal femoral</td>
<td>131</td>
<td>41.8±1.66</td>
<td>149</td>
</tr>
<tr>
<td>Proximal tibial</td>
<td>100</td>
<td>23.5±1.37</td>
<td>141</td>
</tr>
<tr>
<td></td>
<td>159</td>
<td>48.9±0.90</td>
<td>232</td>
</tr>
<tr>
<td></td>
<td>83</td>
<td>51.8±1.43</td>
<td>93</td>
</tr>
<tr>
<td></td>
<td>82</td>
<td>46.7±1.37</td>
<td>117</td>
</tr>
</tbody>
</table>

p derived from Mann-Whitney 'U' test

Table B.4. Patient age, percentage of bone resected and gender with respect to knee hinge configuration and implant.

<table>
<thead>
<tr>
<th></th>
<th>Fixed hinged knee</th>
<th>Rotating hinged knee</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>mean</td>
<td>S.E.</td>
</tr>
<tr>
<td>Distal femoral</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age (years)</td>
<td>499</td>
<td>27.2</td>
<td>0.78</td>
</tr>
<tr>
<td>Resection (%)</td>
<td>397</td>
<td>49.6</td>
<td>0.61</td>
</tr>
<tr>
<td>Sex (n)</td>
<td>F: M</td>
<td>F: M</td>
<td></td>
</tr>
<tr>
<td>Proximal tibial</td>
<td>219</td>
<td>292</td>
<td>1:0.75</td>
</tr>
<tr>
<td>Age (years)</td>
<td>241</td>
<td>23.4</td>
<td>0.93</td>
</tr>
<tr>
<td>Resection (%)</td>
<td>199</td>
<td>48.2</td>
<td>0.9</td>
</tr>
<tr>
<td>Sex (n)</td>
<td>F: M</td>
<td>F: M</td>
<td></td>
</tr>
</tbody>
</table>

p derived from Wilcoxon test

345
Appendix C.

C.1. Introduction

The survivorship study (Chapter 2) identified that there was a marked differences between the two most prolific surgeons in terms of the probability of surviving aseptic loosening. Sixty one surgeons inserted the 1149 custom-made endo-prostheses of the study group at centres throughout Britain and abroad.

Below summarises the indication, patient status, clinical evaluation and radiographic evaluation of the two most prolific surgeons in the study described in Chapter 2.

C.2. Patients

The cases of the two surgeons who had inserted the most uncoated distal femoral replacements that utilised the Stanmore fixed knee hinge were selected. The commonality between the two surgeons were the Stanmore endo-prostheses, that had been designed and manufactured to the same criteria.

Diagnosis. There was a significant difference between the two surgeons with respect to diagnosis (p<0.01, n=275) (Table C.1), and the greatest variations were the percentage of osteosarcoma, osteoclastoma and chondrosarcoma cases treated.

Gender. There was no significant difference in the proportion of males to females with respect to surgeon, either overall or in the three most commonly treated tumours.
Patient age and percentage of bone resected. Patients of Surgeon A were significantly younger and had a greater percentage of bone resected than those of Surgeon B (Table C.2). Surgeon A treated a higher proportion of cases with osteosarcoma, who generally were younger and had a higher percentage of bone resected than osteoclastoma or chondrosarcoma cases (Table C.1), that were proportionally more frequently operated upon by surgeon B. In all four diagnostic groups, surgeon A resected a higher proportion of the distal femoral shaft than surgeon B.

C.3. Results

C.3.1. Patient Status

The status of the patient of the two surgeons showed a number of differences (Table C.3). The proportion of amputations, those with complications and those lost to follow-up were similar. There was variance in the proportion of revisions, deaths and those who had no prosthetic related problems. With respect to those dying of their disease surgeon A treated a higher proportion of cases with osteosarcoma which has a high mortality rate and treated fewer patients with osteoclastoma which has a low mortality rate. Surgeon A revised over 26% whilst surgeon B revised less than 12%.

C.3.2. Revisions

Eighty percentage of surgeon A's revisions (21.2% of the total group), were a result of aseptic loosening, whilst aseptic loosening accounted for 50% (5.8% of the total group) of surgeon B's revisions. However, when excluding aseptic loosening both surgeons had similar revision rates (A=5.3%, B=5.8%) (Table 5.4). Surgeon A revised for aseptic loosening significantly earlier than Surgeon B (p=0.03, n=45) (Surgeon A =71 months ±5.6, range 15.8 - 186.8; Surgeon B =118 months ±15.9, range 75.5 - 159.6).
C.3.3. Radiographic

Using the BME radiographic grading system there was no significant difference between the two surgeons in terms of radiographic score (p=0.65, n=141). Surgeon B had a higher proportion of cases with a 'fair' grade and lower proportion with 'excellent' or 'poor' grades (Figure C.1).

However, the radiographs of surgeon B were marginally shorter in duration (32 months) compared to surgeon A (38 months). Correlating radiographic score against time, identified that the scores were very similar with respect to time. Using linear interpolation, surgeon A had a marginally higher radiographic scores for the first 6 years than surgeon B. (Figure C.2).

The radiolucent line scores of the two surgeons cases were remarkable similar with surgeon B have a marginally lower score but also a slighter shorter average duration (Surgeon A=3.5±0.6, Surgeon B=3.2±1.1, p=0.82).

C.3.4. Clinical

There were no significant differences between the two surgeons with respect the ISOLS clinical score (p=0.12). However, 83.3% of Surgeon B’s cases were graded either 'excellent' or 'good' compared to 64.5% for surgeon A (Figure C.3). In addition, surgeon B’s cases had greater range of movement, less pain and better function scores than surgeon A’s. However, the number of cases assessed was small and therefore little significance can be placed on the clinical findings.

C.4. Discussion

Clearly, there were differences between the two surgeons in terms of revision for aseptic loosening.

The variation between the two surgeons may be as a result of -
a. Surgical technique - the radiographic scores of one surgeon would be poorer throughout, but both surgeons would revise at the same level of deterioration.

b. Differing revision criteria - the surgical technique would be the same and reflected in the radiographic score but the surgeons would revise with markedly differing criteria.

c. A combination of a & b.

d. None of the suggested above hypotheses.

The similarity of the radiographic scores, the percentage of revisions excluding aseptic loosening and to a lesser extent the clinical scores and would indicate that the surgical performance of the two surgeons was similar and the overriding factor was the decision by the surgeon of when to revise.

The surgeons decision on when to revise a loosened endo-prosthetic replacement has considerable effect on the probability of survival of the primary endo-prosthesis. As a result of the significant difference in aseptic loosening rates between the two surgeons treating bone tumours of the distal femur using the same manufacturers implant, a comparison of loosening rates between different implant types inserted and managed by different surgeons is probably invalid. What may be valid, however, is a comparison of event related failures such mechanical fracture of the implant stem.

Revising an endo-prosthetic replacement early in the short term looks poor, however, in the long term this may be more successful. The ultimate aim of the limb-salvage is to preserve life and limb, but by revising an endo-prostheses 'early' provides the surgeon with more substantial bone stock from which to revise. In general, less shaft bone would require resecting and the bone quality of the shaft would be more competent and intact than if the revision procedure was left for a longer period of time. A greater resection of the distal femur
would increase the probability of loosening, as identified in Chapter 2. The success of revisions of massive endo-prostheses is dealt with in Appendix F.
Figure C.1. Radiographic grades with respect to surgeon.

Figure C.2. The radiographic score with respect to implant duration and surgeon (linear regression with 95% confidence interval curves).
Figure C.3. Clinical grades with respect to surgeon.
Table C.1. Diagnosis with respect to surgeon.

<table>
<thead>
<tr>
<th>Tumour type</th>
<th>Surgeon</th>
<th>A</th>
<th>B</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>%</td>
<td>%</td>
</tr>
<tr>
<td>Osteosarcoma</td>
<td></td>
<td>67.7</td>
<td>41.9</td>
</tr>
<tr>
<td>Osteoclastoma</td>
<td></td>
<td>6.9</td>
<td>18.6</td>
</tr>
<tr>
<td>Chondrosarcoma</td>
<td></td>
<td>5.4</td>
<td>9.3</td>
</tr>
<tr>
<td>Other tumours</td>
<td></td>
<td>20.0</td>
<td>30.2</td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td>100.0</td>
<td>100.0</td>
</tr>
</tbody>
</table>

Table C.2. The age of the patient and percentage of bone resected for all diagnoses and the three most commonly occurring tumours with respect to surgeon.

