CHARACTERISATION OF BONE TISSUE USING COHERENTLY SCATTERED X-RAY PHOTONS

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Errata

Page 15: Line 12: 'Thompson' should read 'Thomson'.

Page 17: Line 5: 'Thompson' should read 'Thomson'.

Page 18: Line 13: 'Thompson' should read 'Thomson'.

Page 19: Line 6: 'Thompson' should read 'Thomson'.

Page 18: Figure 1.6: X axis should read 'Momentum Transfer [Å^2]'.

Page 36: Line 3: 'Later' should read 'latter'.

Page 56: Line 14: 'FWHM and energy' should read 'FWHM and the square root of energy'.

Page 58: Line 10: 'asses' should read 'assess'.

Page 78: Line 3: 'increasing the momentum transfer separation' should read 'increasing the energy separation'

Page 81: Line 6: 'Institute' should read 'Institute'.

Page 112: Figure 4.14: Caption should read 'Average accuracy of the 9 test phantoms for the calcaneus using the three models'.

Page 115: Figure 4.16: X axis should read 'Average Accuracy (FBML)'.

Page 127: Line 16: 'can be located useful' should read 'can be located in useful'.
Abstract

An energy dispersive x-ray diffractometer was designed and built to measure bone mineral density in the trabecular region of the bone and to assess the suitability of the technique as a clinical in-vivo method. Trabecular bone has a higher turnover rate than that of cortical bone, and to detect excessive bone mass loss, with the prevention of osteoporosis in mind, it would be advantageous to be able to measure trabecular bone mineral density in isolation from cortical bone density. At present the only method capable of achieving this in-vivo is quantitative computerised tomography.

Initially measurements were made of trabecular bone mineral density on dry excised bone samples consisting of femurs, vertebrae and radii. These measurements were compared to measurements made using dual energy x-ray absorptiometry (DEXA) and photodensitometry techniques. The energy dispersive x-ray diffraction (EDXRD) measurements were the most accurate when correlated to the actual trabecular densities of the femur and vertebrae with correlation coefficients of r=0.84 and r=0.92 respectively. This compares with r=0.64 and r=0.74 for the DEXA measurements and r=0.77 and r=0.85 for the photodensitometry measurements. For the radii samples the correlation coefficients for all the methods were approximately the same at r=0.75.

In-vivo measurements were simulated using a specially designed phantom. The results were analysed using multivariate calibration techniques and the radiation dose to the patient estimated using thermoluminescent dosimetry (TLD). Two main clinical sites were targeted, the calcaneus (heel) and the radius (forearm). It was found that the technique was capable of producing results with the required accuracy and precision (approximately 1% of peak bone mass) but the radiation dose to the patient was high compared to other diagnostic radiographic procedures. The calcaneus measurements produced an effective dose of 270 μSv. for an accuracy of between 1% and 2% fractional bone mass loss, and the radius measurement resulted in an effective dose of 3.3 mSv. for an accuracy of approximately 2% fractional bone mass loss.
Measurements were made on recently excised femoral heads from total hip replacements, with 5 cm of tissue equivalent material. Predictions of bone mineral density were made from a calibration model created using phantom measurements. The predictions were compared to CT numbers obtained from QCT measurements and the correlation coefficient was calculated to be 0.94 significant to the 0.1 % level.

It is concluded that EDXRD is a technique that, with suggested refinements, has the potential to be able to make clinical measurements giving good accuracy and precision at an acceptable radiation dose to the patient.
It is far better to be educated beyond your class than beyond your intelligence.

D. Walsh BA, MSc. 1996
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Introduction

The objective of this study was to design and build an energy dispersive x-ray diffractometer that could be used to characterise bone tissue, and to assess the suitability of such a system for in-vivo bone mineral density measurements. Bone mass is a major determinant with respect to the strength of bone and risk of bone fracture, and is an important parameter in the diagnosis and management of osteoporosis (Christiansen 1995).

Osteoporosis is one of the major problems facing women and older people of both sexes. In the USA 1.5 million fractures per year are attributed to osteoporosis with a lifetime risk of fracture of the spine, hip, and distal radius of 40% for white women and 13% for white men from 50 years of age onwards (Riggs and Melton 1995). The consequences of fractures are severe, e.g. after a hip fracture there is a 10 - 20% mortality rate over the subsequent 6 months. Furthermore, 50% of sufferers will be unable to walk without assistance and 25% will require long term care. In the US the annual cost to the healthcare system is at least $5 to $10 billion and it is estimated that fractures will increase fourfold world-wide during the next 50 years which could threaten the stability of healthcare systems throughout the world.

Bone mass or density can be determined at many skeletal sites e.g. forearm, heel, hip, spine or the total skeleton. All techniques used to measure bone density are subject to limitations that hamper measurements of changes in bone mass, and a common criterion in all types of measurement is their precision and accuracy (Hassager and Christiansen 1995). Most established methods of measuring bone mineral density are based on photon absorptiometry, which, with the exception of Quantitative Computerised Tomography (QCT), includes a measure of both cortical and trabecular bone. Studies have shown that the severity of osteoporosis can best be determined by measuring the density of trabecular bone in isolation from cortical density
The technique used in this work is designed to investigate a volume of bone within the trabecular region of a chosen clinical site.

EDXRD is a technique that makes use of the coherently scattered x-ray photons emerging from a material that is subjected to incident radiation. Coherent, or Rayleigh scattering is the scattering of photons from bound atomic electrons which results in no change in energy of the incident photon, but due to the spatial distribution of the scattering centres and the scattering angle, interference effects become apparent between the individual wavelets from the scattering centres. For materials with long range structure e.g. crystalline materials, the effects of interference from the atomic sites in a unit cell of the lattice leads to the phenomenon of Bragg diffraction. X-ray diffraction has been used as a tool for investigating materials for many years and more recently has been used as an industrial tool for substance identification (Luggar and Gilboy 1994). Examples of such on-going work are the detection of contaminants in food and the detection of energetic materials (explosives) in luggage (Luggar et al 1996).

Coherent scatter in diagnostic radiology was, until recently, overlooked because its cross section was small and it was assumed to be indistinguishable from incident radiation due to its elastic nature. However Johns and Yaffe (1983) showed that coherent scatter represented a significant fraction of the total scattering in body tissues at diagnostic energies and the amount of work being undertaken involving the applications of coherent scattering in medicine has increased considerably since then. Scattering profiles of body tissue and some tissue substitute materials have been reported (Kosanetzky et al 1987) and small angle scattering measurements have been made on breast tissues (Evans et al 1991). Tomographic techniques have also been explored using energy dispersive x-ray diffraction on test objects consisting of water and various plastic materials (Harding et al 1990).

The use of coherent scattering for measuring bone mineral density has been investigated. Kerr et al (1980) used gamma rays which were scattered coherently and incoherently from the calcaneus of three cadaver feet and showed that coherently scattered photons were more sensitive to changes in bone mineral composition than a method using the ratio of coherent to incoherent scattered photons. Royle and Speller (1991) showed results of low angle x-ray scattering measurements on bone and bone substitute materials using a polyenergetic x-ray source. Two methods were investigated: measuring the scatter profiles at a single scattering angle and measuring...
the number of photons scattered within chosen energy values for a range of angles between 1 and 11 degrees. The conclusion was made that changes in bone mineral were more apparent in the scatter profiles and it is this method that has been adopted in this study. More recent work has investigated quantitative x-ray diffraction analysis of bone and marrow volumes in the femoral head (Royle and Speller 1995). Quantitative data of the ratio of bone and marrow volumes was obtained from the trabecular region of the femoral head by measuring the relative intensities of the two peaks due to bone mineral and bone marrow, and it was proposed that this measure could provide a parameter for the determination of the osteoporotic state of the bone.

The problems of applying an EDXRD technique to measure bone mineral density in a clinical in-vivo environment are significant. The information contained in a scatter profile obtained from a measurement volume defined in the trabecular region, suffers from degradation due to attenuation caused by the physical size of the trabecular region itself, the thickness of cortical bone encasing the trabecular region and the soft tissue surrounding the bone. These influences are all variables over which we have little or no control. This study investigates the use of multivariate calibration techniques in an attempt to overcome the problems of obtaining quantitative measures of bone mineral density in-vivo.

The remainder of this chapter gives an overview of the points relevant to the study. It introduces the anatomy and physiology of bone and the concept of bone loss which can lead to osteoporosis. The existing methods of measuring bone mineral density are briefly reviewed. The theory of scattering and x-ray diffraction is introduced and the experimental set up of the energy dispersive x-ray diffractometer used in this work is described. The chapter includes an introduction to multivariate analysis and illustrates the technique via a simple experimental example and concludes with an introduction to dosimetry.

1.1 Bone

The skeletal system is the framework for the body. Without it we would be unable to perform tasks such as walking, grasping or even standing. The skeletal system also acts as protection for delicate organs e.g. the skull is a protective cage for the brain and the vertebrae protects the spinal cord. Bone also acts as a storage facility for
minerals which can be distributed to parts of the body on demand. Bone marrow plays an important role in the correct functioning of the body e.g. red marrow produces red blood cells, white blood cells and platelets and the lipids stored in yellow marrow are a source of energy.

1.1.1 Bone structure

Bone is a connective tissue which is made rigid by the deposition of minerals. Bone can be split into two categories, cortical bone and trabecular bone. Both types are constantly being destroyed and renewed in a process known as remodelling. The anatomy of the femoral head and neck, which is typical of a long bone, is shown in figure 1.1. The diaphysis is the shaft of the bone and the epiphysis is the extremity or end of the bone. A thin layer of articular cartilage covers the epiphysis where the bone forms a joint with another bone and the periosteum is a dense fibrous covering around the surface of the bone not covered by articular cartilage. The medullary cavity is the space inside the diaphysis that contains yellow marrow in adult bone.

Cortical bone is a dense bone tissue that makes up approximately 80% of the skeletal mass. It is found on the exterior of all bone and is generally thicker in the diaphysis than the epiphysis. Adult cortical bone has a concentric ring structure which gives it immense strength. Blood vessels and nerves penetrate cortical bone through the Volkmanns and Haversian canals (not shown in figure 1.1).

Trabecular bone contains many spaces between bony struts which make a rigid network of bone and constitutes most of the bone in short, flat, irregular shaped bones e.g. vertebrae and the calcaneus (heel), and is found in the epiphysis of long bones for example the head and neck of the femur. Trabecular bone contributes approximately 20% of the total skeletal mass. The irregular latticework of trabecular bone is made up of thin plates called trabeculae which provide a large surface area and are the most metabolically active part of the skeleton. The trabeculae account for approximately 33% of the mass of trabecular bone and 20% of the volume (Woodard and White 1982) and are typically 100-200 μm thick and enclose spaces which are 600-1000 μm across. The spaces enclosed by the trabeculae are filled with marrow. In the early years of life all marrow is used to produce blood cells in a process called haemopoiesis and this marrow is known as red marrow. In adult bone the red marrow is nearly all replaced by fibrous tissue and fat known as yellow marrow.
Figure 1.1: The anatomy of the femoral head and neck.

Figure 1.2 shows a slice of bone taken through the neck of the femur. The outer cortical bone and the trabecular bone are clearly visible. The spaces between the trabeculea are filled with bone marrow.
Chapter one

Introduction

Figure 1.2: A slice through the femoral neck shows the cortical bone forming the outer shell, and the inner trabecular bone. The enclosed cells are filled with marrow.

1.1.2 Mineral composition of bone

Bone fibres consist of a protein called collagen which is encrusted with a crystalline mineral or bone salt. The specific feature that distinguishes bone from other connective tissue is the presence of bone mineral. Mature bone mineral is hydroxylapatite, formed from calcium carbonate and calcium phosphate. Mineral is deposited on the collagenous matrix which gives it structural rigidity and provides a reservoir for 99% of the body calcium. As well as calcium and phosphorous, bone contains magnesium, sodium, potassium, carbon, chlorine, hydrogen and oxygen. Table 1.1 shows the elemental composition of bone (% by mass), the data was taken from Woodard and White (1986).

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<td>(3.4)</td>
<td>(0.2)</td>
</tr>
<tr>
<td></td>
<td>Cl</td>
<td>K</td>
<td>Ca</td>
<td>Fe</td>
<td></td>
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<tr>
<td></td>
<td>(0.2)</td>
<td>(0.1)</td>
<td>(7.4)</td>
<td>(0.1)</td>
<td></td>
<td></td>
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</tr>
</tbody>
</table>

*Table 1.1 Elemental Composition of Bone, % by mass (Woodard and White 1986)*
1.1.3 Bone growth and remodelling

Bone growth occurs during the first 20 years of life with an accelerated spurt during adolescence. This is followed by a period of consolidation during which time an individual's peak bone mass is reached, which in an adult is at about 35 years of age. Black populations have a higher bone mass than Caucasians or Asians (Cohn et al 1977, Reid et al 1986) and males have bigger, denser skeletons than females (Mazess 1982). Each individual has their own genetic potential for peak bone mass and the degree to which it is reached is dictated by hormonal, nutritional and mechanical factors (Goldsmith and Johnston 1975, Sandler et al 1985, Nilson and Westlin 1971). The body must manufacture the correct amount of the hormones responsible for bone growing activities as too little or too much human growth hormone during childhood results in abnormally short or tall adults. The important nutritional determinant is dietary calcium and phosphorous as well as sufficient amounts of vitamins, particularly vitamin D, which participates in the absorption of calcium from dietary intake into the blood as well as calcium removal from the bone and kidney re-absorption of calcium that would otherwise be lost in the urine. Insufficient vitamin C results in decreased production of collagen and hence bone matrix. The mechanical demands put on a bone also influence its growth, and immobilisation due to illness will result in bone loss. Higher bone mass has been observed in athletic individuals, and when placed under mechanical stress the formation of mineral salts and collagen fibre increases.

Bone has the property of renewing itself throughout adult life and is never metabolically at rest. Remodelling is the term that describes the replacement of old bone tissue with new bone tissue and takes place at different rates in various regions of the body. Some parts of the femur are replaced approximately every four months, in contrast to the shaft which may not be completely replaced over an individual's lifetime (Tortora and Anagnostakos 1990). Remodelling allows injured bone to be removed and replaced with new bone and allows bone to act as a calcium reservoir from which blood continually exchanges calcium, removing it when required and re-supplying it with dietary calcium to prevent loss.

1.1.4 Ageing and the skeletal system

Throughout life females have lower bone mass than males but with advancing age this difference widens. Over a lifetime a female will lose approximately 35% of their peak
cortical bone and approximately 50% of their trabecular bone while a male will lose approximately three quarters of this amount (Riggs and Melton 1986). Factors that influence rate of loss include oestrogen deficiency, body mass, physical activity levels, dietary intake of calcium and phosphorous, smoking, alcohol intake, certain diseases and medications.

Both cortical and trabecular bone mass decline with age in both sexes. For cortical bone (Mazess 1982, Smith et al 1975) this loss usually begins to occur after the age of 30 years in females and is approximately 0.3-0.5% of peak bone mass per year until it accelerates greatly around 40 to 45 years of age as oestrogen levels decrease. The loss rate may increase to 2-3% of peak mass per year but will slowly revert to the lower rates after 10 years. In males the rate of cortical loss does not rise above the 0.3-0.5% annual rate. For trabecular bone (Riggs et al 1986, Mazess 1982) the rate of loss ranges from 1.0- 3.0% per year in women and is approximately 1.2% in men.

1.1.5 Osteoporosis

Osteoporosis is an age related disorder that is characterised by decreased bone mass resulting in an increased risk of fracture following trauma. The disorder affects mainly middle aged and elderly people with females being affected more than males and white populations in general more than black populations. The first symptom of osteoporosis occurs when the bone mass is reduced to the extent that the skeleton can no longer withstand the mechanical stresses of everyday living, and a fracture occurs. Sites particularly at risk are the femur and distal radius. Osteoporosis can also cause vertebrae to crush resulting in shrinkage of the backbone, consequent loss of height and hunched backs. In an individual suffering from osteoporosis there is a loss of mineral from both cortical and trabecular bone with some trabeculea being lost completely. Figure 1.3 shows slices of bone from the neck of the femur. Figure 1.3a shows a healthy bone with many thick trabeculae and a generally thick cortex contrasting with figure 1.3b which shows the thinning and complete disappearance of some trabeculea as well as cortical thinning in some areas.
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![Figure 1.3: a) Healthy bone with many thick trabeculae enclosing marrow cavities. b) Osteoporotic bone with reduced trabeculae. Both slices are taken from the neck of the femur.](image)

1.2 Methods of determining bone mass

The following is a brief outline of the methods that are currently available to measure bone mineral density. For a more detailed description and comparisons of the methods the reader is referred to Hassager and Christiansen (1995), Lang et al (1991), Speller et al (1989) and Ott et al (1987).

1.2.1 Radiogrammetry

Radiogrammetry determines the amount of bone present by measuring the thickness of cortical bone from conventional X-ray images normally of the metacarpal bones. The advantages of radiogrammetry are that it is cheap and simple to carry out with equipment that is widely available. The radiation dose to the patient is low, approximately 0.4 mSv. The disadvantages are that it does not measure any changes in trabecular bone mass and there are potential sources of error in making the measurement of cortical width, movement during exposure and incorrect film processing.
1.2.2 Photodensitometry

A radiograph is taken of the clinical site, normally the metacarpals, radius or ulna, which is placed next to a step wedge of bone mineral equivalent material. Both arm and step wedge are placed in a water bath, which has similar attenuating properties to soft tissue at the energies used, eliminating the differences in soft tissue thickness around the bone. The optical density of the bone is read from the radiograph and compared with the calibration curve obtained from optical densities from the step wedge so that bone density can be given as a thickness of the bone equivalent material. The advantages and disadvantages are the same as those for radiogrammetry with the added disadvantage that each film requires calibration with the reference step wedge. However, this method does include trabecular bone as well as cortical bone in the measurement.

1.2.3 Photon absorptiometry

This is the most widely used technique for assessing bone mineral content and makes use of the exponential law of photon attenuation. A highly collimated source of radiation is passed through the chosen clinical site and the transmitted intensity is recorded by a highly collimated NaI crystal scintillation detector.

In single photon absorptiometry the isotope source normally used is iodine 125 which emits photons of energy 27.4 keV. The site being measured has to be immersed in water to eliminate the effects of surrounding soft tissue on the measurement. The method is restricted to appendicular sites typically the distal radius and the mid point of the radius. An extension to this technique is dual photon absorptiometry which eliminates the need for immersion in a water bath enabling more clinically relevant sites deeper within the body, such as the femur and lumbar vertebrae, to be measured.

A further development of this technique is dual energy X-ray absorptiometry (DEXA). Instead of two isotope sources being used a stable X-ray tube is rapidly switched between two kVp settings or a single kVp setting is used along with suitable k-edge filters. The method produces a higher photon flux than isotopes which reduces scanning times. DEXA is the most widely used method for monitoring bone mineral density as it gives a low radiation dose to the patient (approximately 4.0 μSv) and has a reported precision of 1% \( (\text{Mazess et al 1988, Franck et al 1994}). \)
1.2.4 Quantitative Computerised Tomography (QCT)

Computerised Tomography produces an attenuation profile through a cross section of the chosen site in angular steps. Each profile is back projected and an image reconstructed with each pixel in the image being allocated a CT number. Because the main interactions that occur in the body are Compton scattered events, which are dependent on the physical density of the scattering medium, the CT number can be directly related to the density of the tissue. The area of the bone which is of interest can be allocated a mean CT number and compared to the CT number of a phantom calibration material and given the appropriate value of bone mineral density.

One of the main advantages of QCT is that it can localise the bone to be measured so that a measurement of trabecular bone only can be achieved. The method should be more sensitive to changes in bone mineral density because any changes in the trabecular bone will not be masked by the far slower changes in cortical bone. Mazess (1983) reported that large inaccuracies can be caused by biological variation of marrow composition, however the main disadvantages of this method are the high cost of the equipment and the high radiation dose to the patient which typically can be 10 mSv.

1.2.5 Neutron activation analysis

This method detects the quantity of a particular element in the bone being examined. The technique relies on the fact that neutrons entering the body will produce $n,\gamma$ reactions e.g. $^{48}\text{Ca}(n,\gamma)^{49}\text{Ca}$. By measuring the $\gamma$-rays given off from the body, the quantity of the original element can be calculated. The whole body can be bombarded with neutrons and a measure of the total calcium content, hence skeletal mass, can be obtained. The major disadvantage of this method is the high dose to the patient which may be up to 15 mSv.

1.2.6 Broad band ultrasonic attenuation (BUA)

If an ultrasound wave is directed through the body it will undergo attenuation which will be dependent on the type of tissue through which it is passing. The technique relies on the fact that attenuation through osteoporotic bone will be different from that
of normal bone. BUA was first suggested by Langton et al (1984) as a useful index relating to fracture risk. There is a linear relationship between attenuation and frequency of a ultrasound beam, hence, for a healthy bone a gradient of this linear relationship is obtained from which measurements of patients could be compared. The clinical site in common use for ultrasound measurements is the calcaneus (heel) and measurements have been shown to correlated well with other measuring methods and other clinical sites (Moris et al 1995, Mautalen et al 1995, Herd et al 1992). The main advantage of this technique over the others discussed is that the patient receives no dose due to ionising radiation. However, a recent study by Petley et al (1995) calls into question the inherent accuracy of BUA measurements when using large aperture piezo-electric receivers.

1.2.7 A new approach to measuring bone mineral density

With the exception of QCT, all the above techniques assess bone density by measuring both cortical and trabecular bone. It has already been stated that bone loss in post menopausal women is accelerated more in the trabecular region of the bone than in the cortex, therefore a technique that takes a measurement from trabecular bone only could be advantageous in the early detection of changes in bone density. Such a measurement can be achieved using QCT but as stated above, the technique is expensive and results in a high radiation dose to the patient.

The method used in this study is an energy dispersive x-ray diffraction technique which can be configured to take a measurement from the trabecular region of the bone in isolation from the cortex. The technique relies on the fact that diffraction of x-ray photons occur from crystalline materials resulting in an energy dispersive diffraction spectrum which is unique to the material under investigation. Before describing how such a spectrum is obtained, the following sections deal with the interactions of photons with matter and the structure of crystalline materials which leads on to the concept of diffraction.
1.3 Photon interactions with matter

When X-ray photons are incident on any form of matter, they are partly transmitted and partly absorbed, i.e. the incident beam of photons is attenuated by the medium. The removal of photons from the primary beam can be through absorption or scattering events. The number of photons removed from the primary beam is proportional to the thickness of the material through which it has passed hence

$$\frac{-\Delta I}{I} = \mu \Delta x$$  \[1.1\]

where $-\Delta I$ are the photons removed from the primary beam which has intensity $I$, $\Delta x$ is the thickness of the material through which the beam is passing and $\mu$ is a constant of proportionality. For an element of thickness $dx$, and letting the primary intensity be $I_0$ when $x = 0$, integrating equation 1.1 gives

$$I = I_0 e^{-\mu x}.$$  \[1.2\]

The linear attenuation coefficient, $\mu$, has units of length$^{-1}$ and is dependent on the density of the attenuating material. A more fundamental coefficient is the mass attenuation coefficient, $\mu_m$, which is independent of the physical state and is given by $\mu_m = \mu / \rho$ where $\rho$ is the density of the attenuating medium.

Attenuation coefficients vary depending on the attenuating medium and the energy of the primary beam of photons. The probability of a photon being removed from the primary beam is given the term cross section per atom or molecule. The total cross section, $\sigma_{tot}$, is made up from the cross sections due to the individual processes that occur in the attenuation of the primary beam e.g. photoelectric absorption, Compton scatter and pair production. The total linear attenuation coefficient is therefore dependent on the cross section and the number of sites at which an attenuation process can occur i.e.

$$\mu = N\sigma_{tot}$$  \[1.3\]

where $N$ is the number of attenuating sites per unit volume. Figure 1.4 shows the linear attenuation coefficients for cortical bone as a function of photon energy in the range of interest for this study i.e. 0-150 keV. There are three interaction processes
that will occur to produce attenuation, these are photoelectric absorption, Compton scattering and coherent scattering (also called Rayleigh or elastic scattering).

Figure 1.4: The cross section as a function of energy for cortical bone.

### 1.3.1 Photoelectric absorption

In a photoelectric event, a photon of incident energy \( h\nu \) interacts with an atom in the absorber and ejects one of the bound electrons from one of the inner shells of the atom, usually the K, L, or M shell. The ejected photoelectron emerges with energy \( h\nu - E_{BE} \) where \( E_{BE} \) is the binding energy of the shell from which the electron is ejected. The emitted photoelectron loses energy to the surrounding atoms and its kinetic energy is very rapidly degraded to thermal energy. The vacancy left in the shell is filled by rapid rearrangement of electrons in outer shells resulting in either the production of characteristic x-rays or Auger electrons. The energy of the characteristic x-rays correspond to the energy difference between the shells.

As a result of a photoelectric interaction the incident photon is completely absorbed and therefore will not directly contribute to an energy dispersive diffraction spectrum but will cause attenuation of the signal. The photoelectric cross section varies as a
function of energy as $h\nu^n$ where $n$ varies between 1 and 3 depending on the energy of the incident photon. For the energy range used in this study $n$ can be taken to be 3 (see figure 1.4). The effect of this energy dependence results in low energies being preferentially absorbed affecting the profile of the scattered spectrum. The photoelectric cross section is also a function of the atomic number of the absorbing material and varies approximately as $Z^4$. Consequently a material such as bone which has an effective atomic number of approximately 13 will attenuate photons far more readily than soft tissue which has an effective atomic number of approximately 7.

1.3.2 Scattering

If a photon is incident on a free electron, the electric field will cause the electron to oscillate at the same frequency as the incident wave and will consequently radiate energy of the same phase and frequency as the incident photon. This process is called Thompson scattering. The electric field of the photon can be represented by two equal electric vectors $E_1$ and $E_2$ at right angles. When these two vectors pass over a free electron at point P, (see figure 1.5) the electron will have a force of $F_1=keE_1$ due to the electric vector $E_1$ and will be given an acceleration $a_1=keE_1e/m_0$. The constant $k$ arises from Coulomb's law which states that a force between two charges $Q$ and $Q'$ a distance $r$ apart is $F=kQQ'/r^2$, and $k$ has the value $8.9875\times10^9$ Nm$^2$/C$^2$. The accelerated electron will radiate energy in the form of an electromagnetic wave, and at the point $S$ the electric vector of this wave will be

$$E_1 = \frac{ke^2}{m_0c^2} \frac{E_1}{r} \sin \varphi \quad [1.4]$$

where $c$ is the speed of light, $r$ is the distance PS and $\varphi$ is the angle between the electric vector $E_1$ and the direction PS. The quantity $ke^2/m_0c^2$ is called the classical electron radius $r_0$ and has the value $2.81794\times10^{-15}$ m. Equation 1.4 can now be written

$$E_1 = \frac{r_0}{r} E_1 \sin \varphi \quad [1.5]$$

Similarly $E_2$ will result in an electric field component
The intensity of the original wave at the point $P$ is given by $\frac{c}{4\pi} [E'_2^2 + E'_1^2]$ and the intensity at point $S$ of the scattered wave is given by $\frac{c}{4\pi} \frac{r}{r^2} [E'_2^2 + E'_1^2 \sin^2 \varphi]$. For an unpolarised beam $E_1$ and $E_2$ the fraction of the incident energy scattered into unit area at $S$ is the ratio of these two intensities which is

$$\frac{I_S}{I_P} = \frac{r_0^2}{2r^2} (1 + \cos^2 \theta)$$  \[1.7\]

*Figure 1.5: Diagrammatic representation of the classical scattering process.*

The quantity represented by equation 1.7 is the fraction of the incident energy that is scattered by the electron into the solid angle $d\Omega$, where $d\Omega = 1/r^2$. This fraction is represented by

$$\frac{d\sigma_0}{d\Omega} = \frac{r_0}{2} (1 + \cos^2 \theta)$$  \[1.8\]

The quantity $d\sigma_0/d\Omega$ is called the classical scattering coefficient per unit solid angle per electron.
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The total cross section is obtained by integrating equation 1.8 over all values of $\theta$ from 0 to 180 degrees. The solid angle $d\Omega$ between the cones of angles $\theta$ and $\theta + d\theta$ is given by $d\Omega = 2\pi \sin \theta \, d\theta$. Equation 1.8 can be written as

$$\frac{d\sigma_0}{d\theta} = \frac{r_0^2}{2} (1 + \cos^2 \theta) 2\pi \sin \theta$$  \hspace{1cm} [1.9]$$

The total cross section, $\sigma_0$, called the Thompson classical scattering coefficient for a free electron is obtained by integrating equation 1.9 for $\theta$ between values 0 to 180 degrees and is

$$\sigma_0 = \frac{8\pi}{3} r_0^2$$

1.3.3 Coherent (Rayleigh) scattering

The scattering process described in section 1.3.2 is for a free electron. If the electron is bound to an atom the situation is more complex. If a photon is incident on an atom of atomic number $Z$, the amplitude of the scattered wave will not necessarily be the amplitude of the scatter from an electron multiplied by $Z$ because interference effects can now take place. If each electron in the atom scatters a wave in the forward direction they will be in phase and will constructively interfere, but in any other direction the scatter from each electron will be out of phase to some extent so that a certain amount of destructive interference will occur, resulting in reduced amplitude. As the scatter angle increases the effect of destructive interference increases so that coherent scattering is predominantly in the forward direction.

The loss of amplitude in a coherent scattered event is described by the atomic form factor which is a function of atomic number, $Z$, and the momentum transfer, $x$ which is the momentum transferred to the photon such that it is deflected through an angle $\theta$ and is defined as

$$x = \frac{1}{\lambda} \sin \left[ \frac{\theta}{2} \right]$$  \hspace{1cm} [1.10]$$

and is in units of inverse Angstroms since the wavelength, $\lambda$, of the photon is in Angstroms. (It should be noted that the SI unit is now nm for wavelength, however published data for form factors are given as a function of momentum transfer in units
of inverse Angstroms.) The momentum transfer is a function of both photon energy and scatter angle and the values of form factors for all the elements have been calculated and are quoted in this form (Hubbell et al 1975). Figure 1.6 shows the atomic form factor as a function of momentum transfer for the elements oxygen, aluminium and copper and it can be seen that the form factor decreases with increasing $\theta$ (for constant $\lambda$) and in the forward direction the form factor is numerically equal to the atomic number of the material.

![Figure 1.6: Atomic form factors for oxygen, aluminium and copper as a function of momentum transfer. (Data taken from Hubbell et al 1975).](image)

The form factor is also a function of the electronic distribution of the atom. The charge distribution of the hydrogen atom has been determined by a solution of the Schrödinger equation, but for atoms with more than one electron it is not possible to find an exact solution and models have been developed to approximate the charge distribution. These models will not be discussed here, suffice to say that the form factor approximation to correct for Thompson scattering is generally good over the range of energies used in this study. However, if the scattering medium is made up of several elements the form factor becomes a more complicated calculation. Unlike the elements, molecular form factors have not been tabulated and a common method of
approximating them is to use the mixture rule whereby each element in the compound is weighted according to the molecular construction. The mixture rule can be applied at various levels of sophistication and has been shown to be inaccurate at low angles of scatter unless inter molecular interference effects, which lead to a maximum amplitude of scatter being at non-zero scatter angle are accounted for (Johns and Yaffe 1983).

To relate the Thompson cross section described by equation 1.8 to the atomic cross section the form factor must be incorporated. The form factor can be considered as the ratio of the scattered amplitude by the atom to the scattered amplitude of a free electron thus, the form factor is proportional to the square root of the scattering intensity so the differential cross section per atom is given by

\[
\frac{d\sigma}{d\Omega} = \frac{d\sigma_{\text{son}}}{d\Omega} [F(x,z)]^2
\]

\[
= \frac{F_0}{2} (1 + \cos \theta) [F(x,z)]^2
\]

[1.11]

The coherent cross section varies as a function of \( E^{-2} \) and is shown in figure 1.4. At small angles of scatter the cross section varies as a function of \( Z^2 \). Coherent scattered photons are the most important in this study as it is this type of scattering that leads to the phenomena of diffraction from regular order substances such as bone mineral.

1.3.4 Incoherent (Compton) scattering

In the Compton process, an incident photon scatters inelastically with an electron which causes the incident photon to undergo a loss in energy and a change of direction, and the electron to gain kinetic energy. This electron carries away part of the incident energy while the rest is carried away by the scattered photon at an angle \( \theta \). Compton scattering from an atom is dependent on the atomic number i.e. the electron density of the material. The cross section per atom is therefore the cross section per electron multiplied by a factor given by \( Z \). For the energies used in this study, the probability of Compton scattering occurring within the scatter angles of interest i.e. up to 10 degrees, can be taken to be constant and the energy lost by the incident photon at these angles is small. Some Compton scattered photons will contribute to the measured energy dispersive diffraction spectra and will be described more fully in chapter 2.
The three interactions described above will contribute to some degree in the measurements made in this work. However as stated, it is the coherent scattering events that lead to diffraction and this topic is now introduced.

1.4 X-ray diffraction

Diffraction effects can most readily be observed from materials with high range order i.e. crystalline materials. The structure of such materials are introduced in the following section.

1.4.1 Crystal structure

A crystal can be defined as a solid that is made up of atoms arranged in a periodic pattern in three dimensions. When imagining crystals it is normal to think of a set of points in space which act as a framework on which the crystal is built. Such a set of points is called a point lattice and can be defined as an array of points in space such that the view from each point is identical. An example of a point lattice is shown in figure 1.7. The cells within the lattice are identical and any one is called a unit cell which is described by three vectors \( \mathbf{a} \), \( \mathbf{b} \), and \( \mathbf{c} \) taken from the corner of the cell which acts as an origin.

![Figure 1.7: A point lattice and unit cell described by vectors \( a \), \( b \) and \( c \)](image)
The three sets of planes which define the unit cell can be arranged in many ways producing different shapes of unit cell. If the planes are equally spaced and mutually perpendicular then the resulting unit cell is a cubic one. By placing a point at the corners of a unit cell a point lattice is created, but points placed at other locations can still satisfy the criterion of a point lattice. There are 14 possible point lattices called Bravais lattices, a well known example of which is the body centred cubic lattice.

The direction of any line in a lattice can be described by passing through the origin of a unit cell and a point with co-ordinates \(u,v,w\) (called the indices of the line). The orientation of the planes in the lattice can be expressed by a system called the Miller indices. The orientation of a plane can be described by stating the distances from the origin at which the plane intercepts the three crystallographic axes \(a,b,c\). If the plane is parallel to one of these axes the two will never intercept, so the intercept distance is described as infinite. The use of infinity is avoided by quoting the reciprocal of the distance which is zero when the plane and axis are parallel. The Miller indices are then described as the reciprocal of the fractional intercepts which the planes make with the crystallographic axis. Miller indices are normally written \((hkl)\) and examples are shown in figure 1.8.

![Figure 1.8: Examples of planes designated by Miller indices.](image)

A crystal can be described by a type of Bravais lattice and the arrangement of atoms within each unit cell of the lattice. The unit of the crystal is called the basis and the crystal structure is made up of copies of the basis which are located at all points on the lattice. The simplest crystals are ones in which the basis is a single atom of one element and many metals crystallise in this way forming body centred cubic and face centred cubic structures. More complex structures arise when two or more identical atoms are associated with each lattice point. Again this is common to many metals and results in a hexagonal close packed structure. The structure of compounds are also built up on the sites of the lattice e.g. CsCl and NaCl. In the structure of the later, sodium ions and chloride ions are situated at alternate points on a simple cubic lattice such that each ion has six of the other kind as its nearest neighbours. Materials with such high range structural order give rise to diffraction.
1.4.2 Bragg diffraction

In the scattering discussed in section 1.3.3, the interference effects from electrons within the same atom were considered. However if the scattering material has structure, particularly crystalline structure as described in section 1.4.1, the interference effects from the surrounding atoms or molecules are significant and can lead to the occurrence of diffraction.