<table>
<thead>
<tr>
<th>Tumour</th>
<th>Surgeon</th>
<th>Age (years ±S.E.)</th>
<th>Resection (% ±S.E.)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>A</td>
<td>B</td>
<td>p</td>
</tr>
<tr>
<td>Osteosarcoma</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(n=164)</td>
<td></td>
<td>17.6±0.85</td>
<td>19.1±1.61</td>
<td>0.06</td>
</tr>
<tr>
<td>Osteoclastoma</td>
<td></td>
<td>40.3±4.36</td>
<td>37.3±3.6</td>
<td>0.77</td>
</tr>
<tr>
<td>(n=32)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chondrosarcoma</td>
<td></td>
<td>40.2±6.57</td>
<td>52.6±7.85</td>
<td>0.20</td>
</tr>
<tr>
<td>(n=18)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td></td>
<td>33.7±2.84</td>
<td>40.0±3.77</td>
<td>0.15</td>
</tr>
<tr>
<td>(n=61)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>All diagnoses</td>
<td></td>
<td>23.7±1.9</td>
<td>31.4±1.78</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>(n=275)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

p derived from Mann-Whitney 'U' test
Table C.3. A summary of the patient status with respect to surgeon.

<table>
<thead>
<tr>
<th>Healthcare event</th>
<th>Surgeon A</th>
<th>Surgeon B</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amputation (all causes)</td>
<td>9.0</td>
<td>9.3</td>
</tr>
<tr>
<td>Died of disease</td>
<td>20.1</td>
<td>4.7</td>
</tr>
<tr>
<td>Prosthetic related problems</td>
<td>5.8</td>
<td>3.5</td>
</tr>
<tr>
<td>No prosthetic related problems</td>
<td>29.6</td>
<td>59.3</td>
</tr>
<tr>
<td>Revision</td>
<td>26.5</td>
<td>11.6</td>
</tr>
<tr>
<td>No follow-up</td>
<td>9.0</td>
<td>11.6</td>
</tr>
<tr>
<td>Total</td>
<td>100.0</td>
<td>100.0</td>
</tr>
</tbody>
</table>

Table C.4. A summary of the causes of revision with respect to surgeon.

<table>
<thead>
<tr>
<th>Mode of failure</th>
<th>Surgeon A</th>
<th>Surgeon B</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Revisions Frequency (%)</td>
<td>Study group Frequency (%)</td>
</tr>
<tr>
<td>Aseptic loosening</td>
<td>80</td>
<td>21.2</td>
</tr>
<tr>
<td>Femoral fracture</td>
<td>2</td>
<td>1.1</td>
</tr>
<tr>
<td>Infection</td>
<td>8</td>
<td>4.2</td>
</tr>
<tr>
<td>Implant fracture</td>
<td>8</td>
<td>4.2</td>
</tr>
<tr>
<td>Extendible implant complications</td>
<td>2</td>
<td>1.1</td>
</tr>
<tr>
<td>Recurrence</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Total</td>
<td>100</td>
<td>31.8</td>
</tr>
</tbody>
</table>
Appendix D.

Clinical assessment tables.

Table D.1. The ISOLS clinical assessment grading system.

<table>
<thead>
<tr>
<th></th>
<th>Clinical grade and score</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Excellent</td>
</tr>
<tr>
<td><strong>FUNCTIONAL</strong></td>
<td></td>
</tr>
<tr>
<td>Walk distance</td>
<td>≥ 1 mile</td>
</tr>
<tr>
<td>Walking up stairs</td>
<td>Normally</td>
</tr>
<tr>
<td><strong>ACTIVITY</strong></td>
<td></td>
</tr>
<tr>
<td>Walking Aid</td>
<td>None</td>
</tr>
<tr>
<td>Restrictions</td>
<td>None</td>
</tr>
<tr>
<td><strong>STABILITY</strong></td>
<td>None</td>
</tr>
<tr>
<td><strong>PAIN</strong></td>
<td>None</td>
</tr>
<tr>
<td>ROM (active only)</td>
<td>&gt;90°</td>
</tr>
<tr>
<td><strong>DEFORMITY</strong></td>
<td>None</td>
</tr>
<tr>
<td>Shortening or FFD</td>
<td>&lt;10°</td>
</tr>
<tr>
<td><strong>EMOTIONAL ACCEPTANCE</strong></td>
<td>Enthusiastic</td>
</tr>
</tbody>
</table>

FFD = Fixed Flexion Deformity; ADL = Activities of Daily Living; ROM = Range of Movement

The range of movement and flexion contractures were measured to the nearest 5° and the length of shortening was recorded to the nearest 2 millimetres.
Table D.2. The Biomedical Engineering clinical grading system based upon the ISOLS clinical grading system

<table>
<thead>
<tr>
<th>FUNCTIONAL</th>
<th>BME Clinical grade and score</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Excellent = 4 Good = 3 Fair = 2 Poor = 1</td>
</tr>
<tr>
<td>Walk distance</td>
<td>≥1 mile</td>
</tr>
<tr>
<td>Walking up stairs</td>
<td>Normally</td>
</tr>
<tr>
<td>Stability</td>
<td>None</td>
</tr>
<tr>
<td>ACTIVITY</td>
<td>Walking Aid</td>
</tr>
<tr>
<td>Restrictions</td>
<td>None</td>
</tr>
<tr>
<td>PAIN</td>
<td>None</td>
</tr>
<tr>
<td>ROM</td>
<td>Active</td>
</tr>
<tr>
<td></td>
<td>Passive</td>
</tr>
</tbody>
</table>

FFD = Fixed Flexion Deformity; ADL = Activities of Daily Living; ROM = Range of Movement.

The range of movement and flexion contractures were measured to the nearest 5° and the length of shortening was recorded to the nearest 2 millimetres.
Appendix E.

The definition of the radiographic parameters

**Pedicle or New bone formation**

This refers to the pedicle of bone that grows from the shoulder of the prosthesis along the shaft. It is measured parallel to the prosthesis shaft from the plateau to the tip of the continuous bone structure. The width measurement is an average of three measurements taken at the shoulder of the pedicle, approximately half way along its length and at its tip.

**Pedicle gap**

The pedicle gap is the radiolucent line between the pedicle and the shaft of the prosthesis. It is measured perpendicular to the prosthesis shaft in the proximal region of the pedicle.

**Increased shaft diameter**

The lengths and widths of any expansion of the shaft bone in the region of the intra-medullary stem that has appeared since the immediate post-operative radiographs are measured.

**Radiolucent lines**

The length and width of any radiolucent line is measured and are identified between the cement and bone or between the cement and the intra-medullary stem.
Cavitation

Cavitations differ from radiolucent lines in that cavities have a low aspect ratio and can be in complete isolation of other radiographic features and they are usually associated with radiolucent lines.

Reduced bone density

Regions of osteopaenia are recorded but not measured.

Reduced shaft diameter

This is the reverse of the increased shaft diameter, any narrowing of the shaft is measured along its length and width.

Plateau gap

Radiolucent lines that are parallel to the prosthesis shoulder are recorded separately from radiolucent lines and are measured perpendicular to the prosthesis shoulder at its maximum height.

Cement

If cement identifiable as a uniform layer on the prosthesis shoulder is present the maximum height measured perpendicular to the prosthesis shoulder is recorded.
Appendix F.

This study of revision lower limb massive endo-prostheses was first presented at the 6th International Symposium on Limb Salvage in 1991 (Montreal), and again at the 7th International Symposium on Limb Salvage in 1993 (Singapore) (Unwin et al 1991, Unwin et al 1993). The following has been updated and provides additional data in support of the move from cemented intra-medullary stemmed fixation to uncemented intra-medullary stemmed or extra-cortical fixation.

Revisions of bone tumour massive endo-prosthetic replacements.

F.1. Introduction

At present, the most common method of revising a 'failed' massive endo-prosthetic replacement is to reinsert the original or insert a revision endo-prosthetic replacement. The increasing use of revision prostheses over the last decade for failed bone tumour replacements raises the question - how successful are the revisions of failed massive replacements? The principal aim of the revision replacement is to continue the preservation of the limb.

F.1.1. Aim

The aim of this study was to identify the successfulness revision replacements.