Diffraction is a consequence of the phase relationship between two or more waves. If two waves of equal amplitude are completely in phase and are superimposed on one another the resultant wave will have an amplitude of twice its original. In such a case complete constructive interference is said to have occurred. If the two waves are completely out of phase then the resultant amplitude will be zero and complete destructive interference is said to have occurred. If the two waves are somewhere in between these two extremes then partial interference will occur. In a regular array of periodic atoms such as in a crystal there will be certain directions of scatter such that the path difference between waves that have been scattered from different centres are an integral number of wavelengths, thus constructive interference will result.

Scattering of x-rays from crystalline materials was investigated by Bragg who developed the Bragg Law of diffraction. Bragg considered a crystal as consisting of...
parallel planes of atoms spaced a distance $d$ apart. Figure 1.9 is a diagrammatic representation of such a crystal with a monoenergetic source of x-rays incident on it at an angle $\theta$ measured between the incident beam and the crystal plane. Consider diffraction from one plane of atoms e.g. plane A in figure 1.9. Photons along $a$ and $b$ will be incident on the atoms at sites L and M and scatter photons in all directions. It is only in the directions $a'$ and $b'$ that the scattered beams are in phase and hence constructively interfere. However for full constructive interference to take place, all the scattered waves from all the planes have to be in phase. Consider incident waves $a$ and $c$ which are scattered by atoms at sites M and O. The path difference between the two planes travelled by the incident and scattered waves is $NO + OP = d\sin \theta + d\sin \theta$ and if this path difference is an integral number of wavelengths then the scattered beams will be in phase i.e.

$$n\lambda = 2d\sin \theta$$

and it is only when this above condition is satisfied for the scattered waves from the atoms in the crystal that constructive interference will occur. Equation 1.12 is known as the Bragg Law. For a given material there will be a set of planes which will each have one specific angle (the Bragg angle) that satisfies the Bragg law resulting in a diffraction pattern that has a number of peaks at the scattering angle that corresponds to a particular plane.

The relative intensities of the peaks in a diffraction pattern are a result of a complicated process that is dependent on the scattering medium itself, and will only be dealt with briefly here. A more detailed explanation can be found in standard texts e.g. Cullity (1978). The relative intensity, $I$, of the diffraction peaks is given by

$$I = |S|^2 \cdot M \cdot p \cdot L$$

where $|S|^2$ is called the structure factor, $M$ is the multiplicity factor, $p$ the polarisation factor and $L$ the Lorentz factor. The structure factor represents the scattered wave from all the atoms in a unit cell. The amplitude of each scattered wave depends on the atomic form factor $|F(x,Z)|$, for a particular atom, and its phase is dependent on which plane the wave is scattered from and the atom's co-ordinates in the unit cell. Such a wave can be described by $|F(x,Z)|e^{2\pi i(hu+kv+lw)}$ where $uvw$ and $hkl$ are the indices as described in section 1.4.1. If the unit cell contains $n$ atoms then the structure factor is given by
\[ |SI| = \sum_{\Gamma} F(x, Z) e^{2\pi i (\mathbf{h}_\Gamma \cdot \mathbf{r} + k \gamma + l \lambda)} \]  

The intensity of the diffraction lines is proportional to the square of the amplitude hence the \(|SI|^2\) term in equation 1.13. The multiplicity factor allows for the fact that different planes can sometimes diffract at the same angle which results in an increased intensity at that angle. The polarisation factor takes into consideration the fact that the incident wave is unpolarised. The intensity of a scattered wave at a given point was given in equation 1.7 where the \((1+\cos^2\theta)/2\) term is called the polarisation factor and is included in the intensity calculation to account for the unpolarised incident wave. The intensity peaks in a diffraction pattern have a line spread function that is Gaussian in shape due to the fact that crystals near the Bragg angle will still cause constructive interference to occur. This is accounted for by the Lorentz factor in equation 1.13.

The fact that diffraction occurs due to interference effects of coherently scattered x-rays is the basis of the experimental method used in this study. The following sections discuss the EDXRD technique and the experimental setup used in detail.

1.5 Energy dispersive diffraction

1.5.1 Energy dispersive techniques

The theory of diffraction discussed above is based on an incident beam of photons which is monoenergetic. The Bragg condition for diffraction dictates that there are certain angles that will satisfy the condition for constructive interference to occur for the given wavelength of the incident beam. In diffraction studies such as crystallography, which use a monoenergetic source of photons, the angular distribution of the scattered rays are measured together with their relative intensities so that a plot of the intensity as a function of scatter angle can be produced. From this information, the scattering plane separation distances can be calculated and the internal structure of a crystal determined. Data for a large number of substances have been tabulated in powder diffraction files. These files have been compiled by the international centre for diffraction data. \((JCPDS 1961)\). The information includes the scattering plane.
separation, \( d \), the relative intensities of the scattered beams from those planes, and the Miller indices of the planes.

This study uses an energy dispersive technique to obtain low angle scattering spectra from sample materials. The technique uses a polyenergetic beam of x-ray photons and an energy sensitive detector that is placed such that it detects the scattered photons from an object at a fixed angle. The Bragg condition still applies, the difference being in this technique is that only certain wavelengths will satisfy the condition for constructive interference from the scattering planes. The energies that satisfy the Bragg condition for diffraction are detected and an intensity as a function of energy spectrum can be obtained.

### 1.5.2 The range of scattering angle

The range of energies of interest in the study are those produced by a typical diagnostic x-ray tube, i.e. up to 150 keV. The Bragg condition dictates the scattering angles at which diffraction will occur for a given wavelength (hence energy). The value of \( \lambda \) can be calculated for a particular energy, \( E \) using

\[
\lambda = \frac{hc}{Ee}
\]

where \( h \) is Planck's constant, \( c \), the speed of light, and \( e \), the electronic charge in Coulombs, and \( \theta \) calculated using the Bragg condition. Table 1.2 shows the value of \( \theta \) for a range of energies with a range of plane spacing \( d \).

It can be seen from the table that for this study, the angle chosen to measure the scattered spectra will need to be low. Diffraction data for hydroxylapatite (the main mineral content in bone) shows that the scatter plane spacing is between 0.1 and 0.3 nm (JCPDS, 1961). The x-ray tube used in the study has a maximum tube voltage of 160 keV, giving the range of \( 2\theta \) scatter angle that would enable a spectrum to be recorded from 2 degrees to approximately 10 degrees.
Table 1.2: Scattering angles (in degrees) for range of energies and plane spacing.

<table>
<thead>
<tr>
<th></th>
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<tbody>
<tr>
<td></td>
<td></td>
<td>d = 0.1 [nm]</td>
</tr>
<tr>
<td>30</td>
<td>0.0413</td>
<td>11.9</td>
</tr>
<tr>
<td>50</td>
<td>0.0248</td>
<td>7.1</td>
</tr>
<tr>
<td>70</td>
<td>0.0177</td>
<td>5.0</td>
</tr>
<tr>
<td>90</td>
<td>0.0138</td>
<td>4.0</td>
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<tr>
<td>110</td>
<td>0.0113</td>
<td>3.2</td>
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<tr>
<td>130</td>
<td>0.0094</td>
<td>2.7</td>
</tr>
<tr>
<td>150</td>
<td>0.0082</td>
<td>2.3</td>
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In practice, measuring very low angles is difficult. The incident and scattered beam collimation widths needs to be very small, the photon source to object distance and object to detector distance need to be large to give good angular resolution. When using larger angles, the diffraction peaks that occur, do so at lower energies which can cause problems due to attenuation caused by the scattering object.

1.5.3 Experimental set up

Figure 1.10 shows a schematic diagram of the laboratory experimental set up. The X-ray tube is a Comet industrial metal-ceramic tube. It operates in fluoroscopic mode and will run continuously at a maximum output of 160 kV at 15 mA. The nominal focal spot size is 3.0 x 3.0 mm. The target material is tungsten with 1.0 mm Be inherent filtration. The tube is mounted on an optical table via a purpose built stand which can rotate and tilt the tube so that the direction of the output beam can be adjusted. The output photons are initially collimated by a 5 mm diameter lead aperture and 2.5 mm of aluminium was added for a filter. The term primary photon beam used in this thesis refers to the collimated beam from the x-ray tube as described above.

The primary and scattered beam collimators each consist of two sets of lead slit collimators. The slits are on sliding mounts on the ends of a dural tube enabling the width of the slits to be set up to a width of 1.0 mm using feeler gauges. The height of the slits is 20 mm and this collimation set up leads to a ribbon beam being produced.
Each collimator tube is mounted on an optical bench via micrometer translation and rotation devices, enabling accurate positioning of the slits to be achieved. The collimation arrangement leads to a measurement volume being defined which can be configured to lie within the sample itself, i.e. in the case of bone, within the trabecular region.

![Diagram of energy dispersive x-ray diffractometer](image)

Figure 1.10: Schematic diagram of the energy dispersive x-ray diffractometer.

The scattered beam is detected using an EG&G Ortec GLP series high purity germanium detector. The active crystal diameter is 36 mm and is 10 mm thick. The energy resolution (FWHM) was measured to be 400 eV and 495 eV at 14 keV and 59.5 keV respectively. This type of detector is used because of its excellent energy resolution although it should be noted that in a clinical situation the liquid nitrogen operating temperatures needed for the detector may be inconvenient. The signal from the detector is processed using a PC based multi-channel analyser (EG&G Ortec 92X Spectrum Master).

The final profile of the diffraction spectrum that is recorded depends on many parameters, and is dealt with fully in the next chapter. However, in general the collimated primary beam is incident on the sample material under investigation and for the scatter angle \( \theta \), there will be certain wavelengths in the incident spectrum that
satisfy the Bragg condition for constructive interference to occur. It is at these wavelengths, hence momentum transfer values (see equation 1.10) that peaks occur in the diffraction spectrum and will consequently be unique for a particular material. Figure 1.11 shows a typical diffraction spectrum obtained from an excised, dry femur. The measurement was made through the femoral neck, and clearly shows two peaks that are characteristics of the bone mineral hydroxylapatite. The geometry for this measurement was a scatter angle of 5 degrees with the primary and scattered collimator slits set at 0.5 mm and slit separation distances of 300 mm. The x-ray tube voltage was 70 kV. The intensity of the peaks in the spectrum will be dependent on the number of scattering centres in the scattering volume. The spectrum has been normalised such that the total integrated intensity is unity and all of the spectra presented in this thesis will be in this form unless otherwise stated.

*Figure 1.11: A typical diffraction spectrum obtained from a dry femur showing characteristic hydroxylapatite peaks.*

Two such energy dispersive diffractometers were used in this study, one was designed and constructed at the medical physics department of University College London, and the second was built to a similar design using the same equipment at the clinical physics department, St Bartholomew's Hospital.
Because the intensity of the peaks in the spectrum shown in figure 1.11 is an important quantity when trying to determine the amount of material present in a scattering volume, the stability of the output from the x-ray tube needs to be monitored and any fluctuations between measurements corrected for. The following section describes some tests carried out on the x-ray tube.

1.5.4 Stability of the x-ray tube output

The output of the x-ray tube was measured using an ionisation chamber placed adjacent to the end of the primary collimator 2, (see figure 1.10). The tube was run from a cold start and readings, in Grays, were taken every 300 seconds for a total run time of 190 minutes. This process was carried out for kV values of 70, 100, and 130. The tube was run at 15 mA for all measurements. Figure 1.12 shows how the output of the tube varies with time from the cold start up, all results are normalised to the initial output reading. The figure shows that the output drops by approximately 20% in the initial 160 minutes of running. After this the output was stable to within approximately 2%.

![Figure 1.12: The output of the x-ray tube as a function of time for 70, 100, and 130 kV (15 mA).](image)

Figure 1.13 shows 10 repeated measurements made on a powdered calcium carbonate sample. The time for each measurement was 600 seconds live time and were taken
over a period of 9 hours. The integrated number of counts was calculated for each of
the spectra. The mean and standard deviation of these integrated counts was
calculated and two standard deviations were expressed as a percentage of the mean
giving a measure of variation between the 10 spectra of approximately ± 1.6%.

The fluctuations observed in these output tests mean that when comparing intensities
of measured spectra a correction procedure must be applied. This could be achieved
by continually monitoring the output with an ionisation chamber, or the spectra must
be normalised so that the total intensity is unity.

![Image of a graph showing measurements repeated 10 times on a calcium carbonate sample over a period of 9 hours.]

**Figure 1.13**: Measurements repeated 10 times on a calcium carbonate sample over a period of 9 hours.

### 1.5.5 Focal spot alignment

To maximise the number of photons incident on the target sample for a given kV and
mA, the focal spot intensity needs to be mapped so that the most intense part of the
beam can be directed along a known path. An accurate and reproducible method of
measuring the radiation intensity distribution at the point of production is by using a
CCD (charged couple device) focal spot camera (*Speller et al 1995*). For this
particular application the camera was set up as shown in figure 1.14. A Degussa 30 μm
pinhole was mounted on two micro translator devices which in turn were mounted
over the output window of the x-ray tube. This arrangement enabled the pinhole to be moved to any position in front of the output window. Mounted behind the pinhole is the CCD camera (Photon camera, EEV Ltd, Chelmsford) the output from which is digitised using a frame grabber. The camera was also mounted on a device that enabled movement horizontally and vertically so that the position of the CCD could be kept the same relative to the pinhole. The video signal from the camera could be displayed on a monitor which gave real time images of the focal spot. This enabled any size or intensity variation in the focal spot with kV and mA to be observed.

Focal spot images were taken at 100 pinhole positions in front of the output window on a 10 x 10 mm grid. At each position six images were taken and then averaged to account for any time variations in the intensity of the beam. The images were then analysed by integrating a vertical and horizontal intensity profile plot and obtaining an overall intensity reading for each position. Figure 1.15 shows a typical averaged focal spot image, and figure 1.16 shows the intensity plots in the horizontal and vertical directions.

With the position of the highest intensity image now located, the x-ray tube has to be positioned such that the beam is directed along the centre and parallel to the optical bench. X-ray film was placed in front of the pinhole and an exposure made. The film was then moved a distance down the optical bench and the exposure repeated. If the beam is not parallel to the optical bench, the centre of the two focal spot images will not be in the same place on the film, (see figure 1.17 a where the dotted line shows the
position of the focal spot image with the film placed close to the pinhole). The position of the x-ray tube was adjusted until the required beam direction was achieved and the two focal spot images were centred on the film (see figure 1.17 b).

![Averaged focal spot image taken with the CCD focal spot camera.](image)

**Figure 1.15**: Averaged focal spot image taken with the CCD focal spot camera.

![Horizontal and vertical intensity profile plots. These plots are integrated to obtain an intensity reading for each pinhole position.](image)

**Figure 1.16**: Horizontal and vertical intensity profile plots. These plots are integrated to obtain an intensity reading for each pinhole position.
A small pencil beam laser was converted to a slit beam via a beam splitting lens and directed down the path of the photon beam. The collimators were then placed on the optical bench and the position and orientation of the slits adjusted until in line with the laser beam. Fine tuning of the position of the collimators was achieved by placing an ionisation chamber at the end of the primary collimators and adjusting for maximum throughput. The ionisation chamber was then moved to the end of the scattering collimators and the process repeated.

Once a spectrum has successfully been recorded, the next stage is to analyse the data to obtain the required measurements. This may mean correcting for attenuation which is reasonably straightforward in the simple case such as the dry bone sample shown in figure 1.11 but as previously stated becomes ever more complex in the clinical situation due to surrounding cortex and soft tissue. A possible solution to this problem was attempted by using multivariate analysis, which is introduced in the next section.
1.6 Multivariate analysis

The quantity we wish to obtain from an energy dispersive diffraction spectra taken in-vivo is the amount of bone mineral present in a known measurement volume i.e. the bone mineral density (BMD). In the spectrum shown in figure 1.11 the peaks are due to the mineral hydroxylapatite present in the dry bone hence a quantitative measure of the mineral present could be the number of counts in a region of interest that includes both peaks. (Note the spectrum has to be corrected for attenuation and this process is explained in detail in chapter 3). This information would also be present in a spectrum recorded in-vivo but can be masked by factors over which there is little control. Assuming the diffractometer can be arranged so that the measurement volume is situated in the trabecular region of a given clinical site, there are several factors that need to be considered. There is no clinical site on which a measurement of this type could be made that has the same parameters for every individual because bones vary in size, the cortical thickness of the bone varies between individuals and the amount of soft tissue surrounding the bone will differ. All of these factors will cause attenuation of the measured spectrum which would be very difficult and complicated to correct for. The only factor here that there may be any control over is the surrounding soft tissue as this can in effect be rendered constant by immersing the site in water or other tissue equivalent materials. However this procedure tends to limit the sites available for measurement to appendicular regions. A possible way round this problem was investigated by using a software package that performs multivariate analysis on spectroscopic data. This section introduces the concept of multivariate calibration as used in the software package and the reader is referred to Martins and Naes 1991 for a more detailed explanation.

1.6.1 Multivariate Calibration

In a calibration process, empirical data is used (e.g. measured spectra) together with prior knowledge (e.g. quantities known to represent that spectra) to predict unknown quantitative information from future measurements, through the use of a mathematical function. Multivariate calibration means to use many variable measurements $X\{x(1), x(2), \ldots, x(n)\}$ to quantify a target variable(s) $Y\{y(1), \ldots, y(k)\}$. In this study the $X$ measurements are the measured diffraction spectra with $x(1), x(2), \ldots, x(n)$ being the momentum transfer values in the spectra, and the $y$ variables will be the bone mineral content, marrow content, cortical thickness etc. In order to predict information $Y$
from measurements $X$, the prediction formula $Y = f(X)$ needs to be determined. To do this task we need a model that links how $X$ relates to $Y$. An example of this may be a regression model of the form $y = Xb + c$. During calibration the unknown parameters $b$ and $c$ are estimated from the calibration data giving a calibration model which can then be used for future predictions of $y$ assuming the objects from which the predictions are made are of the same form as those used for the calibration. There are several statistical calibration methods available for creating a model (Martins and Naes 1991) and this study concentrates on the use of partial least squares regression (PLSR).

1.6.1.1 Data reduction

There are common problems associated with the prediction of variables via a calibration model. It may be that no single $X$ variable is sufficient to predict $Y$ because $Y$ is caused by several phenomena that is represented by different $X$ variables or that the $X$ measurements are affected by several factors. It could be the case that two $X$ variables have the same correlation to a given $Y$ variable resulting in what is called redundancy. Multivariate analysis is based around the idea of reducing the amount of data used in the calibration and the basic concept for data reduction is that information contained in the many variable $X$ data $X\{x(1)..........x(n)\}$ is concentrated onto a few underlying variables called principal components, scores or factors $T\{t(1)..........t(k)\}$. i.e.

$$\{t(1)..........t(k)\} = h(1)[\{x(1)............x(n)\}]$$

and it is these principal components that are used as the regressors in the regression

$$\{y(1)........y(j)\}=h(2)[\{t(1)........t(k)\}] + f$$

where $f$ represent the contributions of $y$ that cannot be explained by the principal components $T$. The number of principal components represent the variation in the $X$ data that is important for predicting the $y$ variables. The two functions $h(1)$ and $h(2)$ form the predictor $y=f(x)$, with $f(x)=h(2)[h(1)(x)]$. The data compression of the many $X$ variables into a few $T$ variables simplifies the statistical calibration by reducing the number of model parameters in the $X$-$Y$ regression.
A method of data compression is concentrated on in this study that comes under the heading of bilinear methods. The two basic methods are principal component regression (PCR) and partial least squares regression (PLSR) of which the later is used in this study.

![Diagram of multivariate calibration approaches]

Figure 1.18: Different approaches to multivariate calibration. 
(Taken from Martins and Naes 1991)

Figure 1.18 shows diagrammatically the different approaches to multivariate calibration modelling. In all four approaches it is assumed that one Y variable is to be determined from four measured X variables which contain information concerning two types of variation, one of which we want to determine and the other is a contaminant of some type we are not interested in quantifying. In a) all four variables are used to determine the desired quantity and the contaminant is ignored. This process leads to incorrect interpretation of the calibration model and the predictive ability is poor due to the contaminant. Diagram b) represents multiple linear regression where the four X variables are assumed to have four independent types of information about Y. This model has a problem because there are only two types of information present in Y plus noise which results in the predictive ability being limited because the data is over fitted i.e. the noise is included in the model. Diagram c) represents principal component regression where two main principal components are found by data reduction analysis.
of the X data. Diagram d) shows PLSR where the principal components are found by examining both the X and Y data i.e. the Y variables are used in the principal component analysis of the X data, which gives rise to one major and one minor principal component from X. Like PCR, these principal components describe both the X and Y data but in PLSR the major principal component accounts for most of the modelling so a simpler calibration model can be used.

1.6.2 The Unscrambler

The Unscrambler (CAMO 1994) is a commercial software package that was used in this work to perform multivariate analysis on spectra obtained using energy dispersive diffraction techniques on bone phantoms. The package contains a number of analytical methods for the analysis of sets of data to find internal relationships within the data. In this study the Unscrambler was used to do two things.

1. Establish the regression relationships between two sets of data. The program achieves this by using two sets of known data consisting of X-variables and Y-variables called a training or calibration set. The X data consists of a number of objects with each object containing a number of variables. In this study an object is a measured diffraction spectrum and the variables are the momentum transfer values in that spectrum. The Y data are quantities that are related to a given spectrum so must therefore contain the same number of objects with each object having the number of variables chosen to be modelled. A single variable model may be the bone mineral content represented in the spectrum, a two variable model could be the bone content and marrow content. A three variable model could be the addition of cortical thickness and a four variable model the further addition of soft tissue thickness surrounding the bone. However many variables we choose to model we have

\[ \text{X-variables + Y-variables} \Rightarrow \text{model} \]

2. The Unscrambler is used to predict unknown values of the Y-variables from new X-variables and the model previously created, i.e. the prediction process is

\[ \text{X-variables + model} \Rightarrow \text{Y-variables} \]
The method of modelling used to perform the above is PLSR as described in section 1.6.1.1. The PLSR method performs a simultaneous and interdependent principal component analysis in both the X and Y matrices in such a way that the information in the Y-matrix is used as a guide for the optimal data reduction of the X-matrix. This method was chosen because it handles several co-varying Y-variables better than principal component regression or multiple linear regression. The Unscrambler has two PLS algorithms, PLS1 which handles only one Y-variable at a time and PLS2 which is used for handling several Y-variables simultaneously.

Once the principal components are found they are stored in a T matrix with which the regression is performed on Y. The T-variables are given the term scores which express the relation between objects. Each column in the T matrix corresponds to one principal component (PC) and each row corresponds to each object in the X-data. The scores in the matrix indicate which objects are responsible for most of the variation in the data set or, scores are a measure of how much of a particular PC is present in a particular object.

A variable called the loading, expresses the relationship between individual variables and the principal components i.e. they tell you which variables are dominantly influencing the model. Loadings are the regression coefficients of each variable to each PC and are stored in matrices P and Q which are computed by the program as a result of the regression of X to T and Y to T respectively. The Q matrix has one line per PC and each line has one element per Y-variable. When the model is used for prediction purposes the values of the predicted Y variables ($Y_{\text{pred}}$) are computed from

$$Y_{\text{pred}} = TQ + Y_{\text{centre}}$$

where $Y_{\text{centre}}$ is the mean value of the known Y-variables in the calibration set.

The X and Y residuals (or residual variance) are the differences between the measured and modelled X and Y data and represent the data that cannot be included in the model or how much of the variation in the data that is unexplained. The residuals are stored in E and F matrices respectively. The residuals serve as a valuable validation function in the modelling procedure. The model is validated to obtain a measure of how good it is and how accurate future predictions made from the model will be. In the Unscrambler the validation process is carried out during calibration and the procedure used in this study is one called cross validation. Cross validation can be used when the
calibration set is large and representative of the future predictions to be made. A series of calibrations is made with different subsets of the calibration objects used as validation objects which in effect allows the calibration model to be tested against real test objects. During the calibration process, the residuals are computed for each PC both for the calibration and validation objects. The optimal number of PC's to use in the model and hence future predictions is the number that gives the smallest residuals.

Another useful measure the Unscrambler computes is the root mean square error of prediction (RMSEP) which is an expression of the expected error in a predicted Y value. The RMSEP is defined as the square root of the average of squared differences between predicted and measured Y-variables (or the square root of the residual Y variance) and is calculated from the validation objects used in the cross validation procedure during calibration. The predicted values given by the Unscrambler are as an absolute value ± a deviation which is calculated using an empirical formula based on the X and Y residual variances.

1.6.3 An example using the Unscrambler

A simple two component system was designed to illustrate and test the use of the Unscrambler. A mixture of two powdered materials, calcium carbonate and polyethylene, was prepared with concentrations of the mixture ranging from 14% by mass of calcium carbonate, 86% polyethylene, to 39.5% by mass calcium carbonate, 60.5% polyethylene. A total of 18 mixtures were made up in steps of increasing calcium carbonate content of 1.5% by mass. These figures were chosen as it could represent a simple model of trabecular bone with the calcium carbonate representing the bone mineral and the polyethylene the bone marrow and typically the bone mineral constitutes approximately 30% of the trabecular mass.

Energy dispersive diffraction spectra were obtained using the diffractometer designed and constructed at the medical physics department, UCL (see section 1.5.3) using a scattering angle of 5 degrees and an incident spectrum of 70 kV. The collimation used was a ribbon beam with a slit width of 0.5 mm, a slit height of 20 mm and slit aperture separation distances of 300 mm. The spectra obtained from these measurements were used as the calibration set in the Unscrambler i.e. the X-data has 18 objects and each object has 250 variables i.e. the number of channels used in the MCA. Figure 1.19 shows the spectra from 3 of the mixtures. The Y-data has 18 objects with each object
consisting of 2 variables i.e. the percentage by mass of calcium carbonate and percentage by mass of polyethylene.

![Normalized Spectra for 26%, 33.5% and 39.5% Calcium Carbonate Content Mixtures](image)

**Figure 1.19: Normalised spectra for the 26%, 33.5% and 39.5% calcium carbonate content mixtures.**

The model was created by using the PLS2 option incorporating the cross validation technique. The program first carries out principal component analysis of the data and reduces the X-data to a given number of principal components. In this particular case the number of principal components was 16 and the user has the choice of using 1-16 principal components in the calibration procedure. The first model created used all 16 components so that the residual variance of each component could be viewed such that the number that minimised the residual variance could be found. In this example the optimal number of PC's was 2 which explained 99% of the variance in the data set.

A further test set of 5 mixtures was made up to evaluate the prediction abilities of the model. The test mixtures consisted of 15, 21, 27, 30 and 35% by mass of calcium carbonate. The percentage mass of calcium carbonate and polyethylene was then predicted by the Unscrambler using 2 PC's. Figure 1.20 shows these predictions with error bars obtained from the quoted deviation. The predictions are accurate to better than 0.5% of the percentage mass.
1.6.4 Conclusions

The results obtained from the example described in section 1.6.3 show that the Unscrambler is capable of handling the type of data obtained from an energy dispersive diffractometer. The theory behind multivariate analysis suggests that this type of example may be extended to include more Y-variables and that it may be useful in analysis of data generated from in-vivo measurements.

Further use of the Unscrambler is discussed in the following chapter where computer generated spectra are obtained for different collimation geometry and modelled using the Unscrambler. This can help optimise the experimental set up such that throughput efficiency is maximised with acceptable prediction accuracy.

1.7 Introduction to dosimetry

In a clinical situation the radiation dose given to the patient is an important consideration and the ALARA principle has to be followed. This principle basically
states that in any procedure the dose to the patient has to be As Low As is Reasonably Achievable and that the disadvantages of the dose received by the patient have to be outweighed by the advantages gained by the patient from the procedure.

1.7.1 Guidelines for dose quantities

The International Commission on Radiological Protection has published recommendations for dose quantities in ICRP publication 60. For an in depth description of these recommendations the reader is referred to the above publication and NRPB (1993). The principal dosimetric quantities now recommended by the ICRP are as follows

1) The absorbed dose in an organ or tissue, $D$
2) The equivalent dose in an organ or tissue, $H$
3) The effective dose, $E$.

The absorbed dose is the fundamental dosimetric quantity and is the energy absorbed per unit mass and has units of joules per kilogram, given the name Gray (Gy). The equivalent dose is a measure that takes into account the type and energy of the radiation causing the dose. This is achieved by weighting the absorbed dose by a factor related to the type of radiation and its energy. For the purposes of this study the weighting factor is 1 so in effect the absorbed and equivalent dose is the same at least numerically. Some organs are more susceptible to radiation damage than others and the ICRP has therefore developed a quantity to reflect the differing risks and this quantity is derived from the equivalent dose and is called the effective dose. Each organ or tissue is weighted according to its risk of radiation damage. A list of weighting factors for 12 organs and tissue types has been compiled by the ICRP and a general weighting factor is assigned to the remainder of organs. The term for the units of effective dose and the equivalent dose is the Sievert (Sv).

The method used in this study to measure dose was thermoluminescent dosimetry (TLD) and is described along with the experimental procedure used in chapter five.
1.8 Work undertaken

The remainder of the work in this thesis has been split broadly into four categories, each dealt with by a different chapter. Chapter two describes computer code written to model the experimental measurements with the aim of gaining an understanding of energy dispersive diffraction, and using the resulting model to optimise the experimental parameters. Chapter three follows the use of the system to make quantitative measurements of bone mineral density in archaeological bone samples and introduces the problem of attenuation in the measured spectra and how this may be compensated for. Chapter four deals with the simulation of in-vivo bone mineral density estimation by taking measurements on specially designed phantoms that represent gradual bone loss within a range of the parameters that cause attenuation problems in-vivo i.e. surrounding soft tissue thickness and cortical thickness. The measurements described in this section are analysed using multivariate calibration techniques. Predictions are also made of the BMD of recently excised femurs from a calibration model made from the phantom measurement data. The radiation dose to the patient is considered in chapter five using TLDs as a dosimetry measuring method. Finally chapter six discusses the results and offers suggestions for further work.
2

Modelling Coherent Scattered Spectra.

From the description of the experimental set-up and the typical spectrum shown in figure 1.11, it is clear that there are certain parameters that will influence the profile of the measured spectrum. Examples of such parameters are the geometry of the collimation, which will lead to angular blurring, the shape of the incident spectrum and the process of attenuation, which will effect the relative intensities of peaks in the measured spectrum, as well as the resolution of the detector and choice of scatter angle. This chapter describes the development of computer code that models the system such that the profile of the measured spectrum can be predicted. The resulting model helps give an understanding of the scattering system and the effects of the various influences on the spectrum and can aid in choosing an optimal experimental set-up.

2.1 The computer model

Computer code was written to model the scattering system so that the scattered spectrum could be predicted for a given set of parameters and to help in the design of an optimum diffraction system for a given application. As stated above, there are several parameters in the system that play a part in the final profile of the spectrum. The program uses diffraction data for a chosen material obtained from the powder diffraction files, \textit{(JCPDS 1961)}. The data used in the program are the scattering plane spacings, $d$, and the relative intensities of the scattering from those planes. The program calculates the scattered spectrum for a given incident x-ray spectrum up to 150 kV and any scatter angle from 3 to 10 degrees. The program also enables the geometry of the collimation to be changed. Three types of photon beam are modelled, a pencil beam, a ribbon beam, and a conical beam (obtained using annular collimation). Different shapes of target sample are also modelled, so that for a given material the parameters can be varied until the optimum spectrum for a given application is achieved.
The format of the modelled data is either intensity as a function of energy or intensity as a function of momentum transfer. The energy or momentum transfer axis has 512 values to simulate the number of channels in the multi channel analyser being used in this study. In principle, this number of channels could be changed in the model to suit any number of channels used in the MCA.

2.1.1. The diffraction data line spectrum

The spectrum produced from the JCPDS diffraction data is one which gives a line of a certain intensity at each energy from the incident x-ray spectrum that satisfies the Bragg law for the material under investigation. The model first calculates this line spectrum for a particular material up to the end point energy of the incident spectrum and a given scatter angle. The diffraction data is read in and the wavelengths that satisfy the Bragg law (see equation 1.12) are calculated and converted to energy values using equation 1.15. The model then places the calculated energy values into the appropriate energy channel that simulates the MCA.

Figure 2.1 shows the line spectra for calcium carbonate, polyethylene and hydroxylapatite and compares them to the measured spectra which was measured with an incident spectrum of 70 kV and the angle of scatter 6 degrees. Clearly there are factors that are spreading and blurring the spectrum and these factors have to be considered in the model. The following are considered and their effect on the line spectrum modelled.

- Angular blurring
- The probability of a coherent scattering event occurring as a function of energy.
- The polyenergetic incident spectrum.
- Attenuation of the incident and scattered beam in the sample material.
- The contribution to the spectrum from Compton scattering.
- Detector resolution.
Figure 2.1: Comparison of the line spectrum and measured spectrum for calcium carbonate, polyethylene and hydroxylapatite. The incident spectrum used for the measurement was 70 kV and an angle of scatter 6 degrees. All spectra have been normalised to the highest peak for comparison purposes.

2.1.2 Angular blurring

The line spectra shown in figure 2.1 are for a fixed scattering angle of 6 degrees, i.e. it is assumed that only photons scattered at this angle from the object reach the detector and contribute to the spectrum. In order to try to achieve this ideal in the measured spectrum, both the incident and scattered beams need to be collimated. To obtain good angular resolution the photon beam width needs to be as small as possible, while the distances between the primary collimator apertures and the scattered collimator apertures need to be as large as possible. This has disadvantages in practice because as the photon beam width is reduced and the aperture distances increased, the number of photons that pass through the system decreases. This in turn leads to the need for increased measuring times to obtain acceptable counting statistics. Figure 2.2 shows that because of the finite dimensions of the collimator geometry, there are a range of scattering angles that can reach the detector.

The range of angles that can reach the detector will depend on the type of collimation used, i.e. pencil beam collimation, ribbon beam collimation or annular beam collimation. The range can be calculated from the geometry and figure 2.3 shows the angular deviation for pencil beam geometry either side of the chosen scatter angle for
four beam diameters, and various collimator aperture separation distances. The calculations assume that the distance between the primary beam collimator apertures and the scattered beam collimator apertures are the same.

Figure 2.2: The finite dimensions of the collimation geometry give rise to angular blurring.

Figure 2.3: The range of scatter angles that can reach the detector due to finite pencil beam collimation geometry.
Because there are a range of angles that have to be considered in the Bragg law $n\lambda = 2d\sin \theta$, there will be a corresponding range of wavelengths that will also satisfy the law. For a chosen scatter angle there will be a spread of wavelengths, hence energies, appearing in the spectrum. It can be seen from the Bragg equation that the spread of energies will be dependent on the chosen nominal scatter angle $\theta$, and on the plane separation of the material, $d$. Figure 2.4 shows the maximum deviation in energy for nominal scatter angles from 3 to 10 degrees for 0.15 nm and 0.25 nm plane spacing with collimator aperture separation distances of 300 mm and beam width 0.5 mm.