F.1.2. Purpose

The purpose having identified if revision replacements had a poorer or better prognosis of surviving aseptic loosening than primaries, the results may then assist the surgeon in deciding when to revise a loosened primary replacement.
F.2. Methodology

All revision Stanmore massive endo-prosthetic replacements cases using the following criteria were selected -

- Proximal femoral, distal femoral or proximal tibial replacements
- Cemented intra-medullary stemmed fixation for the original and revision/s protheses
- Original diagnosis was neoplastic in origin
- Failure was either implant or fixation related. Recurrence of the tumour was not classed as an endo-prosthetic related failure.
- Inserted prior to 1994.

In total, 146 massive endo-prosthetic replacements fitting the above criteria were selected for study.

F.2.1. Implants

Of the 146 endo-prostheses, the distal femoral replacements accounted for 83 (56.8%), followed by the proximal tibial replacements with 48, (32.9%), and the remaining 15 (10.3%) were proximal femorals replacements. The first implant in this study was inserted in mid 1977.

F.2.2. Patients

In total, of the 146 revision endo-prostheses, 136 (93.2%) were the first revision prosthesis whilst the remaining 10 (6.8%) were the second.

Diagnosis

The most common complication which necessitated a revision prosthesis was aseptic loosening (57.5%), followed by infection (17.1%) (Table F.1). The complications of the extendible replacements for use in the skeletally immature was jamming of the extending mechanism or a fully extended replacement in
patients who were not skeletally mature. Titanium cysts were only present in the proximal tibial replacement group.

Patient age

The mean age of the patient at the time of the revision procedure was 24.8 years old (±1.05 S.E. range 8-69 years). The youngest patients were those with proximal tibial replacements (mean age =24.0 years), closely followed by those with distal femorals (24.7 years), whilst the oldest were patients with proximal femoral replacements (28.5 years). There was no significant difference between implant types with respect to age (p=0.8).

F.2.3. Patient status and survival analysis

Using the latest available data the status of the patient was categorised. For the survival analysis the latest status of the replacement was categorised either as "surviving" or "failed". A failure was classified when either the endo-prosthetic replacement was removed, recemented or the limb amputated as a result of aseptic loosening.

F.2.4. Radiographic Assessment

Radiographic assessments where performed only on those that were taken a minimum of 3 months post operatively and where both the frontal and lateral radiographs were available clearly showing the replacement and adjacent bone. The ISOLS radiographic grading method was used.

F.2.5. Histological Examination

Retrieved endo-prosthetic replacements with some of their associated bone underwent histological examination. Using a slitting wheel the bone and implant were cut into 5 mm thick transverse slices; these were x-rayed and prepared for decalcified histology (Thin sections prepared by histology technician).
F.3. Results

In total 142 (97.3%), of the 146 revision endo-prosthetic cases had post-operative clinical-related details of duration greater than 3 months after the revision procedure. The average follow-up duration was 28.0 months (±2.18) with the longest follow-up recorded at 191.9 months. Fifty seven percent of patients were fully mobile and had no prosthetic related problems (Table F.2).

Five patients died, 4 of their disease and 1 of natural causes. Pain (45%), infection (18%), and fixed flexion deformities (14%) were the predominant modes of complications.

Thirty two revision implants (21.9%) failed. The predominant modes of failure were aseptic loosening (43.8%), followed by infection (25.0%) (Table F.3). Proportionally, the proximal tibial group had the highest number failures with 14 of the 48 revision implants failing (29.2%). Furthermore, 5 of the 14 proximal tibial failures had amputations, whereas, all of the 15 distal femoral replacement failures were revised.

Of the 32 cases that had failed, 6 were amputations, 9 were revised with a Stanmore cemented intra-medullary stemmed endo-prosthesis, prior to 1994 and therefore included in the study, 12 were revised with a Stanmore cemented intra-medullary stemmed endo-prosthesis, in 1994, and excluded from the study, 3 were revised to a Stanmore total femoral replacement and excluded under the selection criteria, 1 was revised with a Kotz\textsuperscript{2} uncemented modular distal femoral replacement and 1 had the replacement removed and a temporary anti-biotic loaded cement spacer inserted, which was later replaced with a revision proximal tibial replacement in 1994. One of the 9 failed cases that was revised and included in this study, had the second revision distal

\textsuperscript{2}Kotz modular replacements manufactured by Howmedica, Pfizer, Rutherford, USA.
femoral replacement fail and was one of the 3 to receive a total femoral replacement.

Comparing the first and second modes of failure of the 32 cases, it was noted that 13 cases had the same mode of failure (Table F.4). Aseptic loosening of the primary replacement and of the revision replacement was most frequently observed when the modes were of the same type. Failure as a result of infection of the primary replacement and revision replacement occurred twice, whereas, 3 of the primary infected cases failed subsequently by aseptic loosening.

**F.3.1. Survival Analysis**

All three replacements groups had initially similar probabilities of surviving aseptic loosening replacements (Figure F.1). Later, after approximately 3.5 years both the distal femoral and proximal tibial replacement groups had an increasingly poor prognosis of surviving aseptic loosening. The five year probabilities of surviving aseptic loosening were $0.657\pm0.114$ for distal femorals, $0.706\pm0.170$ for proximal tibial and $0.857\pm0.132$ for proximal femoral replacements. There was significant difference between the three implant groups in terms of surviving aseptic loosening with a revision endo-prosthesis ($p=0.52$).

**F.3.2. Radiographic Assessment**

Fifty six sets of radiographs of the intra-medullary stemmed replacements met the criteria for assessment. The majority of cases were graded using the ISOLS system as "Good" (46.4%), or "Poor" (33.9%). However, 4 cases (7.1%), did achieve an "Excellent" grade (Table F.5).

Radiolucent lines observed at the cement/bone interface were present in 67.8% of radiographs examined. In a small number of cases the radiolucent lines could be detected around the entire cement mantle.
F.3.3. Histological Examination

Examination of the contact radiographs of slices through four retrieved specimens, all showed areas of radiolucency adjacent to the cement, that correlated to areas of radiolucency on the radiographs. A shell of sclerotic bone adjacent to the cement mantle was observed in the diaphyseal and metaphyseal bone. In the areas where sclerotic bone was present, interdigitation of cement into the cancellous bone did not occur. The endosteal surface of diaphyseal bone adjacent to the cement was smooth walled.

F.3.4. Comparison of revision and primary replacements

Both distal femoral (Figure F. 2) and proximal tibial revision replacements had significantly poorer prognoses of surviving aseptic loosening than primary replacements (Table F.6).

To compare the radiographs of primary and revision replacements, those of primary replacements were of a duration greater than 3 months and less than 135 months, equalling that of the revision group. There was no significant difference between the revision and primary radiographic ISOLS scores with respect to the proximal femoral and proximal tibial replacements (Table F.7). However, radiographs of revision distal femoral replacements were significantly poorer than primary distal femoral replacements (p=0.01).

F.4. Discussion

Using a revision massive replacement is the most commonly used method of revising a failed primary massive endo-prosthetic replacement. The results presented here indicates that there is a higher probability of the revision replacement failing from a prosthetic associated complication than compared with primary Stanmore replacements used in bone tumour limb salvage.
Similarly, revision of primary joints replacements has also been problematic with increased complication rates of the revision implants reported (Lord et al 1988, Kershaw et al 1991). Substantial bone loss and weakened remaining bone has led to bone fracture when revising knee replacements (Inglis and Walker 1991). As a result of poor revision results of revision total hip replacements, 'second-generation' cementing techniques and improved stem designs have been employed with encouraging results. When extensive bone loss adjacent to total hip replacement has occurred, revision using massive replacements (Table 2.1) or using techniques such as those described by Wagner (Wagner 1993) have been used. However, unlike failed joint replacement cases, much of the bone shaft has been resected with bone tumour cases and therefore often the intra-medullary stem was being placed into a region of bone previously used for fixation.

A possible cause is the poor interdigitation of the bone cement into the remaining dense cortical and cancellous bone. Poor interdigitation in the latter may be due to the layer of sclerotic bone identified in the histological sections of the retrieved specimens. This resulted in cementation of the intra-medullary stemmed revision endo-prosthesis into a smooth tube of bone which ultimately led to an increased rate of implant failure primarily as a result of aseptic loosening.

Alternative limb-salvage methods for the revision of failed cemented massive replacements, such as extracortical bony bridging, uncemented intra-medullary stemmed fixation, extra-cortical fixation or improved cementation techniques require evaluation but may increase implant longevity.
F.5. References


Figure F.1. The probability of surviving aseptic loosening with revision replacements of the lower limb.
Figure F.2. A comparison of the probability of surviving aseptic loosening between primary and revision distal femoral replacements.
Table F.1. The diagnoses of the revision endo-prostheses with respect to implant location.