![Figure 2.4: The maximum deviation of energy around peak energy due to collimation geometry.](image)

In a system that uses ribbon beam collimation, the angular blurring will differ considerably. The deviation of angle smaller than the nominal scatter angle will be the same as that of pencil beam geometry i.e. it will depend on the slit width of the collimator apertures. The deviation larger than the nominal angle will however be greater than that for pencil beam as it will be dependent on the length of the slit as shown in figure 2.5.

The collimation used in this study is a ribbon beam configuration with a 20 mm slit length. Figure 2.6 shows the increase in the scattering angle relative to a nominal scatter angle of 6 degrees for a range of collimator aperture separation distances and a slit width of 0.5 mm.
From input geometry dimensions, the model calculates the deviation from the nominal scatter angle that the geometry will produce. This angular range is divided into a number of intervals and the individual line spectrum is calculated for each interval. 50 intervals was deemed sufficient to produce a smooth line spread function. Different forms of the functions have been assumed by different workers i.e. Speller et al 1993 assumed a 3 component function derived from collimator dimensions. Luggar et al
(1996) showed that the line spread function due to angular blurring is in the form of a Gaussian distribution, and a distribution of the form shown in figure 2.7 is used to give a weighting factor to each of the line spectra calculated as described above. The actual distribution used will depend on the type of collimation being modelled i.e. pencil or ribbon beam. Each angular interval between $\theta$ and $\theta_{\text{max}}$ is given a weighting between 0 and 1 with the nominal scatter angle being given a weight of 1. This in effect is a convolution of the line spectrum with a Gaussian function that has a varying FWHM with energy.

![Gaussian distribution](image)

**Figure 2.7**: Angular blurring distribution function.

The process of angular blurring for annular collimation is assumed to be the same as that for pencil beam collimation. However, it should noted that in reality it is a cross between pencil and ribbon beam as photons will travel "sideways" down the cone. The primary beam collimation is a pencil beam and the scattered beam is a cone shape set at the scatter angle and of a chosen width. Figure 2.8 shows the annular collimation arrangement and it can be seen that the length of the scattered beam collimator has to be kept to a dimension such that the final annular diameter does not exceed the diameter of the detecting crystal. Figure 2.9 shows the effect of angular blurring on the line spectra. Figure 2.9a. is for pencil beam geometry, 2.9b. is for ribbon beam geometry and 2.9c. is for annular geometry. The material modelled is calcium carbonate, with an incident spectrum of 70 kV and a scattering angle 6 degrees. For the pencil and ribbon beam geometry the primary and scattered collimator aperture separation distances are 300 mm, while for the annular collimation, the primary separation is 300 mm and the scattered collimator length is 80 mm. All photon beam widths are taken to be 0.5 mm and the ribbon beam slit length is 20 mm.
It can be seen from figure 2.9 that in the case of a pencil beam the blurring is symmetrical about the lines in the spectrum. However, for the ribbon beam, because of the deviation from the nominal scatter angle being far greater than the minimum deviation, the peaks are skewed to the lower energy side of the lines. The annular collimation produces a greater blurring than pencil beam due to the relatively short dimensions of the scattered beam conical collimator.

Figure 2.8: Schematic diagram of annular collimation arrangement.

Figure 2.9: The effects of angular blurring for a) pencil beam, b) ribbon beam, c) annular collimation geometry.

2.1.3 Coherent scattering probabilities.

The intensity information in the JCPDS diffraction data files is obtained using a monoenergetic source of photons. The probability of a coherent scattering event occurring increases with decreasing incident photon energy. An energy dispersive technique uses a polyenergetic photon source and therefore the intensity of coherent
scattering will vary as a function of the shape of the incident spectrum. A correction has to be made to the relative intensities in the modelled spectrum.

The coherent mass attenuation coefficients for the materials modelled in the program have been calculated using a computer program called XCOM. (Berger and Hubbell 1987). The values are calculated for each of the energy channels used in the MCA i.e. 512 channels from 0 to 150 keV. The calculated coefficients are then used as weighting factors which are applied to the intensity value in each of the energy channels. Figure 2.10a shows the weighting curve superimposed on the spectrum shown in figure 2.9b for calcium carbonate i.e. corrected for angular blurring only. The figure shows how the curve varies across the energy range and figure 2.10b shows the effect of its application. In general terms the effect is to enhance the lower energy information and subdue the features at the higher energies.

![Figure 2.10](image)

**Figure 2.10**: a) The coherent mass attenuation coefficient curve as a function of energy is used to correct the relative intensities of the modelled spectrum. b) The effect of correcting for coherent scattering probabilities.

### 2.1.4 Polyenergetic incident spectrum and attenuation

The photon beam from an x-ray tube has a characteristic energy distribution depending on the target material, target angle, inherent filtration and any added filtration. The x-ray tube used in this study is described in section 1.5.3 and the output spectra for such a tube were generated using a computer program called X-RAY (Birch et al 1979) for a range of values from 50 kV to 150 kV in 5 kV intervals. The distribution of intensity across the energy range means that the number of photons incident on the scattering sample will vary with energy. The more photons that are incident on the sample, the
more probable it is that a scattering event will occur, which will effect the relative intensities of the scattered spectrum.

The scattering volume inside the sample will vary depending on the width of the collimated primary and scattered beams, and the angle of scatter (see figure 2.11). Table 2.1 shows the scattering length for a range of beam widths and scatter angles. The incident spectrum will be attenuated through the sample until it reaches its scatter point within the scattering volume, and the diffracted spectrum is attenuated as it passes out of the sample. Each energy channel of the incident spectrum is corrected for attenuation for the thickness of material in the sample. The linear attenuation coefficients are generated using the XCOM program and the attenuation calculated using $I = I_o e^{-\mu x}$, where $I$ is the incident intensity, $I_o$ the transmitted intensity, $\mu$ the linear attenuation coefficient and $x$ the transmission distance. The attenuation corrected incident spectrum is then used as a weighting curve and applied to the modelled scattered spectrum.

![Figure 2.11: Scattering length depends on collimator aperture widths and scattering angle.](image)

<table>
<thead>
<tr>
<th>Beam width (mm)</th>
<th>Nominal Scatter Angle (degrees)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>3</td>
</tr>
<tr>
<td>0.25</td>
<td>9.54</td>
</tr>
<tr>
<td>0.5</td>
<td>19.10</td>
</tr>
<tr>
<td>0.75</td>
<td>28.64</td>
</tr>
<tr>
<td>1.0</td>
<td>38.19</td>
</tr>
<tr>
<td>2.0</td>
<td>76.33</td>
</tr>
</tbody>
</table>

*Table 2.1: Scattering lengths (in mm) for a range of beam widths and scattering angles.*
If ribbon beam collimation is being modelled, then the shape of the sample needs to be taken into consideration. If the cross section through the sample is circular, and the diameter comparable to that of the ribbon height, then there will be different attenuation distances for different parts of the ribbon beam as shown in figure 2.12. This is accounted for in the model by dividing the ribbon height into 10 intervals and calculating the transmission distance for each interval. Ten intervals was deemed sufficient to represent the change in attenuation across typical dimensions of the samples being modelled. The attenuation correction is carried out for each interval and the mean found.

![Diagram](image)

*Figure 2.12: Attenuation is dependent on the shape of the target sample when using ribbon beam collimation.*

### 2.1.5 Contribution of Compton scattered photons

The contribution of Compton scattered photons which reach the detector and contribute to the measured spectrum was estimated using a Monte Carlo based photon transport model. The experimental set-up shown in figure 1.10 was modelled using the EGS4 package *Nelson et al 1985* over a range of system parameters. By following the individual life histories of the photons through the system, the detected photons which had originated from Compton scatter events were collected and binned to form a spectrum of the Compton contribution *Mooney 1995*. This technique also allowed the multiple Compton scatter contribution to be assessed which was found to be negligible due to the dimensions of the target material and the restricted detector collimation.

The amount of Compton scatter was estimated experimentally by recording a set of diffraction spectra for a given set of parameters. The angle of scatter was then
increased to 25 degrees so that the recorded spectrum could be assumed to be from Compton scattered photons alone. This procedure assumes that at 25 degrees, the intensity of any coherently scattered photons is negligible, and that Compton scattering occurs with equal probability up to this angle. This assumption is reasonable over the range of energies being used. The amount of Compton scattered photons as a percentage of the total measured spectrum was then estimated. These experiments were carried out on three materials, calcium carbonate, hydroxylapatite and polyethylene for a range of incident kV and scatter angle. As expected, the Compton contribution as a percentage of the total measured spectrum increased as the scatter angle increased because the intensity of the coherently scattered spectrum decreases with increased scatter angle. Such experimental Compton contribution data was obtained for the three materials at 3, 5 and 7 degrees and for incident x-ray spectra of 60, 90 and 120 kV. Data for other angles was estimated from the relationship between the measured contribution and the scatter angle using linear interpolation. This information enables the model to add the appropriate amount of Monte Carlo data to the modelled spectrum. Figure 2.13 shows the modelled spectrum with the Compton contribution added. It should also be noted that due to the time taken for the Monte Carlo code to run, the experimental set-up was modelled with only one set of collimator dimensions i.e. slit width 0.5 mm and aperture separation distances of 300 mm. The system was only modelled for a ribbon beam set up as it was this arrangement that was used in the work.

![Figure 2.13: The addition of the Compton scattered photons to the modelled spectrum.](image)

*(The total intensity has been normalised to unity).*
2.1.6 Detector resolution

The model is primarily intended to simulate an ideal detector i.e. it assumes that there will be no Compton continuum and no Compton edge associated with each full energy peak. Any detector has an inherent energy resolution. No detector will produce a line at a particular energy, it will always be spread due to the fluctuation in the number of charge carriers formed from event to event. If it is assumed that the number of charge carriers formed per photon is a Poisson process then the amount of inherent fluctuation in the detector can be estimated. The line spread function will be Gaussian in shape and the resolution of the detector is defined as the full width at half maximum (FWHM) height of the Gaussian distribution. The distribution is described generally by:

$$ G(e) = \frac{A}{\sigma \sqrt{2\pi}} \exp\left(-\frac{(E - E_0)^2}{2\sigma^2}\right) $$  \[2.1\]

In equation 2.1, $\sigma$ is the standard deviation of the Gaussian and determines the FWHM through the relationship (Knoll 1989)

$$ FWHM = 2.35\sigma $$  \[2.2\]

The resolution of a detector i.e. the FWHM will vary as a function of energy. Over the energy range the model is working with it is assumed that the relationship between FWHM and energy is a linear one. The model requires the input of the FWHM for the detector being modelled at two energies, 60 keV and 14 keV. (These were chosen as they are easy to measure from an Americium 241 source). From these two values the program can calculate the FWHM for each energy channel in the spectrum. Each line in the modelled spectrum is then convolved with a Gaussian function of the form in equation 2.1 using the appropriate value of $\sigma$ calculated via equation 2.2.

2.1.7. Detector efficiency

The efficiency of the detector will vary with energy. If the spectrum is measured over a large energy range this will effect the relative intensities of the peaks in such a spectrum. However in this model the efficiency is taken to be 100% over the energy range used. For an incident photon beam energy of 100 keV, approximately 1% of the intensity is transmitted through a Germanium crystal 15 mm thick.
2.2 Comparison of modelled and measured spectra

The final modelled spectrum for calcium carbonate using an incident spectrum of 70 kV and scattering angle of 6 degrees is shown in figure 2.14 and is compared to the measured spectrum. The other parameters used were ribbon beam collimation with 0.5 mm slit widths, 20 mm slit height, 300 mm slit separation distances and a rectangular block of material 20 mm thick. It can be seen that the two spectra are not identical, but the modelled spectrum does show important characteristics of the measured spectrum i.e. the peak positions are correct to within approximately 2 keV. A cause of this difference may be due to experimental limitations in the accuracy of setting the scatter angle. The relative intensities of the peaks are closely matched. Errors here will arise from the fact that, as explained in section 2.1.5 the Compton contribution is only an estimate based on one configuration of collimation geometry. It should also be noted that the model in its present form includes no estimation of noise.

![Measured spectrum vs Modelled spectrum](image)

*Figure 2.14: Final modelled spectrum compared to the measured spectrum.*

Figure 2.15 shows the comparison of the modelled to measured spectra for the same collimation geometry as for figure 2.14, but for different incident spectrum energies and scatter angle. Graph a) shows a scatter angle of 5 degrees with an incident spectrum of 100 kV and graph b) shows a scatter angle of 8 degrees with an incident
spectrum of 60 kV. The limitations of the model are the same as those described for figure 2.14.

![Graph of measured vs modelled spectra](image)

Figure 2.15: Comparison of measured to modelled spectra for different kV values and scatter angles. Graph a) has parameters 100 kV and 5 degree scatter angle, and graph b) has 60 kV and 8 degree scatter angle.

From the work described in section 2.1, it can be seen that the angular blurring due to the collimation geometry has a potentially significant effect on the scattered spectrum. The work in this study involves examining changes in characteristic peak intensities for a given material i.e. bone mineral and bone marrow. These changes in intensity, due to a decrease or increase in the amount of material present, need to be detectable while at the same time maximising the efficiency of photon detection. The main use of the model therefore, will be to analyse peak positions and intensities as a function of incident kV and scatter angle, and assess the resolution of a given geometry. Figure 2.16 shows the effect of changing the slit width of the collimators on the spectrum shown in figure 2.14. It should be noted that the relative intensities of the peak heights does not compare as well as in figure 2.14. This is due to inaccurate addition of the Compton contribution, which is only modelled for 0.5 mm. However, despite these shortcomings the model can be used to help optimise the collimation geometry for a given application as will be shown in the following sections.
2.3 Optimisation using the model

The model can now be used to help decide on the best set of parameters to use for a given application. This study uses a one component system i.e. bone mineral only, in measurements on archaeological bone (see chapter three), and a two component system, i.e. bone tissue and bone marrow, in measurements on bone phantoms simulating in-vivo measurements. The material used to model the bone mineral is hydroxyapatite, which is the main mineral content of bone. The marrow is modelled using polyethylene as this gives a broad diffraction peak of momentum transfer value close to that of marrow fat.

2.3.1 The basis of the optimisation process

Although pencil beam geometry gives the best resolution in a measured spectrum i.e. it provides the minimum of angular blurring and hence improves energy resolution, it has...
the disadvantage that long counting times are necessary to obtain good quality spectra. In any clinical application the measurement time has to be kept to a minimum and consequently for the purposes of this study ribbon beam collimation has been used and therefore all the modelling assumes this geometry. An important aspect of the optimisation procedure is taking into account how the spectra are to be analysed. In this study the diffraction peaks that are present in the spectra due to the two components being measured, i.e. bone mineral and bone marrow, will be analysed. (In the case of the archaeological bone it will be just the mineral). The peaks may or may not require good resolution depending on their position in the spectrum i.e. the proximity to each other or to other peaks present. If the resolution is not important then the collimation geometry can be widened allowing shorter measurement times and better counting statistics.

Chapter three describes work carried out on archaeological bone samples. This is a simple one component system to model i.e. bone mineral only. The model can be used to view peak positions and intensities as a function of scatter angle, and also as a function of the incident spectrum kV. The analysis of the recorded spectra is to quantify the bone mineral present which is achieved by integrating the number of counts in a region of interest (ROI) that contains peaks characteristic of hydroxylapatite. It should be noted for this application, the measuring time is not a limiting factor as it is not a clinical situation.

2.3.2 Variation of hydroxylapatite spectra with angle

Figure 2.17 shows a plot of the modelled spectra for hydroxylapatite with an incident spectrum of 70 kV and a range of scatter angles from 4 degrees to 10 degrees plotted at 0.25 degree intervals. It can be seen how the characteristic peak positions vary as a function of energy. The position of the peak of interest is an important consideration as it is desirable to position it such as to maximise the signal strength. As the peak shifts in relation to the angle the intensity varies as a function of the intensity of the incident spectrum. To demonstrate this more clearly the data has been replotted in figure 2.18 which shows the intensity as a function of momentum transfer and illustrates how the main peak intensity varies as the angle is increased.
Figure 2.17: Variation of the hydroxylapatite spectrum with changing scatter angle.

Figure 2.18: The change in peak intensity as a function of momentum transfer and changing angle for hydroxylapatite.
2.3.3 Variation of spectra with incident kV

It can be seen from figure 2.18 that the intensity of the main hydroxylapatite peak is maximised at a scatter angle of approximately 6 degrees. The peaks in the spectrum are present because the incident spectrum contains the wavelength necessary for the Bragg law to be satisfied. To see how the peaks vary in intensity with varying incident spectrum, and to see if any other peaks become significant, a plot such as that shown in figure 2.19 can be examined. The figure shows the variation of the hydroxylapatite spectra with increasing incident kV from 65 kV to 140 kV. It can be seen that by increasing the energy no further significant peaks appear i.e. there is no additional information in the increased energy range of 70 keV to 140 keV and the influence of the x-ray tubes characteristic lines become apparent.

![Figure 2.19: Variation of the hydroxylapatite spectrum with change in incident kV at a scatter angle of 5 degrees.](image)

2.3.4 Modelling collimation geometry

The information described above is useful in the case of archaeological bone. However, perhaps one of the most useful aspects of the model is to investigate the change in spectra as a function of changing geometry. This is a useful tool because it enables the collimation geometry to be optimised such that the photon throughput of...
the system is maximised while retaining the useful information in the spectrum. In the case of archaeological bone this can be carried out using the model described in section 2.1 and is explained in context in chapter three. To perform this optimisation for a bone phantom simulating an in-vivo situation, it would be useful to be able to model both the bone mineral and the bone marrow as a mixture.

2.4 Modelling a mixture

The program was modified to model a mixture of bone mineral and bone marrow. The materials chosen to represent the mixture were calcium carbonate and polyethylene respectively. The materials are cheap and were in plentiful supply enabling different mixtures to be made from which measurements could be taken to test the model of the diffraction system.