<table>
<thead>
<tr>
<th>Implant</th>
<th>Distal femoral</th>
<th>Proximal femoral</th>
<th>Proximal tibial</th>
<th>All implants</th>
</tr>
</thead>
<tbody>
<tr>
<td>Indication for revision</td>
<td>n</td>
<td>%</td>
<td>n</td>
<td>%</td>
</tr>
<tr>
<td>Aseptic loosening</td>
<td>57</td>
<td>68.7</td>
<td>6</td>
<td>40.0</td>
</tr>
<tr>
<td>Implant fracture</td>
<td>11</td>
<td>13.3</td>
<td>3</td>
<td>20.0</td>
</tr>
<tr>
<td>Infection</td>
<td>11</td>
<td>13.3</td>
<td>2</td>
<td>13.3</td>
</tr>
<tr>
<td>Extendible implant complications</td>
<td>2</td>
<td>2.4</td>
<td>3</td>
<td>20.0</td>
</tr>
<tr>
<td>Bone fracture</td>
<td>1</td>
<td>1.2</td>
<td>1</td>
<td>6.7</td>
</tr>
<tr>
<td>Surgical error</td>
<td>1</td>
<td>1.2</td>
<td>0</td>
<td>0.0</td>
</tr>
<tr>
<td>Ti cyst</td>
<td>0</td>
<td>0.0</td>
<td>0</td>
<td>0.0</td>
</tr>
<tr>
<td>Total</td>
<td>83</td>
<td>100</td>
<td>15</td>
<td>100</td>
</tr>
</tbody>
</table>

Table F.2. The status of the 146 cases

<table>
<thead>
<tr>
<th>Status</th>
<th>Number</th>
<th>Frequency (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>No prosthetic related problems</td>
<td>83</td>
<td>56.9</td>
</tr>
<tr>
<td>Died</td>
<td>5</td>
<td>3.4</td>
</tr>
<tr>
<td>Complications</td>
<td>22</td>
<td>15.1</td>
</tr>
<tr>
<td>Amputations/Revisions</td>
<td>32</td>
<td>21.9</td>
</tr>
<tr>
<td>No Follow-up</td>
<td>4</td>
<td>2.7</td>
</tr>
<tr>
<td>Total</td>
<td>146</td>
<td>100.0</td>
</tr>
</tbody>
</table>
Table F.3. Modes of failure of the revision endo-prostheses with respect to implant type.

<table>
<thead>
<tr>
<th>Status</th>
<th>Implant</th>
<th>Proximal femoral</th>
<th>Distal femoral</th>
<th>Proximal tibial</th>
<th>All implants</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aseptic loosening</td>
<td>1</td>
<td>9</td>
<td>4</td>
<td>14</td>
<td></td>
</tr>
<tr>
<td>Infection</td>
<td>1 (amp)</td>
<td>3</td>
<td>4 (3 amps)</td>
<td>8</td>
<td></td>
</tr>
<tr>
<td>Chronic pain</td>
<td>-</td>
<td>1</td>
<td></td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Implant fracture or hyper-extension of Stanmore knee</td>
<td>-</td>
<td>1</td>
<td>3</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>Titanium cyst</td>
<td>-</td>
<td>-</td>
<td>1 (amp)</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Surgical Complications</td>
<td>-</td>
<td>-</td>
<td>1</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Fully extended extendible implant</td>
<td>1</td>
<td>-</td>
<td>-</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Bone fracture</td>
<td>-</td>
<td>1</td>
<td>1 (amp)</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>No. failed/No. in group</td>
<td>3/15</td>
<td>15/83</td>
<td>14/48</td>
<td>32/146</td>
<td></td>
</tr>
<tr>
<td>Percentage of failure</td>
<td>20.0%</td>
<td>18.1%</td>
<td>29.2%</td>
<td>21.9%</td>
<td></td>
</tr>
</tbody>
</table>

amp/s = amputation/s

Table F.4. A comparison between the first and second modes of failures.

<table>
<thead>
<tr>
<th>First Failure</th>
<th>Second Failure</th>
<th>Revised</th>
<th>Amputated</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aseptic loosening</td>
<td>Aseptic loosening</td>
<td>9</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>Infected</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Knee hyper-extension</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>Bone fracture</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Severe pain</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Infected</td>
<td>Aseptic loosening</td>
<td>3</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>Surgical complications</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>Stanmore knee hyper-extension</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>Fully extended extendible implant</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>Infected</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Fractured</td>
<td>Fractured IM stem</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>intra-medullary stem</td>
<td>Aseptic loosening</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>Infected</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Titanium cyst</td>
<td>Titanium cyst</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Complications with extendible implants</td>
<td>Infected</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Aseptic loosening</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td>26</td>
<td>6</td>
</tr>
</tbody>
</table>

370
Table F.5. ISOLS Radiographic score with respect to implant type.

<table>
<thead>
<tr>
<th>Grade</th>
<th>Implant</th>
<th>Proximal femoral</th>
<th>Distal femoral</th>
<th>Proximal tibial</th>
<th>All implants</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>%</td>
<td>n</td>
<td>%</td>
<td>n</td>
</tr>
<tr>
<td>Excellent</td>
<td>2</td>
<td>33.3</td>
<td>0</td>
<td>0.0</td>
<td>2</td>
</tr>
<tr>
<td>Good</td>
<td>0</td>
<td>0.0</td>
<td>14</td>
<td>40.0</td>
<td>10</td>
</tr>
<tr>
<td>Fair</td>
<td>2</td>
<td>33.3</td>
<td>7</td>
<td>20.0</td>
<td>0</td>
</tr>
<tr>
<td>Poor</td>
<td>2</td>
<td>33.3</td>
<td>14</td>
<td>40.0</td>
<td>3</td>
</tr>
<tr>
<td>Total</td>
<td>6</td>
<td>100.0</td>
<td>35</td>
<td>100.0</td>
<td>15</td>
</tr>
</tbody>
</table>

Table F.6. A comparison of the probabilities (%) of survival at 5 years between revision and primary massive replacements.

<table>
<thead>
<tr>
<th>Implant</th>
<th>Primary</th>
<th>Revision</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Proximal femoral</td>
<td>93.9±8.06</td>
<td>85.7±13.2</td>
<td>0.60</td>
</tr>
<tr>
<td>n=290</td>
<td>n=15</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Distal femoral</td>
<td>89.9±4.81</td>
<td>65.7±11.4</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>n=577</td>
<td>n=83</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Proximal tibial</td>
<td>86.6±9.70</td>
<td>70.6±17.0</td>
<td>0.04</td>
</tr>
<tr>
<td>n=260</td>
<td>n=48</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

p derived from Log-rank test

Table F.7. A comparison of radiographic scores between primary and massive endo-prosthetic revision replacements

<table>
<thead>
<tr>
<th>Implant</th>
<th>Primary</th>
<th>Revision</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Proximal femoral</td>
<td>2.01±0.11</td>
<td>2.33±0.39</td>
<td>0.63</td>
</tr>
<tr>
<td>n=78</td>
<td>n=6</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Distal femoral</td>
<td>2.26±0.05</td>
<td>1.80±0.15</td>
<td>0.01</td>
</tr>
<tr>
<td>n=349</td>
<td>n=35</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Proximal tibial</td>
<td>2.20±0.08</td>
<td>2.67±0.24</td>
<td>0.52</td>
</tr>
<tr>
<td>n=119</td>
<td>n=15</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

p derived from Wilcoxon rank test. (ISOLS grades - Excellent =4, Good =3, Fair =2, Poor =1)
Appendix G.

Additional pedicle data.

Table G.1. The dimensions and scores of pedicle with respect to quadrant and implant.

<table>
<thead>
<tr>
<th>Quadrant</th>
<th>Proximal femoral (n=82)</th>
<th>Distal femoral (n=189)</th>
<th>Proximal tibial (n=96)</th>
<th>p (score)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>LxW score ±S.E.</td>
<td>LxW score ±S.E.</td>
<td>LxW score ±S.E.</td>
<td></td>
</tr>
<tr>
<td>Anterior</td>
<td>34.9 x 3.7 ±0.12</td>
<td>23.7 x 2.9 ±0.05</td>
<td>27.6 x 2.5 ±0.09</td>
<td>0.68</td>
</tr>
<tr>
<td>Posterior</td>
<td>24.9 x 3.9 ±0.08</td>
<td>32.3 x 3.0 ±0.04</td>
<td>20.2 x 2.1 ±0.09</td>
<td>0.07</td>
</tr>
<tr>
<td>Medial</td>
<td>39.6 x 4.9 ±0.07</td>
<td>25.0 x 3.7 ±0.04</td>
<td>34.9 x 2.9 ±0.07</td>
<td>0.26</td>
</tr>
<tr>
<td>Lateral</td>
<td>16.9 x 1.9 ±0.15</td>
<td>24.9 x 2.8 ±0.04</td>
<td>18.1 x 2.7 ±0.08</td>
<td>0.13</td>
</tr>
</tbody>
</table>

p derived from Wilcoxon Rank test. LxW = length x width

Table G.2. The width of the pedicle gap with respect to quadrant and implant.

<table>
<thead>
<tr>
<th>Implant</th>
<th>Quadrant</th>
<th>Anterior ±S.E.</th>
<th>Posterior ±S.E.</th>
<th>Medial ±S.E.</th>
<th>Lateral ±S.E.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Proximal femoral</td>
<td>2.0±0.39</td>
<td>2.5±0.37</td>
<td>4.2±0.85</td>
<td>2.3±0.95</td>
<td></td>
</tr>
<tr>
<td>Distal femoral</td>
<td>1.8±0.16</td>
<td>2.0±0.16</td>
<td>1.5±0.10</td>
<td>1.8±0.14</td>
<td></td>
</tr>
<tr>
<td>Proximal tibial</td>
<td>1.6±0.20</td>
<td>1.7±0.24</td>
<td>1.7±0.17</td>
<td>1.5±0.13</td>
<td></td>
</tr>
</tbody>
</table>

372
Table G.3. The number of quadrants with pedicle present with respect to implant and percentage of bone resected.

<table>
<thead>
<tr>
<th>Quadrants</th>
<th>0 (%)</th>
<th>1 (%)</th>
<th>2 (%)</th>
<th>3 (%)</th>
<th>4 (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Resection (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Proximal femoral</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;40</td>
<td>21.2</td>
<td>36.4</td>
<td>27.3</td>
<td>12.1</td>
<td>3.0</td>
</tr>
<tr>
<td>40-60</td>
<td>38.3</td>
<td>32.4</td>
<td>8.8</td>
<td>17.6</td>
<td>2.9</td>
</tr>
<tr>
<td>&gt;60</td>
<td>26.7</td>
<td>26.7</td>
<td>33.3</td>
<td>13.3</td>
<td>0</td>
</tr>
<tr>
<td>Distal femoral</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;40</td>
<td>19.0</td>
<td>29.7</td>
<td>8.1</td>
<td>29.7</td>
<td>13.5</td>
</tr>
<tr>
<td>40-60</td>
<td>10.1</td>
<td>13.4</td>
<td>14.3</td>
<td>20.2</td>
<td>42.0</td>
</tr>
<tr>
<td>&gt;60</td>
<td>12.1</td>
<td>6.1</td>
<td>12.1</td>
<td>33.3</td>
<td>36.4</td>
</tr>
<tr>
<td>Proximal tibial</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;40</td>
<td>71.5</td>
<td>21.4</td>
<td>0</td>
<td>0</td>
<td>7.1</td>
</tr>
<tr>
<td>40-60</td>
<td>31.8</td>
<td>19.7</td>
<td>21.2</td>
<td>15.2</td>
<td>12.1</td>
</tr>
<tr>
<td>&gt;60</td>
<td>49.9</td>
<td>12.5</td>
<td>18.8</td>
<td>18.8</td>
<td>0</td>
</tr>
</tbody>
</table>

Table G.4. The dimension of the pedicle respect to implant, quadrant and percentage of bone resected.

<table>
<thead>
<tr>
<th>Quadrants</th>
<th>Anterior L x W</th>
<th>Posterior L x W</th>
<th>Medial L x W</th>
<th>Lateral L x W</th>
</tr>
</thead>
<tbody>
<tr>
<td>Resection (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Proximal femoral</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;40</td>
<td>28.4 x 4.4</td>
<td>26.2 x 3.7</td>
<td>32.3 x 4.9</td>
<td>(20.0 x 5.0)</td>
</tr>
<tr>
<td>40-60</td>
<td>50.3 x 4.1</td>
<td>26.7 x 4.6</td>
<td>65.3 x 6.4</td>
<td>17.5 x 2.0</td>
</tr>
<tr>
<td>&gt;60</td>
<td>12.5 x 2.0</td>
<td>15.2 x 2.8</td>
<td>18.3 x 2.1</td>
<td>15.5 x 1.0</td>
</tr>
<tr>
<td>Distal femoral</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;40</td>
<td>16.6 x 5.1</td>
<td>30.8 x 2.8</td>
<td>16.0 x 3.7</td>
<td>19.8 x 3.7</td>
</tr>
<tr>
<td>40-60</td>
<td>22.3 x 2.6</td>
<td>30.8 x 3.0</td>
<td>24.5 x 3.7</td>
<td>23.9 x 2.5</td>
</tr>
<tr>
<td>&gt;60</td>
<td>31.4 x 3.0</td>
<td>39.1 x 3.3</td>
<td>35.1 x 3.5</td>
<td>32.2 x 3.0</td>
</tr>
<tr>
<td>Proximal tibial</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;40</td>
<td>(24.0 x 2.0)</td>
<td>(4.0 x 1.5)</td>
<td>(15.0 x 2.0)</td>
<td>5.0 x 4.0</td>
</tr>
<tr>
<td>40-60</td>
<td>27.8 x 2.6</td>
<td>21.7 x 2.3</td>
<td>32.8 x 3.1</td>
<td>22.4 x 2.5</td>
</tr>
<tr>
<td>&gt;60</td>
<td>27.3 x 2.3</td>
<td>20.0 x 1.3</td>
<td>48.6 x 2.0</td>
<td>7.3 x 2.3</td>
</tr>
</tbody>
</table>
Table G.5. The number of quadrants with pedicle present with respect to implant, and patient age.

<table>
<thead>
<tr>
<th>Quadrants</th>
<th>No pedicle</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Proximal femoral</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤16</td>
<td>40.0</td>
<td>40.0</td>
<td>20.0</td>
<td>0.0</td>
<td>0.0</td>
</tr>
<tr>
<td>&gt;16 ≤25</td>
<td>13.3</td>
<td>26.7</td>
<td>53.3</td>
<td>0.0</td>
<td>6.7</td>
</tr>
<tr>
<td>&gt;25 &lt;60</td>
<td>30.8</td>
<td>34.6</td>
<td>11.5</td>
<td>21.2</td>
<td>1.9</td>
</tr>
<tr>
<td>≥60</td>
<td>40.0</td>
<td>20.0</td>
<td>20.0</td>
<td>20.0</td>
<td>0.0</td>
</tr>
<tr>
<td>Distal femoral</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤16</td>
<td>6.3</td>
<td>12.7</td>
<td>14.3</td>
<td>23.8</td>
<td>42.9</td>
</tr>
<tr>
<td>&gt;16 ≤25</td>
<td>10.0</td>
<td>12.0</td>
<td>6.0</td>
<td>34.0</td>
<td>38.0</td>
</tr>
<tr>
<td>&gt;25 &lt;60</td>
<td>17.2</td>
<td>12.1</td>
<td>19.0</td>
<td>22.4</td>
<td>29.3</td>
</tr>
<tr>
<td>≥60</td>
<td>22.2</td>
<td>44.4</td>
<td>5.6</td>
<td>5.6</td>
<td>22.2</td>
</tr>
<tr>
<td>Proximal tibial</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤16</td>
<td>14.3</td>
<td>25.7</td>
<td>14.3</td>
<td>28.6</td>
<td>17.1</td>
</tr>
<tr>
<td>&gt;16 ≤25</td>
<td>42.3</td>
<td>19.2</td>
<td>26.9</td>
<td>7.7</td>
<td>3.8</td>
</tr>
<tr>
<td>&gt;25 &lt;60</td>
<td>60.0</td>
<td>13.3</td>
<td>16.7</td>
<td>3.3</td>
<td>6.7</td>
</tr>
<tr>
<td>≥60</td>
<td>100.0</td>
<td>0.0</td>
<td>0.0</td>
<td>0.0</td>
<td>0.0</td>
</tr>
</tbody>
</table>

Table G.6. The dimension of pedicle with respect to implant, quadrant and patient age.