To use the computer code to model a mixture of materials a JCPDS diffraction data set needs to be estimated for that mixture. The JCPDS powder diffraction file data sets cannot simply be added together because the intensities of the lines in each set are normalised to the most intense line in a particular set and hence to not relate directly to a mixture of materials. A diffraction data set for the mixture was estimated by using information obtained from a conventional powder diffraction system. The diffractometer used was a Phillips "X'pert", using a photon wavelength of 1.5406 Angstroms (Cu Kα). Diffraction data was obtained for the calcium carbonate and polyethylene powders under identical conditions and over a 2θ range of 15 to 35 degrees. The Phillips diffraction data obtained for the calcium carbonate matched the JCPDS data in the powder diffraction files but the polyethylene data differed slightly. It was decided to use the data from the Phillips diffractometer so as to be sure it matched the polyethylene being used. Figure 2.20 shows the data obtained from the Phillips diffractometer for both materials. It can be seen that there are two significant diffraction peaks for the polyethylene at 2θ values 21.5 and 23.8 degrees with 3324 and 957 counts respectively. The most intense line in the calcium carbonate data has 1824 counts and this is the line represented by the normalised intensity value of 100 in the JCPDS powder diffraction files. The polyethylene data was normalised to this line i.e. if 1824 represents the 100 line, then the 3324 polyethylene line represents 182 and the 957 polyethylene line represents 52. The d values were calculated from the Bragg
law so that this information could now be incorporated into the JCPDS powder diffraction file data for calcium carbonate giving an estimated diffraction data set for the mixture.

![Graph showing diffraction data for calcium carbonate and polyethylene](image)

**Figure 2.20 : Diffraction data obtained using the Phillips X'pert diffractometer for calcium carbonate and polyethylene.**

This estimated diffraction data set is valid for equal quantities of the components in the mixture. To be able to model a range of mixtures an individual diffraction data set was made for 20% to 70% calcium carbonate (by mass) at 2% intervals. The relative intensities of the peaks was adjusted for the varying percentage content of materials using

\[ I = \frac{I_{(o)}}{100} P_\% \]

where \( I_{(o)} \) is the number of counts in the polyethylene peak from the diffractometer and \( P_\% \) is the percentage of polyethylene in the mixture. A similar process is carried out for the calcium carbonate peak. The data is then normalised to the calcium carbonate peak (which is given the value of 100) as described above. For use as an example, consider a 60% calcium carbonate, 40% polyethylene mixture. The polyethylene peaks are corrected in the following manner:

\[ I_{2\theta=21.5} = \frac{3342}{100} \times 40 = 1329 \]
\[ I_{20-23.1} = \frac{957}{100} \times 40 = 382 \]

For the calcium carbonate peak

\[ I = \frac{1824}{100} \times 60 = 1094 \]

i.e. the 1094 count figure is used to represent the I = 100 line in the JCPDS diffraction data. The polyethylene are normalised to this i.e.

\[ I_{20-21.5} = \frac{1329}{1094} \times 100 = 121 \]
\[ I_{28-23.1} = \frac{382}{1094} \times 100 = 34.9 \]

The attenuation data for each mixture also had to be estimated which was achieved using the XCOM program. The Monte Carlo procedures described in section 2.15 were carried out for each mixture. Figure 2.21 shows the modelled spectra for the range of mixtures using an incident spectrum of 70 kV and a scatter angle of 5 degrees and Figure 2.22 shows the modelled spectra compared to the measured spectra for three of the mixtures.

\[ \text{Figure 2.21 The modelled spectra for different percentages of calcium carbonate in a mixture of calcium carbonate and polyethylene.} \]
Chapter Two

Modelling Coherent Scattered Spectra

Figure 2.22a: Modelled and measured spectra for 50% calcium carbonate, 50% polyethylene.

Figure 2.22b: Modelled and measured spectra for 38% calcium carbonate, 62% polyethylene.

Figure 2.22c: Modelled and measured spectra for 20% calcium carbonate, 80% polyethylene.
Chapter Two  
Modelling Coherent Scattered Spectra

2.5 Optimisation of the system for measurements on phantoms simulating an in-vivo situation

Due to the unavailability of the UCL diffractometer, the St. Bartholomew's system was used for the measurements on the phantoms described in chapter four. The system was built at the clinical physics department of St. Bartholomew's Hospital, London, and is of similar design and uses the same equipment as the one constructed at UCL which was used for the work described in chapter three. However the system did have some restrictions, namely the slit collimator aperture separation distances, which are fixed at 150 mm, the primary collimator slit width, which is fixed at 1.0 mm, and the x-ray tube filtration which has 1.0 mm of aluminium compared with the 2.5 mm on the UCL system. The system was modelled to assess its suitability given the above restraints.

2.5.1 Further modifications to the model

Code was implemented to model the attenuation due to varying dimensions of surrounding soft tissue, and varying dimensions of the cortical bone surrounding the trabecular measurement volume. The coefficients used to account for the attenuation due to the cortex were those for the material dural, as it the material used in the phantoms to represent the cortical bone. Other modifications were carried out to suit the measurements to be made on the St. Bartholomew's system. The mixture that is modelled has components made up of calcium carbonate and polyethylene, whereas the materials in the phantoms are hydroxylapatite and animal fat. (A full description of the phantom is given in chapter four, section 4.2). The polyethylene is a suitable substitute for the fat as it produces a broad diffraction peak at the same momentum transfer value. The calcium carbonate produces its main characteristic peak at a lower momentum transfer than that of hydroxylapatite but still provides good contrast with the polyethylene making it acceptable to use for this application. The range of mixtures modelled described in section 2.4 was wide and the mixtures were categorised by percentage of mass content. For the phantoms used to simulate in-vivo measurements, the percentage by mass ranged from 45% hydroxylapatite/55% fat to 30% hydroxylapatite/70% fat. The range of calcium carbonate used in the model was taken from 48% to 30% and modelled at 2% intervals. The model was used to predict spectra for this range of mixtures for a given geometry. Multivariate calibration using the Unscrambler (see chapter one section 1.6) was performed to make a calibration
model and predict the quantities of calcium carbonate and polyethylene in certain test spectra. This process could be repeated for different scatter collimator slit widths.

The model described in section 2.4 takes no account of statistical noise or of the time taken to acquire a spectrum. It would be useful to be able to estimate the differences in spectra due to the time of measurement, as this would then give an idea of how time would affect the predicting capabilities of the Unscrambler. Exploratory measurements on the phantoms showed that an average count time of approximately 1200 seconds gave a total integrated number of counts in a spectrum of 750 000. This number was deemed acceptable as it produced counts in the predominant peaks of the spectra that were generally greater than 10 000. A routine was written for the program that normalised the modelled spectrum so that the total integrated counts was made to equal 750 000. If it is assumed that this number took 1200 seconds to acquire then the count rate is easily established such that the spectrum for any given time can be estimated by correcting the number of counts channel by channel. Each channel was then examined and using a random number generator, noise was added in the range \( \pm \sqrt{N} \), where \( N \) is the number of counts in the given channel. Figure 2.23 shows the difference in a modelled spectra for 45% CaCO\(_3\) for three different times of 250, 50 and 2s and should be compared to figure 4.2 (chapter four section 4.1).

![Figure 2.23: Estimation of spectra for different measurement times using the model.](image)
2.5.2 Modelling the system

A scatter angle of 5 degrees was chosen and an incident spectrum of 70 kV used as this produced good contrast between the predominant peaks of hydroxylapatite and fat. It was shown in section 2.3.2 that the main hydroxylapatite peak has its greatest intensity at a scattering angle of approximately 6 degrees. However, at angles larger than 5 degrees the peak due to the animal fat in the mixture has a relatively low momentum transfer value and is subject to increased attenuation. At angles smaller than 5 degrees the hydroxylapatite peak is pushed to higher momentum transfer values where the intensity of the incident spectrum is reduced resulting in reduced intensity in the scattered spectrum. It was decided that 5 degrees was a good compromise as it gave reasonable intensities for both the hydroxylapatite and fat and enabled them to be resolved easily i.e. they were not set close together. With the fixed slit primary aperture width of 1.0 mm and a 5 degree angle the measurement volume was contained within the simulated trabecular dimensions in the phantom provided the scattered collimator slit width did not exceed 1.0 mm, i.e. the dural, simulating the cortex and the polyethylene container housing the mixture of hydroxylapatite and fat, contribute nothing to the scattered spectrum.

The model was used to produce spectra for a range of soft tissue and cortical thicknesses that could represent measurements made on the forearm i.e. the radius. Three soft tissue thicknesses were used 10, 20 and 30 mm, and for each of these, 3 cortical thicknesses were modelled, 0.5, 1.0 and 1.5 mm. The maximum slit width of 1.0 mm was used. A four variable model was then made using the 10 mixtures described above in the Unscrambler where the y-variables were calcium carbonate content, polyethylene content, cortical thickness and soft tissue thickness. The calibration matrix contained 90 objects (spectra) each having 184 variables (channels). The partial least square modelling option was used with the cross validation procedure. The optimum model was attained using 3 principal components. A test set of 9 mixtures was then generated using the computer model with a 20 mm soft tissue thickness for the three dimensions of cortex, and predictions made for 3 simulated measurement times of 250, 50 and 10 seconds. Figure 2.24 is a scatter plot of predicted calcium carbonate content against actual content. The average accuracy figure is the mean accuracy of all 9 test predictions. The dotted line shows the ideal predictions and the solid line is a regression on the points. The error bars are the deviation estimated by the Unscrambler (see chapter one section 1.6.2).
Four Variable Model

It can be seen from figure 2.24 that the accuracy at 250 seconds is within approximately 1.5% and as expected gets progressively less accurate with time. Figure 2.25 shows the predictions of the cortical thickness made using the four variable model. There is no capability of distinguishing between the 3 cortical thicknesses using this model at any of the 3 count times.

The prediction ability could be hampered by the fact that the attenuation process is occurring because of variations in both soft tissue and cortical dimensions. Another model was made using a constant thickness of soft tissue of 20 mm and the 3 cortex dimensions i.e. the number of objects in the model was reduced to 30 and the attenuation is caused primarily by the thickness of the dural cortex. Figure 2.26 shows the predictions for the 3 variable model. It can be seen there is improvement in the predictive ability in the three variable model at the higher count time of 250 seconds and with the exception of the initial 0.5 mm prediction are accurate to within approximately 0.1 mm.
2.6 Discussion

This chapter has described computer code written to model the spectra being measured in the two applications described in this study. The program allows the different aspects of the system to be examined, and the relative effects of changing a particular
parameter with respect to others. Particular routines can be omitted, enabling the potential effects of a certain parameter to be assessed. It is clear that angular blurring caused by the collimation geometry is the most important consideration in this work.

The geometry used for the archaeological bone measurements was decided on using the model, as well as the incident kV of 70 and scatter angle of 5 degrees. This is described in more detail in chapter three.

The St. Bartholomew's system was modelled with the fixed geometry and the maximum scatter collimator width of 1.0 mm to assess its suitability for measurements on the phantom. The results showed that sufficient accuracy could be achieved using an incident spectrum of 70 kV, a scatter angle of 5 degrees using a measurement time of approximately 50 seconds. (For more detail of the accuracy required see chapter four). It should be noted that this is an estimation only because the time, and noise parameters modelled are only estimated over an average time to collect a fixed number of counts. This length of time will vary depending on the amount of attenuation that occurs due to cortical and soft tissue thickness.

However, despite these and the previously described limitations the model is useful in assessing the feasibility of making the measurements and obtaining results of sufficient accuracy. Having established this the phantoms could now be constructed and this is described fully in chapter four section 4.2.
Measuring Trabecular Bone Mineral Density in Archaeological Bone

3.1 Introduction

The main aim of using the energy dispersive x-ray diffractometer (EDXRD) system in this study is to characterise bone tissue, i.e. quantify the amount of bone and bone marrow within the trabecular structure. The problems of in vivo measurements are significant including the problems of attenuation due to the surrounding soft tissue, surrounding cortical bone and the dimensions of the bone itself. The limits of the systems capabilities need to be established to assess the suitability of the technique for a clinical application.

An initial study of these capabilities was performed on a large supply of archaeological human bones. The bones were being used as part of a study by the Institute of Archaeology at University College London to try to establish if osteoporosis was present in the population of East London in the 1700's. One possible aspect of this determination is the measurement of the trabecular bone content of the samples. The bones were excavated from two sites, one set being from the Redcross Way burial ground in the borough of Southwark, London and were approximately 200 years old with an age range of individuals from 16 years to over 45 years. The burials were in pits of up to 10 coffins across and 7 or 8 deep. On excavation the coffins were found to be in good order with decoration still visible which meant that the majority of the remains were in exceptionally good condition. The second set of bones were from a burial site in Farringdon Street, London, and were also approximately 200 years old with a large range of individual ages.

Comparative measurements of trabecular bone mineral density were carried out on the samples from the Redcross Way site which consisted of 30 femurs, 25 4th lumber vertebrae, and 22 radii. The standard archaeological method used to assess bone
density in their samples is to use radiogrammetry techniques (Ericksen 1976, Mays 1996) or DEXA (Lees et al 1993). Radiogrammetry techniques involve the measurement of cortical thickness from radiographs and the osteoporotic state is inferred by correcting for the estimated size of the individual, and comparing the cortical thickness to a reference set of normal data for the age of the individual. This technique, however, does not give a quantitative measurement of the bone density. DEXA has two main drawbacks if measurements of trabecular bone mineral density are required. Firstly the measurement is one for the whole bone i.e. cortical and trabecular content, and secondly the calibration procedures used and the software used to process the attenuation data might not be suitable for the type of sample being examined.

The archaeological bone samples are the simplest system for the EDXRD technique to deal with i.e. a one component (bone mineral only) system. The aim of this particular part of the study was to test and assess the technique for making simple bone mineral density measurements, and to compare them with DEXA measurements and optical densitometry measurements made on radiographs of slices of the bone samples. Predictions of trabecular bone mineral density were also made from a calibration model so that the accuracy and precision of this simple one component system could be estimated. Bones that have been buried for a considerable time period may undergo mineral changes due to contact with ground water and chemicals in the ground (Bell 1990, Hanson and Buikstra 1987). The different minerals in the bone will not be detected by using DEXA but should be detectable using energy dispersive diffraction measurements as the different minerals will produce different diffraction peaks in the spectrum. If the system can be used in this way it will offer a non invasive technique for indicating the mineral types in a sample.

### 3.2 Experimental Procedure

#### 3.2.1 The measurement sites

Figure 3.1 shows one sample from each of the sets of femurs, vertebrae and radii. The femoral measurement site was a slice through the neck 5 mm wide. The slice through
the vertebra was in the centre of the body of the bone and was again 5 mm wide. The radius site was just below the styloid process. Each site was marked on the bone.

3.2.2 Whole bone radiographs

Each of the bone samples was radiographed together with an aluminium calibration step wedge. The exposure parameters used were 60 kV, 3 mA, 30 seconds for the femurs, 50 kV, 3 mA, 35 seconds for the vertebrae, and 50 kV, 3 mA, 35 seconds for the radii. The x-ray tube had 0.2 mm aluminium filtration. The measurement sites in each sample were then analysed using an optical densitometer (DT 1100 R.Y.Parry LTD, Newbury) and assigned an equivalent thickness of aluminium taken from the step wedge. The step wedge had 15 graduations in height from 1 mm to 15 mm stepping in 1 mm intervals. Each step had an area 15 mm wide by 10 mm deep. The optical
densitometer with a 3 mm diameter aperture was used to take three measurements from each step in the wedge and then the mean found. The mean values were then plotted as a function of aluminium thickness. A curve was fitted to the points using a quadratic regression procedure. The range of optical densities for the wedge were from 0.5 to 4.5. Each bone sample was analysed using the optical densitometer on a matrix of 2x5 positions where measurements were taken over the measuring site and the mean found. This mean value was then read off the step wedge calibration curve and the sample allocated an equivalent thickness of aluminium. The purpose of this measurement was to use it in attenuation correction procedures for the EDXRD measurements at a later stage, (see section 3.3).

3.2.3 DEXA measurements

DEXA measurements were taken on each sample on a Lunar DPX-L at St. Mary's Hospital, Paddington, London. The system is calibrated by staff at the hospital using phantoms supplied by the manufacturer (Lunar Corporation, Madison, Wisconsin). The scanner uses a pencil beam collimator which performs a raster scan of the area of interest. The DPX-L has various scanning options depending on the site of the body that is being scanned. The forearm option was chosen for all the samples of bone as the software used in processing the data assumes no soft tissue surrounding the bone. Instead of having to simulate soft tissue, the option only requires the use of the tissue equivalent platform, made of delrin, which is placed such that the forearm of the patient rests on the platform. A high resolution scan was used for each sample which is recommended for measurements with a small region of interest.

Two measurements were made for each sample which were placed on the delrin platform, one being rotated 180 degrees relative to the other (i.e. turned over). Regions of interest were set over the measurement site for each scan and two bone mineral density readings recorded that were then averaged. The region of interest was a rectangle 5 mm by 20 mm. This matches the dimensions of the slice thickness, and the slit height of the ribbon beam collimator used in the diffractometer.

An estimation of the precision of the DEXA measurements was made by recording 10 bone mineral density readings of a chosen bone sample over the same region. This was repeated for 7 bone samples with varying initial bone mineral density values from 0.032 gcm$^2$ to 0.9 gcm$^2$ and the mean and standard deviation of the readings were
calculated. Assuming the readings are normally distributed, it can be said with a 95% confidence level that a bone mineral density reading will lie within ± two standard deviations of the mean. Two standard deviations were expressed as a percentage of the mean for the value of the precision and plotted as a function of the mean bone mineral density. This plot is shown in figure 3.2. From this curve the precision of the bone mineral density readings could be estimated for each of the bone samples. It can be seen that the precision is poor particularly with low bone mineral density samples. The precision for normal DEXA readings on calibration phantoms is approximately 1% (see section 1.2.3) which would indicate that, although using the forearm option of the machine, the software routines in the analysis may not be suitable for low bone mass archaeological samples. Some of the very low bone mass samples did show a zero bone density reading using DEXA and is described in section 3.4.