<table>
<thead>
<tr>
<th>Quadrants</th>
<th>Anterior LxW</th>
<th>Posterior LxW</th>
<th>Medial LxW</th>
<th>Lateral LxW</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Proximal femoral</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤16</td>
<td>8.0 x 2.5</td>
<td>7.3 x 1.3</td>
<td>15.5 x 5</td>
<td>2.0 x 1.0</td>
</tr>
<tr>
<td>&gt;16 ≤25</td>
<td>9.5 x 5.0</td>
<td>31.1 x 3.6</td>
<td>37.9 x 3.4</td>
<td>12.5 x 3.0</td>
</tr>
<tr>
<td>&gt;25 &lt;60</td>
<td>43.6 x 3.9</td>
<td>20.8 x 3.8</td>
<td>41.0 x 5.5</td>
<td>20.8 x 1.7</td>
</tr>
<tr>
<td>≥60</td>
<td>36.0 x 1.0</td>
<td>68.5 x 11.0</td>
<td>49.0 x 4.0</td>
<td>-</td>
</tr>
<tr>
<td>Distal femoral</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤16</td>
<td>28.4 x 3.0</td>
<td>34.7 x 2.8</td>
<td>29.4 x 3.6</td>
<td>31.3 x 2.9</td>
</tr>
<tr>
<td>&gt;16 ≤25</td>
<td>17.3 x 2.4</td>
<td>28.9 x 3.0</td>
<td>26.9 x 4.3</td>
<td>19.5 x 2.3</td>
</tr>
<tr>
<td>&gt;25 &lt;60</td>
<td>25.0 x 3.5</td>
<td>35.5 x 3.2</td>
<td>21.0 x 3.3</td>
<td>21.4 x 3.0</td>
</tr>
<tr>
<td>≥60</td>
<td>7.5 x 1.5</td>
<td>19.8 x 3.8</td>
<td>13.7 x 3.3</td>
<td>33.4 x 3.2</td>
</tr>
<tr>
<td>Proximal tibial</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤16</td>
<td>27.4 x 2.4</td>
<td>25.4 x 2.1</td>
<td>44.3 x 2.7</td>
<td>19.6 x 2.2</td>
</tr>
<tr>
<td>&gt;16 ≤25</td>
<td>34.3 x 3.9</td>
<td>5.5 x 2.0</td>
<td>29.2 x 3.7</td>
<td>14.0 x 3.2</td>
</tr>
<tr>
<td>&gt;25 &lt;60</td>
<td>19.2 x 1.2</td>
<td>14.5 x 2.5</td>
<td>15.5 x 2.4</td>
<td>18.5 x 3.2</td>
</tr>
<tr>
<td>≥60</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>
Appendix H.

Additional data of uncemented intra-medullary massive endo-prostheses used in laboratory trials and for limb salvage procedures.

Table H.1. The designs of the 5 trial replacements.

<table>
<thead>
<tr>
<th>Implant number</th>
<th>Skeletal location</th>
<th>Form of anti-rotation device</th>
<th>Plateau design</th>
<th>Stem length</th>
<th>Stem design</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Proximal femoral</td>
<td>2 AR lugs (A &amp; P)</td>
<td>Flat</td>
<td>150 mm</td>
<td>Straight</td>
</tr>
<tr>
<td>2</td>
<td>Distal femoral</td>
<td>2 AR lugs (A &amp; P)</td>
<td>Flat</td>
<td>150 mm</td>
<td>Curved</td>
</tr>
<tr>
<td>3</td>
<td>Proximal femoral</td>
<td>Transverse screw (A-P)</td>
<td>Shaped</td>
<td>150 mm</td>
<td>Straight</td>
</tr>
<tr>
<td>4</td>
<td>Distal femoral</td>
<td>Transverse screw (A-P)</td>
<td>Flat</td>
<td>150 mm</td>
<td>Straight</td>
</tr>
<tr>
<td>5</td>
<td>Proximal femoral</td>
<td>Transverse screw (A-P)</td>
<td>Flat</td>
<td>110 mm</td>
<td>Straight</td>
</tr>
</tbody>
</table>

AR = anti-rotation, A = anterior, P = posterior, A-P = anterior through to posterior
Table H.2. Details of the 20 uncemented implants inserted between May 1991 and September 1994.

<table>
<thead>
<tr>
<th>No.</th>
<th>Implant</th>
<th>Age</th>
<th>Sex</th>
<th>Diagnosis</th>
<th>Knee type</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>humerus proximal</td>
<td>34</td>
<td>F</td>
<td>bone metastasis</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>femur distal</td>
<td>71</td>
<td>M</td>
<td>M.F.H.</td>
<td>Smiles</td>
</tr>
<tr>
<td>3</td>
<td>femur distal</td>
<td>19</td>
<td>M</td>
<td>osteosarcoma</td>
<td>Smiles</td>
</tr>
<tr>
<td>4</td>
<td>femur distal</td>
<td>10</td>
<td>M</td>
<td>osteosarcoma</td>
<td>Smiles</td>
</tr>
<tr>
<td>5</td>
<td>femur distal</td>
<td>10</td>
<td>M</td>
<td>osteosarcoma</td>
<td>Smiles</td>
</tr>
<tr>
<td>6</td>
<td>femur distal</td>
<td>43</td>
<td>F</td>
<td>revision (aseptic loosening)</td>
<td>Stanmore</td>
</tr>
<tr>
<td>7</td>
<td>tibia proximal</td>
<td>10</td>
<td>F</td>
<td>osteosarcoma</td>
<td>Smiles</td>
</tr>
<tr>
<td>8</td>
<td>tibia proximal</td>
<td>17</td>
<td>F</td>
<td>osteosarcoma</td>
<td>Smiles</td>
</tr>
<tr>
<td>9</td>
<td>humerus proximal</td>
<td>13</td>
<td>M</td>
<td>osteosarcoma</td>
<td></td>
</tr>
<tr>
<td>10</td>
<td>humerus distal</td>
<td>22</td>
<td>F</td>
<td>osteosarcoma</td>
<td></td>
</tr>
<tr>
<td>11</td>
<td>femur proximal</td>
<td>16</td>
<td>M</td>
<td>Ewing's sarcoma</td>
<td></td>
</tr>
<tr>
<td>12</td>
<td>femur distal</td>
<td>22</td>
<td>F</td>
<td>parosteal sarcoma</td>
<td>Smiles</td>
</tr>
<tr>
<td>13</td>
<td>humerus proximal</td>
<td>47</td>
<td>F</td>
<td>M.F.H.</td>
<td></td>
</tr>
<tr>
<td>14</td>
<td>femur proximal</td>
<td>20</td>
<td>F</td>
<td>osteosarcoma</td>
<td></td>
</tr>
<tr>
<td>15</td>
<td>femur distal</td>
<td>9</td>
<td>M</td>
<td>osteosarcoma</td>
<td>Smiles</td>
</tr>
<tr>
<td>16</td>
<td>tibia mid-shaft</td>
<td>14</td>
<td>F</td>
<td>Ewing's sarcoma</td>
<td></td>
</tr>
<tr>
<td>17</td>
<td>femur distal</td>
<td>14</td>
<td>M</td>
<td>osteosarcoma</td>
<td>Smiles</td>
</tr>
<tr>
<td>18</td>
<td>femur distal</td>
<td>51</td>
<td>F</td>
<td>revision (loosening)</td>
<td>Stanmore</td>
</tr>
<tr>
<td>19</td>
<td>tibia proximal</td>
<td>20</td>
<td>M</td>
<td>osteosarcoma</td>
<td>Smiles</td>
</tr>
<tr>
<td>20</td>
<td>femur proximal</td>
<td>42</td>
<td>F</td>
<td>chondrosarcoma</td>
<td></td>
</tr>
</tbody>
</table>
Table H.3. The design modifications of the first 20 uncemented endoprostheses.

<table>
<thead>
<tr>
<th>No.</th>
<th>Skeletal location</th>
<th>Anti-rotation device</th>
<th>Coating of the IM stem</th>
<th>Plateau design</th>
<th>Stem shape</th>
<th>Stem sleeve</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>PH</td>
<td>AR screw (A-P)</td>
<td>None</td>
<td>Flat</td>
<td>Parallel</td>
<td>Yes</td>
</tr>
<tr>
<td>2</td>
<td>DF</td>
<td>AR screw (A-P)</td>
<td>None</td>
<td>Flat</td>
<td>Parallel</td>
<td>Yes</td>
</tr>
<tr>
<td>3</td>
<td>DF</td>
<td>2 AR lugs (A-P)</td>
<td>Precision region</td>
<td>Flat</td>
<td>Parallel</td>
<td>Yes</td>
</tr>
<tr>
<td>4</td>
<td>DF</td>
<td>2 AR lugs (A-P)</td>
<td>Precision region</td>
<td>Flat</td>
<td>Parallel</td>
<td>No</td>
</tr>
<tr>
<td>5</td>
<td>DF</td>
<td>2 AR lugs (A-P)</td>
<td>Precision region</td>
<td>Flat</td>
<td>Parallel</td>
<td>No</td>
</tr>
<tr>
<td>6</td>
<td>DF</td>
<td>2 AR lugs (A-P)</td>
<td>Precision region</td>
<td>Coned</td>
<td>Parallel</td>
<td>No</td>
</tr>
<tr>
<td>7</td>
<td>PT</td>
<td>2 AR lugs (A-P)</td>
<td>All stem</td>
<td>Flat</td>
<td>Parallel</td>
<td>No</td>
</tr>
<tr>
<td>8</td>
<td>PT</td>
<td>2 AR lugs (A-P)</td>
<td>All stem*</td>
<td>Flat</td>
<td>Parallel</td>
<td>No</td>
</tr>
<tr>
<td>9</td>
<td>PH</td>
<td>2 AR lugs (A-P)</td>
<td>All stem</td>
<td>Flat</td>
<td>Parallel</td>
<td>No</td>
</tr>
<tr>
<td>10</td>
<td>DH</td>
<td>2 AR lugs (A-P)</td>
<td>All stem</td>
<td>Flat</td>
<td>Parallel</td>
<td>No</td>
</tr>
<tr>
<td>11</td>
<td>PF</td>
<td>2 AR lugs (A-P)</td>
<td>All stem</td>
<td>Coned</td>
<td>Parallel</td>
<td>No</td>
</tr>
<tr>
<td>12</td>
<td>DF</td>
<td>2 Extra-cortical plates (A&amp;L)</td>
<td>All stem</td>
<td>Flat</td>
<td>Parallel</td>
<td>No</td>
</tr>
<tr>
<td>13</td>
<td>PF</td>
<td>2 AR lugs (A-P)</td>
<td>All stem</td>
<td>Flat</td>
<td>Parallel</td>
<td>No</td>
</tr>
<tr>
<td>14</td>
<td>PH</td>
<td>2 AR lugs (A-P)</td>
<td>All stem</td>
<td>Flat</td>
<td>Parallel</td>
<td>No</td>
</tr>
<tr>
<td>15</td>
<td>DF</td>
<td>2 AR lugs (A-P)</td>
<td>All stem</td>
<td>Flat</td>
<td>Parallel</td>
<td>No</td>
</tr>
<tr>
<td>16</td>
<td>M-ST</td>
<td>2 AR lugs (M-L)</td>
<td>All stem</td>
<td>Flat</td>
<td>Parallel</td>
<td>No</td>
</tr>
<tr>
<td>17</td>
<td>DF</td>
<td>2 AR lugs (A-P)</td>
<td>All stem</td>
<td>Flat</td>
<td>Tapered</td>
<td>No</td>
</tr>
<tr>
<td>18</td>
<td>DF</td>
<td>2 AR lugs (A-P)</td>
<td>All stem</td>
<td>Flat</td>
<td>Parallel</td>
<td>No</td>
</tr>
<tr>
<td>19</td>
<td>PT</td>
<td>2 AR lugs (A-P)</td>
<td>All stem</td>
<td>Flat</td>
<td>Tapered</td>
<td>No</td>
</tr>
<tr>
<td>20</td>
<td>PF</td>
<td>2 AR lugs (A-P)</td>
<td>All stem</td>
<td>Flat</td>
<td>Tapered</td>
<td>No</td>
</tr>
</tbody>
</table>

HA = hydroxyapatite, AR = anti-rotation, A = anterior, P = posterior, M = medial, L = lateral
DF = distal femoral, PF proximal femoral, PT = proximal tibial, M-S T = mid-shaft tibial, PH = proximal humeral, DH = distal humeral.
* All the stem was coated except 9 mm adjacent to the plateau, see text.
Table H.4. A summary of the dimensions of the reamer and intra-medullary stem. (All dimensions in millimetres).

<table>
<thead>
<tr>
<th>No.</th>
<th>Implant</th>
<th>Precision reamer Ø</th>
<th>Uncoated precision stem Ø</th>
<th>Precision region length</th>
<th>Total stem length</th>
<th>Coating thickness</th>
<th>Ø of coated stem</th>
<th>Stem Ø - reamer Ø</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>PH</td>
<td>10.93</td>
<td>11.00</td>
<td>35</td>
<td>100</td>
<td>-</td>
<td>-</td>
<td>0.07</td>
</tr>
<tr>
<td>2</td>
<td>DF</td>
<td>15.48</td>
<td>15.50</td>
<td>40</td>
<td>110</td>
<td>-</td>
<td>-</td>
<td>0.02</td>
</tr>
<tr>
<td>3</td>
<td>DF</td>
<td>11.98</td>
<td>12.00</td>
<td>40</td>
<td>110</td>
<td>0.150</td>
<td>12.15</td>
<td>0.17</td>
</tr>
<tr>
<td>4</td>
<td>DF</td>
<td>9.18</td>
<td>9.20</td>
<td>43</td>
<td>100</td>
<td>0.150</td>
<td>9.35</td>
<td>0.17</td>
</tr>
<tr>
<td>5</td>
<td>DF</td>
<td>10.67</td>
<td>11.05</td>
<td>50</td>
<td>100</td>
<td>0.150</td>
<td>11.20</td>
<td>0.53</td>
</tr>
<tr>
<td>6</td>
<td>DF</td>
<td>16.00</td>
<td>16.00</td>
<td>60</td>
<td>120</td>
<td>0.150</td>
<td>16.15</td>
<td>0.15</td>
</tr>
<tr>
<td>7</td>
<td>PT</td>
<td>9.30</td>
<td>9.51</td>
<td>60</td>
<td>100</td>
<td>0.150</td>
<td>9.66</td>
<td>0.36</td>
</tr>
<tr>
<td>8</td>
<td>PT</td>
<td>15.73</td>
<td>15.75</td>
<td>50</td>
<td>100</td>
<td>0.150</td>
<td>15.90</td>
<td>0.17</td>
</tr>
<tr>
<td>9</td>
<td>PH</td>
<td>10.37</td>
<td>10.49</td>
<td>50</td>
<td>90</td>
<td>0.150</td>
<td>10.64</td>
<td>0.27</td>
</tr>
<tr>
<td>10</td>
<td>DH</td>
<td>11.98</td>
<td>12.0</td>
<td>50</td>
<td>90</td>
<td>0.110</td>
<td>12.11</td>
<td>0.13</td>
</tr>
<tr>
<td>11</td>
<td>PH</td>
<td>14.92</td>
<td>15.03</td>
<td>70</td>
<td>141</td>
<td>0.150</td>
<td>15.180</td>
<td>0.26</td>
</tr>
<tr>
<td>12</td>
<td>DF</td>
<td>10.98</td>
<td>11.00</td>
<td>68</td>
<td>135</td>
<td>0.075</td>
<td>11.075</td>
<td>0.095</td>
</tr>
<tr>
<td>13</td>
<td>PF</td>
<td>11.98</td>
<td>12.07</td>
<td>70</td>
<td>136</td>
<td>0.150</td>
<td>12.22</td>
<td>0.24</td>
</tr>
<tr>
<td>14</td>
<td>PH</td>
<td>9.00</td>
<td>9.02</td>
<td>35</td>
<td>70</td>
<td>0.075</td>
<td>9.095</td>
<td>0.095</td>
</tr>
<tr>
<td>15</td>
<td>DF</td>
<td>10.37</td>
<td>10.48</td>
<td>50</td>
<td>100</td>
<td>0.135</td>
<td>10.615</td>
<td>0.245</td>
</tr>
<tr>
<td>16</td>
<td>M-S T</td>
<td>11.85</td>
<td>11.91</td>
<td>50</td>
<td>100</td>
<td>0.085</td>
<td>11.995</td>
<td>0.145</td>
</tr>
<tr>
<td>17</td>
<td>DF</td>
<td>14.66 &gt; 12.30</td>
<td>14.56 &gt; 12.15</td>
<td>60</td>
<td>120</td>
<td>0.150</td>
<td>14.71 &gt; 12.30</td>
<td>0.05</td>
</tr>
<tr>
<td>18</td>
<td>DF</td>
<td>16.00</td>
<td>15.99</td>
<td>60</td>
<td>120</td>
<td>0.19</td>
<td>6.18</td>
<td>0.18</td>
</tr>
<tr>
<td>19</td>
<td>PT</td>
<td>18.30 &gt; 13.16</td>
<td>18.15 &gt; 13.00</td>
<td>60</td>
<td>110</td>
<td>0.11</td>
<td>18.25 &gt; 13.11</td>
<td>0.05</td>
</tr>
<tr>
<td>20</td>
<td>PF</td>
<td>10.65</td>
<td>10.60</td>
<td>60</td>
<td>110</td>
<td>0.15</td>
<td>10.70</td>
<td>0.05</td>
</tr>
</tbody>
</table>

DF = distal femoral, PF proximal femoral, PT = proximal tibial, M-S T = mid-shaft tibial, PH = proximal humeral, DH = distal humeral.
Appendix J.