![Figure 3.2: Estimated precision for DEXA measurements as a function of bone mineral density.](image)

### 3.2.4 EDXRD measurements

The computer model (see chapter two) was used to help find the optimal parameters to be used in measuring the samples. It is a simple system i.e. one component only, with no restrictions on the length of counting time allowing the geometry to be set such that good resolution can be achieved if needed. The exposure factors chosen were a 70 kV input spectrum and scatter angle of 5 degrees. It can be seen from figure 2.17 that these parameters give a high intensity of the predominant hydroxylapatite peak. Although 6 degrees gives a slightly higher intensity, 5 degrees was used because the
diffractometer was being used for other applications and continual resetting of the geometry was impractical. Using 5 degrees instead of 6 has the effect of increasing the momentum transfer separation between the two main hydroxylapatite peaks. The geometry used was a 0.5 mm slit width, and a collimator aperture separation distance of 300 mm which gives an acceptable count rate while keeping the resolution of the two main hydroxylapatite peaks. Figure 3.3 shows the modelled spectra for hydroxylapatite with varying collimation geometry.

![Modelled spectra for hydroxylapatite with exposure parameters of 70 kV and scatter angle of 5 degrees. The three collimator geometry configurations show the resolving capabilities of the two main hydroxylapatite peaks.](image)

To make the experimental measurements, each sample was positioned in the diffractometer such that the measurement volume, defined by the collimation geometry, was located in the centre of the measurement slice. The sample was positioned using a translator device that enable the sample to be moved at intervals of 0.5 mm until the slice width was covered, hence defining a measurement volume within the sample. The total live time pre-set for counting was set at 1000 seconds which gave counting statistics for all of the sets of bones such that the error in each of the peaks of interest was approximately 1%. The mA setting used was 15 mA to give
a maximum flux of photons while keeping the dead time of the MCA to approximately 2%. Figure 3.4 shows a typical spectrum which was recorded from femur sample number f100 using 70 kV, 15 mA, 1000 second live time and 5 degree scatter angle. Measurements were taken for all of the femur, vertebrae and radius samples using these parameters.

![Graph showing typical energy dispersive diffraction spectrum](image)

**Figure 3.4**: A typical energy dispersive diffraction spectrum taken from one of the bone samples (femur sample f100 using 70 kV, 15 mA, 1000 seconds live time and a scatter angle of 5 degrees).

### 3.2.5. Optical densitometry techniques applied to the measurement volume.

The slice of bone that contained the measurement volume was physically cut from the whole bone sample. The bone slices were then radiographed together with an aluminium calibration step wedge (exposure factors 60 kV, 3 mA for 25 seconds). The step wedge used for this procedure had 15 graduations in thickness from 0.2 mm to 3.0 mm and was analysed as for the whole bone radiographs (section 3.2.2). The measurement volume was marked out on each slice image and using a matrix of 6 x 3 positions, optical density measurements were made which were then averaged. The measurement volume is dictated by the thickness of the slice, the collimator slit height,
the collimator slit width and the scattering angle. An equivalent thickness of aluminium, which was a representation of the amount of material present in the measurement volume could then be given to each sample. Figure 3.5 shows a femoral neck slice with the measurement volume marked on it. An estimation of the precision of this technique was made by repeating the measurement of one sample 10 times and finding the mean and standard deviation. The precision was established as for the method described in section 3.2.3 and was estimated to be ±2% for all samples. It should be noted here that the measurement volume shown is not the precise shape of the actual volume in a sample. The collimation geometry does not result in a rectangular slab but has a rhomboid shape which is enclosed within the trabecular structure. However by estimating the volume with a rectangular slab, the optical densitometry was easier to perform and it enabled the removal of the measurement volume to be achieved at a later stage.

\[\text{Figure 3.5: Femoral neck slice with the measurement volume indicated. The 20 mm dimension is set by the collimator slit height and the 10 mm dimension is set by the collimation geometry i.e. slit widths and scattering angle.}\]
3.2.6 Bone density measurements (base line data)

The final stage of the experimental procedure was to physically remove the measurement volume from the slices of the femurs and the vertebrae, (this was not possible for the radii, see section 3.4.6.). The thickness of the slice was measured and its mass determined before and after the removal of the measurement volume. This enabled a direct measurement of bone density to be made. (This work was carried out by M.Brickley, The Institute of Archaeology, UCL, London). The measurements of density from this procedure were compared with values from the other modalities.

3.3 Analysis of the EDXRD data

The EDXRD spectra, as they are in their raw form, cannot be compared to each other. This is because the bone, through which both the incident and scattered photons have to pass, leads to attenuation of the measured spectra. The cortical or compact bone plays a particularly significant role in this as figure 3.6 shows. The sample used to make the measurements shown in the figure was a femur and the measurement was taken through the femoral neck. The parameters for each of the measurements were the same, the only difference being the removal of the cortical bone around the measurement site. It can be seen that the lower energy peaks are absorbed preferentially and some information may be lost completely (as seen around momentum transfer value approximately 1.15 nm\(^{-1}\)).

To correct for attenuation, each energy channel was corrected individually using 
\[ I = I_0 e^{-\mu x}, \]
where \( I \) is the attenuated intensity, \( I_0 \) is the original intensity, \( \mu \) the linear attenuation coefficient, and \( x \) is the transmission thickness. The method by which each bone sample was given an equivalent thickness of aluminium is described in section 3.2.2. The appropriate linear attenuation coefficients for aluminium were used for each channel and the equivalent thickness of aluminium for each sample.

The region of the spectra with momentum transfer values less than 1.2 nm\(^{-1}\) is excluded as it is in this region where information may be too severely attenuated to be recovered (see figure 3.6). The region of the spectra with momentum transfer values higher than
1.9 nm$^3$ is excluded because it contains no characteristic peaks that are resolved and what information it may contain does not appear above the background.

The method of correcting for attenuation using the optical densitometry techniques on the radiographs could be inconvenient in that the bone has to be radiographed, the film developed and the equivalent thickness of aluminium measured. This is time consuming and requires resources. An alternative method of attenuation correction was attempted and the results compared. Figure 3.6 shows that the lower energy peak of the hydroxylapatite is attenuated preferentially to the higher energy peak. The amount of relative attenuation between the two peaks will be dependent on the amount of attenuating material through which the photons have to pass i.e. the amount of bone present. The ratio of the number of photon counts in these two peaks was used as a representation of the transmission thickness, $x$, in the attenuation formula $I = I_0e^{-ux}$. The attenuation coefficients were derived using the elemental composition (percentage by mass) of the skeletal femur for an adult aged 30 years (ICRU Report 1986).

![Figure 3.6: Attenuation of the measured spectrum due to the cortical bone around the femoral neck.](image-url)
The region of interest to be analysed on the attenuation corrected spectra was taken to include both the two hydroxyapatite peaks. The region was defined on all the attenuation corrected spectra between momentum transfer values of 1.34 nm\(^{-1}\) (channel number 245) and 1.83 nm\(^{-1}\) (channel number 335) as shown in figure 3.7. The signal \(S\) is the number of counts in the region of interest and is calculated using:

\[
S = T - B \pm \sqrt{T + B} = T - B \pm \sqrt{S + 2B} \quad [3.1]
\]

where \(T\) is total counts i.e. the background \(B\) plus signal. The relative error is given by:

\[
e = \frac{\sqrt{T + B}}{S} = \frac{\sqrt{S + 2B}}{S} \quad [3.2]
\]

Figure 3.7: Defining the ROI which includes the two hydroxyapatite peaks.
3.4 Results of BMD measurements

3.4.1 The density of the excised trabecular measurement volume for the femurs (base line data)

Figure 3.8 shows a bar chart of the densities of the femur samples excised trabecular measurement volume, which will be called the base line data as it is the data to which the other modalities will be compared. They are placed in order of increasing bone mass and it can be seen that there is a wide variation and cross section of bone density values. Figure 3.9 shows the cross section of the measurement slice of samples f28 and fnn and clearly shows the thinning and complete loss of some of the trabeculea in sample fnn which has a measured bone density of 0.0683 g/cm³ compared to a density of 0.3011 g/cm³ for the sample f28.

Figure 3.8: Bar chart showing the densities of the femur samples measurement volume (base line data).

Figure 3.9: Measurement slice cross sections of two samples showing significant trabecular thinning in the right hand slice of femur No. fnn
3.4.2 A comparison with DEXA measurements for the femurs

The total bone mass of the base line data of the femur samples as shown in figure 3.8 was normalised to unity for the purposes of comparing the data with other modalities. The DEXA density values were also normalised so the total density was unity and then plotted in the same order as that shown in figure 3.8. Figure 3.10 shows a scatter plot of the base line data density and the DEXA bone density. The error bars are the estimation made of the precision of each DEXA measurement. The correlation coefficient was calculated to be \( r = 0.64 \). It can be seen from the plot that the precision is poor ranging from ± 50% for samples with low density to ± 10% for the higher densities.

![Figure 3.10: Scatter plot of the femoral neck base line data and DEXA bone mineral density.](image)

3.4.3 A comparison with the optical densitometry measurements on the femur sample slices

Figure 3.11 shows a scatter plot of the optical densitometry slice data to the base line data with the estimated precision on the optical densitometry data. The correlation coefficient was calculated to be \( r = 0.78 \).
3.4.4 A comparison with EDXRD measurements for the femur samples

The EDXRD measurements are represented in two sets of data, one for the original spectra being corrected for attenuation by using the equivalent thickness of aluminium for each sample, and the other corrected using information derived from the peak ratio within the measured spectrum as described in section 3.3. Figure 3.12 shows the scatter plot of the two sets of corrected data and the base line data. The correlation coefficient for the aluminium thickness corrected measurements was calculated to be \( r = 0.84 \) and for the peak ratio corrected measurements, \( r = 0.8 \). The EDXRD measurements correlate better than the other two methods and there is little difference between the two methods of attenuation correction.

Table 3.1 shows a summary of the results and includes the correlation coefficient for the EDXRD data not corrected for attenuation. It can be seen the correlation is poorer for uncorrected data and shows the necessity of performing an attenuation correction procedure.
0.06
0.05
0.04
0.03
0.02
0.01

Density from base line data [gcm$^{-3}$ normalised to unity]

• Attenuation correction by thickness of Al (r=0.84)
— Regression through Al corrected data
• Attenuation correction by peak ratio (r=0.8)
— Regression through peak ratio data

Figure 3.12: Scatter plot of the femoral neck base line data and EDXRD data.

<table>
<thead>
<tr>
<th>Method</th>
<th>Standard Deviation $\sigma$</th>
<th>Correlation Coefficient $r$</th>
</tr>
</thead>
<tbody>
<tr>
<td>DEXA</td>
<td>0.02</td>
<td>0.64</td>
</tr>
<tr>
<td>Optical densitometry</td>
<td>0.01</td>
<td>0.78</td>
</tr>
<tr>
<td>EDXRD : raw data</td>
<td>0.01</td>
<td>0.73</td>
</tr>
<tr>
<td>EDXRD : Al corrected</td>
<td>0.01</td>
<td>0.84</td>
</tr>
<tr>
<td>EDXRD : peak ratio corrected</td>
<td>0.01</td>
<td>0.80</td>
</tr>
</tbody>
</table>

Table 3.1: Summary of correlation results for the femur samples.

3.4.5 The density of the excised trabecular measurement volume for the vertebrae (base line data) compared to the other modalities

The results for the 25 vertebrae samples were analysed as for the femurs. Figures 3.13 through 3.15 show scatter plots comparing the base line data with the other modalities. Table 3.2 summarises the results.
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Figure 3.13: Scatter plot of the vertebrae base line data and DEXA bone mineral density.

Figure 3.14: Scatter plot of the vertebrae base line data and optical densitometry data.
3.4.6 Measurements on the radius bone samples

The measurements on the radius samples was different to the femur and vertebrae in that the measurement volume was not confined to the trabecular bone only. The radii are smaller bones and the measurement volume encompassed some cortical bone as...
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Measuring Trabecular Bone Mineral Density in Archaeological Bone

well as trabecular bone. A slice of one of the radius samples with the measurement volume marked on it is shown in figure 3.16. The region of bone that is measured using DEXA is also shown. It has the same volume length as the EDXRD measurement volume but passes through the entire bone. The amount of cortical bone included depends on the physical size of the bone. For the radius sample the whole slice was weighed and the volume of the slice calculated, enabling a density for the whole slice to be established. The DEXA data for the radius samples was compared to the slice densities and a correlation coefficient of \( r = 0.784 \) was calculated. The EDXRD measurements gave a value of \( r = 0.56 \). Certain radii were selected from the set so that samples which were larger than the measurement volume were excluded i.e. only samples which approximately fitted in the measurement volume were included. The EDXRD readings now compared better resulting in a value of \( r = 0.75 \). All of the correlation values calculated were significant at the 0.1% level except the two EDXRD measurements made with the radii samples, which were significant at the 1.0% level. Table 3.3 summarises the results for the radii samples.

![Figure 3.16: Measurement volume of a radius slice and the area measured by DEXA.](image)

Table 3.3 summarises the results for the radii samples.

3.4.7 Discussion

The energy dispersive diffraction technique for measuring trabecular bone content in the femur and vertebrae samples has the best correlation with the base line data (see tables 3.1 and 3.2). The peak ratio attenuation correction procedure gives a slightly smaller value of correlation coefficient than the equivalent thickness of aluminium.
method. The advantages of being able to use the peak ratio method compensates for this lower correlation as it avoids the need for exposing film etc. The DEXA measurements for estimating trabecular bone content are poor because the method measures the cortical content of the bone as well as the trabecular content. The DEXA performed better on the vertebrae samples and this is probably because there is little or no cortex over the main body of the vertebrae. However several of the DEXA readings were zero, suggesting there is a lower limit to which the DEXA clinical system is sensitive enough to detect any bone mass. An improvement might be made on this lower limit by using the small animal software option that is available for many DEXA machines. If the measurement volume of the EDXRD system were to include the cortex then we would expect the DEXA correlation to improve (see section 3.4.6). The photodensitometry method showed better correlation with the base line data than the DEXA correlation with the base line data because the readings were taken over the EDXRD measurement volume only. However the main disadvantage of this method is that it can only be used on excised bone samples.

<table>
<thead>
<tr>
<th>Method</th>
<th>Correlation Coeff (r)</th>
</tr>
</thead>
<tbody>
<tr>
<td>DEXA</td>
<td>0.78</td>
</tr>
<tr>
<td>EDXRD (whole set)</td>
<td>0.55</td>
</tr>
<tr>
<td>EDXRD (edited set)</td>
<td>0.75</td>
</tr>
<tr>
<td>Optical densitometry</td>
<td>0.78</td>
</tr>
</tbody>
</table>

Table 3.3: Summary of correlation coefficients for radius bone measurements.

The results of the radius measurements was poorer. The main cause of this is that the configuration of the system was not optimal for that particular bone, i.e. the EDXRD measurement volume was not always confined to the trabecular structure. In the edited set of data the results were improved and the correlation to the base line data was comparable to that of the DEXA and optical densitometry techniques.

In principal the measurement volume could be made to fit inside any bone sample by changing the collimation geometry of the EDXRD experimental set up. The slit height could be changed and the angle of scatter increased to create a change in measurement volume enabling trabecular bone density measurements to be made. Conversely, if the density of both cortex and trabecular bone was required, the geometry could be changed such that the volume included such a measurement. The problems of attenuation in the measurement can be overcome in this simple one component system by the methods described although it should be noted that the peak ratio method may
not be suitable for more complex systems. Because the diffraction profile is a unique signature for a given material, the system can be used to determine the types of mineral that make up a particular bone sample. Preliminary work on this is described in the next section.

3.5 A further application of the EDXRD system for archaeological bone

Figure 3.4 shows a typical energy dispersive diffraction spectrum from one of the femur samples. It can be seen by comparing this to figure 3.3 that the predominant peaks at momentum transfer values of approximately 1.4 nm\(^{-1}\) and 1.8 nm\(^{-1}\) are due to the mineral hydroxylapatite. There were some samples that showed a different diffraction pattern, as shown in figure 3.17. The characteristic change in the spectra was the appearance of a peak at momentum transfer value around 1.6 nm\(^{-1}\). The following section deals with the analysis leading to the determination of the origin of this peak.

Figure 3.17: The change in the diffraction pattern in the form of a peak of unknown origin.
3.5.1 Detection of mineral types

In order to determine the mineral responsible for the unknown peak in some of the spectra, conventional x-ray diffraction techniques were used. A small sample of bone was removed from the measurement volume of two bones, one being a femur sample which produced a typical hydroxylapatite spectrum, and one being a radius sample that produced a change in the diffraction pattern. These samples were ground to a fine powder and placed in a Phillips X’pert powder diffractometer which uses a photon wavelength of 1.5406 Angstroms (Cu Kα) to irradiate the sample. A spectrum was recorded with a 2θ range of 10 to 60 degrees for each sample. The difference between the two spectra is clearly seen in figure 3.18 where similar underlying structure is visible for both of the samples but for the radius pattern several clear peaks are superimposed. (The pattern for the normal bone sample has been offset for clarity). A peak search was performed on the spectra using the X’pers software and the lines of the femur spectrum were subtracted from the lines of the radius spectrum. This in effect left the lines that were found in the radius sample that were not present in the femur sample. A material identification routine was then used, which compares the data from the peak search with a library of diffraction data to find a match. The best match was found to be calcium carbonate (CaCO3 JCPDS diffraction file 24-0027).

![Diffraction Pattern](attachment:diffraction_pattern.png)

*Figure 3.18: The diffraction pattern obtained using the Phillips X’pert diffractometer for a typical bone sample and a sample with the extra peak in the energy dispersive diffraction pattern. (The normal bone sample has been offset for clarity).*
With this information, any future measurements taken can identify the presence of calcium carbonate although it is possible that all of the samples contain some calcium carbonate but the peak is not intense enough to be resolved using the current geometry. This process could be repeated with other minerals found in archaeological bone enabling a quick and non invasive way of determining the mineral types in the sample.