The operative procedure to insert the mid-shaft replacements

Adult female (skeletally mature) goats of the larger breeds were chosen. The breeds used were predominantly Saanen and Toggenberg. The Saanen goats were slightly taller and more robust (approximate weight = 50 kg) than the Toggenbergs (45 kg), however, the difference in tibial dimensions were minimal. One Anglo-Nubian was used, that was of similar size and stature to the Saanen breed. Goats were bought in and kept on an outdoor concrete apron or indoors depending on the season for a period of at least 1 month before the planned operation, for acclimatisation, over which time their health and weight were monitored regularly. The acclimatisation time provided sufficient time for the design, fabrication and coating of the custom-made mid-shaft tibial endo-prosthesis.

Prior to the operation the goat were starved of food for 12 hours but provided with water and the goats were also moved to a pen without bedding and isolated from other goats. The surgical team consisted of a surgeon, a surgeons assistant, an anaesthetist and a theatre assistant. All staff in the operating theatre wore theatre greens, a face mask and surgical hoods.

Prior to intubation, the goat was given xylazine, an intra-muscular sedative (Rompon, Bayer, 0.01 ml/kg) that took approximately 15 minutes to provide satisfactory sedation. For anaesthesia, intravenous ketamine (Vetlar, Parke Davis Veterinary, 1.0 ml/kg) was administered providing full anaesthesia and analgesia to permit intubation of a trachea tube. In addition, ketamine was a
A muscular relaxant that permitted the lower jaw to be opened widely, to ease intubation. Once intubated, the goat was maintained on oxygen and halothane. The right hind limb was shaved in its entirety and washed in a diluted antimicrobial solution (Betadine), ensuring the hoof was thoroughly scrubbed. Undiluted anti-microbial solution, applied with a swab to the anterior and flanks of the tibia, starting at the predetermined location of surgery and worked outwards ensured the site was not reworked with a dirty swab. Whilst the cleansing was in progress, an antibiotic (Baytril) was administered subcutaneously. This ensured that the antibiotic was at its peak whilst surgery was taking place. On completion of the preparation the limb was kept elevated whilst the goat was transported into theatre and transferred to the operating table. The limb was then passed to the surgeon for further cleaning and draping with sterilised sheets.

The surgeon opened the subcutaneous layers with a longitudinal anterior incision, parting the muscles and upon reaching the tibia, peeled back the periosteum off the bone. The location of the proximal transection was measured from an anterior notch distal to the tibial tuberosity, identifiable on lateral radiographs. The bone was resected with a transverse cut using a micro-oscillating air powered saw. Irrigation of the blade and bone cut with sterile water was maintained whilst transecting the bone. The distal resection was measured from the proximal cut. The proximal section of the mid-shaft replacement was trialled and then secured into location with bone screws. The screw holes were pre-tapped to ensure the bone did not fracture. Preparation of the distal cavity was by reaming and lavaging. Thoroughly mixed low viscosity acrylic bone cement was applied with a sterile syringe. Using a hypodermic needle, blood that had accumulated in the distal region of the bone cavity was drawn off to reduce the pressure and assist interdigitation of the cement. The intra-medullary stemmed component was then pushed into its
correct orientation. Once the cement had set the two component were screwed together.

On closing up, the periosteum was drawn together and sutured over the prosthesis. The soft tissue layers sutured back together and finished with under suturing skin layer. Analgesia (Finadyne) was administered subcutaneously whilst the closing of the soft tissues was in progress. The limb was wrapped in soft bandage and secured with sticky elastic bandage. Anaesthesia was halted and once the gagging reflex had returned the trachea tube was withdrawn and the animal transported back to a clean and freshly bedded pen. The animal, positioned in a recumbent position, was monitored closely for the next three hours. Once recovered, the animals frequently stood within 3 hours of the operation and began feeding. The goats received analgesia (subcutaneous) for a further 3 to 5 days and antibiotics (subcutaneous) for 4 days. They remained in isolation for a minimum of 1 month, after which they were moved to an outdoor covered apron with 1 or 2 other goats. After 2 months, depending on the weather the goats were allowed into a nearby paddock throughout the day and returned to the concrete floored covered apron for overnight shelter and security.
Table J.1. The dimensions of the extra-cortical plates of the mid-shaft tibial replacements used in the animal model.

<table>
<thead>
<tr>
<th>Implant number</th>
<th>Number of plates</th>
<th>Plate dimensions (mm)</th>
<th>Screw location (mm)</th>
<th>Grooved</th>
<th>Length and width of groove (mm)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Length</td>
<td>Width</td>
<td>Breadth at plateau</td>
<td>Breadth at tip</td>
</tr>
<tr>
<td>G73</td>
<td>3</td>
<td>60</td>
<td>12</td>
<td>2</td>
<td>1.25</td>
</tr>
<tr>
<td></td>
<td></td>
<td>50</td>
<td>12</td>
<td>2</td>
<td>1.25</td>
</tr>
<tr>
<td>G77</td>
<td>2</td>
<td>60</td>
<td>12</td>
<td>2</td>
<td>1.25</td>
</tr>
<tr>
<td></td>
<td></td>
<td>50</td>
<td>12</td>
<td>2</td>
<td>1.25</td>
</tr>
<tr>
<td>G40</td>
<td>2</td>
<td>60</td>
<td>12</td>
<td>2</td>
<td>1.25</td>
</tr>
<tr>
<td></td>
<td></td>
<td>50</td>
<td>12</td>
<td>2</td>
<td>1.25</td>
</tr>
<tr>
<td>G7</td>
<td>3</td>
<td>60</td>
<td>12</td>
<td>3</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td></td>
<td>50</td>
<td>12</td>
<td>3</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td></td>
<td>50</td>
<td>12</td>
<td>3</td>
<td>2</td>
</tr>
<tr>
<td>G62</td>
<td>2</td>
<td>60</td>
<td>12</td>
<td>2.5</td>
<td>1.5</td>
</tr>
<tr>
<td></td>
<td></td>
<td>50</td>
<td>12</td>
<td>2.5</td>
<td>1.5</td>
</tr>
<tr>
<td>G64</td>
<td>3</td>
<td>60</td>
<td>12</td>
<td>2.5</td>
<td>1.5</td>
</tr>
<tr>
<td></td>
<td></td>
<td>50</td>
<td>12</td>
<td>2.5</td>
<td>1.5</td>
</tr>
<tr>
<td>G29</td>
<td>2</td>
<td>60</td>
<td>12</td>
<td>2.5</td>
<td>1.5</td>
</tr>
<tr>
<td></td>
<td></td>
<td>60</td>
<td>12</td>
<td>2.5</td>
<td>1.5</td>
</tr>
<tr>
<td>G78</td>
<td>3</td>
<td>60</td>
<td>12</td>
<td>2.5</td>
<td>1.5</td>
</tr>
<tr>
<td></td>
<td></td>
<td>50</td>
<td>12</td>
<td>2.5</td>
<td>1.5</td>
</tr>
<tr>
<td>G59</td>
<td>2</td>
<td>60</td>
<td>12</td>
<td>2.5</td>
<td>1.5</td>
</tr>
<tr>
<td></td>
<td></td>
<td>50</td>
<td>12</td>
<td>2.5</td>
<td>1.5</td>
</tr>
<tr>
<td>G74</td>
<td>2</td>
<td>60</td>
<td>12</td>
<td>2.5</td>
<td>1.5</td>
</tr>
<tr>
<td></td>
<td></td>
<td>50</td>
<td>12</td>
<td>2.5</td>
<td>1.5</td>
</tr>
</tbody>
</table>