### 3.6 Prediction of bone mineral density from a calibration model

The bone samples from Farringdon Street were used for this part of the study and consisted of 68 fourth lumber vertebrae. Energy dispersive diffraction spectra were collected for all the samples using the same parameters as for the Redcross Way samples except the pre-count live time was extended from 1000 seconds to 1500 seconds to provide improved counting statistics for the calibration model (section 3.2.4). The spectra were corrected for attenuation using the peak ratio method described in section 3.3. The trabecular bone mineral density of the measurement volume was calculated by removing the measurement slice and weighing the slice before and after the volume was removed as described in section 3.2.6. A model was made with a calibration set using the Unscrambler (section 1.6.2) with 50 of the spectra which had a bone mineral density (BMD) ranging from 0.0667 g cm$^{-3}$ to 0.4888 g cm$^{-3}$. The 50 samples were chosen to provide a good calibration set with densities that provided uniform coverage over the full range. By using these 50, there were 18 samples left from which to make predictions of BMD. The set was modelled with one variable i.e. the BMD calculated from the removal of the measurement volume. The remaining 18 spectra, with densities spread across the calibration range, were used as a test set for prediction purposes. Each of the test set vertebrae had 10 spectra recorded, from which predictions of BMD were made and the precision estimated as described in section 3.2.3. Figure 3.19 shows the predicted BMD values obtained from the calibration model, the error bars are the estimated precision. The accuracy of each sample prediction was calculated and the mean of the accuracy was found to be within approximately 2%.

The predictions from the calibration model were accurate to within approximately 2% and the precision was estimated to be approximately ± 5%. A source of error in the
prediction is that the calibration model is based on one variable. If the samples did consist of the same minerals with the same content ratios this would be accurate, however it was shown in section 3.5.1 that calcium carbonate may vary in content over the samples. The intensity of photons scattered from calcium carbonate is greater than that of the hydroxyapatite hence a small increase in calcium carbonate content would produce a variation in the spectra out of context for the modelling variable. One way around this problem would be to determine the mineral contents of the calibration set and then create a model using two or more variables. This however is beyond the scope of this study.

![Graph](image.png)

Average accuracy of prediction = +/- 2.1%

Figure 3.19: Predictions of BMD made from the 18 test set samples.

This work on archaeological samples has shown that the EDXRD system has the potential to make accurate and precise measurements of trabecular bone density for
this simple system. The next chapter explores the far more complex, multivariable case of in-vivo measurements.
4 Simulation of In-Vivo Measurements

4.1 Introduction

The primary aim of the work described in this thesis is to assess the feasibility of using the energy dispersive diffraction system in a clinical in vivo environment to determine bone mass loss with the aim of predicting the onset of osteoporosis at an early stage. Methods of measuring bone mass were described in chapter one and it was stated that it would be advantageous to develop a method that could measure trabecular bone density in isolation from the cortical bone. At present, QCT is the only clinical method available to do this and it has the disadvantage that it is costly and the radiation dose to the patient is relatively high. The modelling work described in chapter two (section 2.5) showed that the technique is feasible, and this chapter describes measurements taken from specially constructed phantoms that simulate bone loss in an in-vivo situation. To predict the early signs of osteoporosis, bone mineral density measurements would either have to be taken in the form of a screening program to assess an individuals bone mineral loss rate, or as a one off measurement which is then compared to population norms (Hassager and Christiansen 1995). In either case both, the radiation dose to the patient and the accuracy of the measurement need to be within acceptable limits. The average rate of trabecular bone loss in women is 1-3% per year of peak bone mass and is greatly accelerated in post menopausal years (see chapter one section 1.1.4). Ideally an energy dispersive diffractometer in clinical use would need be to be able to predict a bone mineral density with an accuracy and precision of at least this annual bone mass loss. The considerations of radiation dose are dealt with in chapter five.

The primary problems of obtaining a sufficiently accurate measurement are those of signal attenuation, due to the cortical shell of the bone and soft tissue surrounding the measurement site, and the time available for the measurement. Figure 4.1 shows the
recorded spectra for a constant trabecular bone density with varying cortical bone and soft tissue dimensions. The attenuation problem is clearly seen because the same predicted density has to be derived from each of these measurements. To keep the radiation dose to the patient within acceptable limits and the physical discomfort of the patient to a minimum, the time of the measurement needs to be kept as short as possible which in turn leads to a reduction in the signal to noise ratio. Figure 4.2 shows the variation in the spectra for a given trabecular density with different measurement times of 250, 50 and 2 seconds.

A potential solution to this problem was attempted by analysing the spectra using multivariate analysis techniques (see chapter one section 1.6). By measuring a large number of spectra over a wide range of appropriate variables a calibration model can be produced from which subsequent predictions can be made. Because the analysis is carried out using multivariate analysis and one of the variables in that analysis is the cortical thickness of the bone, it is possible to make predictions of the cortical thickness surrounding the trabecular site. This would mean that as well as monitoring trabecular bone loss in a patient, cortical thinning could also be observed.
Three clinical sites were simulated using multi-component phantoms in the analysis of the measurements taken: the calcaneus, the forearm i.e. the radius, and the femoral neck. The calcaneus is the site used for determining bone mineral density using ultrasound techniques and the forearm and femoral neck are common sites for DEXA measurements (Bouxsein et al 1995, Speller et al 1989). The lumbar spine is an important clinical site used with existing techniques, however it differs from the sites mentioned above in that it is not an appendicular site and has radiosensitive organs in close proximity. The spine is also located in the trunk of the body which means the dimensions of any phantoms are large, consequently in this preliminary feasibility study simulating measurements at this site was not attempted.

4.2 The design and construction of the phantoms

Figure 4.3 shows the components of the phantoms which consist of a simulated trabecular core, housed in polyethylene pots, over which fits a dural sleeve to represent cortical bone. The soft tissue is simulated in the form of tissue equivalent slabs, made of "Mix D" (Jones and Raine 1949) approximately 10 mm thick. The trabecular core
is made up from a mixture of hydroxylapatite powder and animal fat. The hydroxylapatite represents the quantity of bone mineral present in the trabecular structure and the animal fat simulates the presence of bone marrow, which is predominately lipids, and fills the spaces between the trabeculae.

In normal healthy trabecular bone, the bone mineral occupies approximately 20% of the volume (Woodard and White 1982). The volume of the polyethylene pots was calculated and the mass of hydroxylapatite that would fill 20% of that volume established. Similarly the corresponding amount of animal fat that would fill the remaining 80% of the volume was calculated. These quantities were mixed together (with the animal fat melted) and placed in a polyethylene pot, 0.5 mm wall thickness, creating a trabecular core that represented a normal healthy bone i.e. a bone at its peak bone mass. The mass of a 1% reduction in hydroxylapatite and the corresponding increase in mass of fat that would fill the resulting reduced volume of hydroxylapatite was calculated. This enabled a set of trabecular core phantoms to be mixed that simulated a gradual reduction in bone mineral with an associated increase in bone marrow. The densities of hydroxylapatite and fat were calculated for the phantoms and these are shown in table 4.1. It can be seen that a 1% loss of hydroxylapatite is a very small quantity, approximately 0.1 g, which is a density reduction in the phantom of approximately 0.006 g cm$^{-3}$. A chemical balance was used to measure the quantities to be mixed with accuracy of 0.01 g, which, if trying to weigh 0.1 g differences, leads to an accuracy of ±10%. This means that in terms of density a 1% loss in the phantom is $0.006 ± 0.0006$ g cm$^{-3}$. 

*Figure 4.3: Components of the constructed phantoms.*
Although hydroxylapatite is the main mineral content in bone, it should be noted that human bone contains more elements than those that make up the hydroxylapatite e.g. carbon, magnesium and iron. The density of bone is less than that of hydroxylapatite and the linear attenuation coefficients are less and are shown for the energy range used in this study in figure 4.4. The attenuation coefficient for hydroxylapatite is approximately 2.5 times the value of the bone at the lower energies and approximately 1.7 times the values at the higher energies. However, the predominant diffraction peaks that are obtained from measuring bone are the ones due to the hydroxylapatite content which makes it a suitable bone mineral substitute in this investigation. The difference in the attenuation coefficients will result in an increased beam hardening effect on the diffraction spectra i.e. increased attenuation particularly at the lower energies in the spectrum.

<table>
<thead>
<tr>
<th>% Loss</th>
<th>Density HA [gcm(^{-3})]</th>
<th>Density Fat [gcm(^{-3})]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Peak bone mass</td>
<td>0.597</td>
<td>0.716</td>
</tr>
<tr>
<td>2</td>
<td>0.585</td>
<td>0.721</td>
</tr>
<tr>
<td>3</td>
<td>0.579</td>
<td>0.723</td>
</tr>
<tr>
<td>5</td>
<td>0.5673</td>
<td>0.728</td>
</tr>
<tr>
<td>6</td>
<td>0.561</td>
<td>0.730</td>
</tr>
<tr>
<td>7</td>
<td>0.555</td>
<td>0.732</td>
</tr>
<tr>
<td>9</td>
<td>0.543</td>
<td>0.736</td>
</tr>
<tr>
<td>10</td>
<td>0.537</td>
<td>0.739</td>
</tr>
<tr>
<td>12</td>
<td>0.525</td>
<td>0.743</td>
</tr>
<tr>
<td>14</td>
<td>0.514</td>
<td>0.748</td>
</tr>
<tr>
<td>16</td>
<td>0.502</td>
<td>0.752</td>
</tr>
<tr>
<td>18</td>
<td>0.490</td>
<td>0.757</td>
</tr>
<tr>
<td>20</td>
<td>0.478</td>
<td>0.761</td>
</tr>
<tr>
<td>22</td>
<td>0.466</td>
<td>0.766</td>
</tr>
<tr>
<td>26</td>
<td>0.442</td>
<td>0.774</td>
</tr>
<tr>
<td>28</td>
<td>0.430</td>
<td>0.779</td>
</tr>
<tr>
<td>34</td>
<td>0.394</td>
<td>0.792</td>
</tr>
<tr>
<td>35</td>
<td>0.388</td>
<td>0.794</td>
</tr>
<tr>
<td>38</td>
<td>0.370</td>
<td>0.801</td>
</tr>
</tbody>
</table>

*Table 4.1: The hydroxylapatite and animal fat densities of the constructed phantoms*
The cortical bone surrounding the trabecular structure is simulated in the form of dural sleeves of varying dimensions that fit over the polyethylene pots containing the trabecular core. (It should be noted here that the polyethylene pot will cause some attenuation, however the effect will be small and is a constant for all measurements consequently the effect is disregarded in the analysis). Dural is an alloy of aluminium and copper with the aluminium making up approximately 95% of the material. Figure 4.5 shows the total linear attenuation coefficients for cortical bone and dural for the energy range used and it can be seen that dural has a higher linear attenuation coefficient than that of cortical bone by a factor of approximately 2 at 20 keV dropping to a factor of approximately 1.5 at 70 keV. Despite these differences it was felt that dural would be suitable to use for a range of substitute cortical dimensions in the phantom and it has the advantage that it is cheap, readily available and can be easily machined. Four thicknesses of dural sleeve were made: 0.5, 1.0, 1.5 and 2.0 mm.

The soft tissue equivalent slabs were made of a tissue substitute material called Mix D and consists of carbon (77.7942%), hydrogen (13.4144%), oxygen (3.5021%), magnesium (3.8605%) and titanium (1.438%). Figure 4.6 shows the linear attenuation coefficients for soft tissue and Mix D. A maximum of five slabs were used for the measurements each approximately 10 mm thick.
4.3 The range of measurements taken

4.3.1 Scanning the phantom

Scanning was carried out to compensate for any inhomogeneity in the mixture of hydroxylapatite and fat in the phantom. In a clinical system this would be necessary
because trabeculae are not uniform in their dimensions so a volume would need to be scanned to obtain a mean density reading. The other reason for this procedure is that in a screening system measurements would have to be repeated in the same location for comparison purposes and the repositioning error would be less over a scanned volume than for a fixed position of the slit beam. An alternative to scanning the site in a clinical system would be to use a multiple slit collimator system which would have the advantage of reducing the measurement time. Figure 4.7 shows the irradiation geometry of the experimental set-up. Over the course of a measurement the phantom was scanned for a distance of 10 mm along its length. The geometry of the set up determines a scattering length of approximately 23 mm (see section 2.1.4) hence with a slit height of 20 mm the measurement volume created by scanning is approximately 4.6 cm³. The speed of scan (maximum 1 mms⁻¹) could be varied such that measurement times as low a 10 seconds could be scanned for the full 10 mm. Measurement times of 5 and 2 seconds had a scan length of approximately 5 mm and 2 mm respectively which would result in any inhomogeneity in the mixture becoming a source of error in the predictions of density, but was considered small enough to ignore at this stage.

4.3.2 Trabecular core measurements

To evaluate the prediction capabilities of the system under the most favourable conditions measurements were taken on the trabecular cores only i.e. no soft tissue slabs and no dural cortex rings. The calibration data set consisted of ten measured spectra from ten phantoms with a range in hydroxylapatite density from 0.5852 gcm⁻³ to 0.3703 gcm⁻³ in intervals of 0.0238 gcm⁻³, which represents a 4% loss of hydroxylapatite between each calibration phantom. A pre-set was enabled on the MCA so that each measurement continued until the number of counts under the spectrum totalled 750,000 which took approximately 5 minutes. Figure 4.8 shows the 10 spectra that make up the calibration set. A test set of nine spectra, from which predictions of hydroxylapatite density were to be made, were measured on phantoms with a 3, 5, 7, 9, 12, 16, 20, 28 and 35% bone mass loss. Measurements were made on each phantom for scanning times of 250, 100, 50, 20, 10, 5 and 2 seconds. All of the spectra were then normalised enabling predictions to be made from all spectra, regardless of the scanning time.
The Unscrambler was used to create a model using the calibration spectra and two associated variables i.e. the density of hydroxylapatite and the density of animal fat. The model was optimised using two principal components and used the partial least squares option with the cross validation procedure. The test spectra were fed into the model and the appropriate predictions made using the optimum two principal components.
An estimate of the precision of the density predictions was made by repeating the measurements on the test set ten times. Predictions were made from these ten spectra from which the mean and standard deviation was calculated. The precision was estimated by presenting two standard deviations as a percentage of the mean.

![Graph showing calibration data set for the trabecular core phantoms.](image)

**Figure 4.8**: Calibration data set for the trabecular core phantoms.

### 4.3.3 Full phantom measurements

Figure 4.9 shows the variable matrix over which measurements were made. The shaded areas in the figure show the regions applicable to the different clinical sites. The calcaneus has a very thin cortex ranging from 0 to 0.5 mm with surrounding soft tissue from a few mm to 10 mm. The radius may have a cortex of 0.5 mm to 1.5 mm with surrounding soft tissue between 10 mm and 30 mm. These two sites are completely covered in the matrix. The femur may have a cortical thickness of up to 2.0 mm with soft tissue thickness of up to 100 mm. The cortical thickness is covered in the matrix but the soft tissue range does not extend that far and hence the maximum thickness of soft tissue available is used i.e. 50 mm. For each cell in the matrix, i.e. for each soft tissue thickness and each cortex thickness, ten calibration spectra were measured as described in section 4.3.2.
From this matrix of spectra, three models were made. A four variable model used the full 200 spectra represented in the matrix with the four associated variables, i.e. density of hydroxylapatite, density of animal fat, cortical thickness and soft tissue thickness. It was found that 6 principal components minimised the residual variance in the model and hence was the optimum number of principal components to use in prediction. If a single soft tissue thickness is assumed for a given site then a three variable model can be made using 40 calibration spectra and the three associated variables i.e. density of hydroxylapatite, density of animal fat and cortical thickness. This assumption is reasonable for the calcaneus and radius site because if necessary they could be immersed in a water bath of fixed dimensions or the site could be packed with a tissue equivalent gel to a fixed dimension. In the three variable model three principal components minimised the residual variance. In the case of the calcaneus it may be reasonable to assume a constant cortical thickness as well as soft tissue thickness because the cortex on the calcaneus is very thin. If this assumption is made then the site can be modelled using a two variable model with the 10 calibration spectra from the cell and the two density variables. The two variable model minimised the residual variance using one principal component.

Figure 4.9: Variable matrix showing the range of measurements made, the applicable clinical sites, and the three models made.
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The test sets were the same as described in section 4.3.2 with the addition of a 750 and 500 second scanning time for the 5, 7, 12, 20, 28 and 35% bone mass loss phantoms.

4.4 Results

4.4.1 Presentation of accuracy

It has been stated in section 4.1 that the average loss of trabecular bone is between 1 and 3% of peak bone mass per year and that the predictions of trabecular bone density need to be accurate to within this limit. It was also shown in section 4.2 that a 1% loss of hydroxylapatite was equivalent to 0.006 ± 0.0006 g cm⁻³. For this accuracy criterion to be achieved it means that the numerical difference between the actual phantom hydroxylapatite density and the predicted hydroxylapatite density be less than or equal to 0.006 ± 0.0006 g cm⁻³. If \( \rho_{\text{phant}} \) is the density of the phantom, \( \rho_{\text{pred}} \) the predicted density and \( \rho_{\text{ave loss/year}} \) is density of average peak bone mass loss per year i.e. 0.006 ± 0.0006 g cm⁻³ then we can write

\[
\left| \frac{\rho_{\text{pred}} - \rho_{\text{phant}}}{\rho_{\text{ave loss/year}}} \right| \leq 1 \quad [4.1]
\]

If the quantity described by equation 4.1 is defined as fractional bone mass loss (FBML), then it can be said that predictions need to be accurate to within a fractional bone mass loss of 1.0 if the average loss per year is taken as 1%, 2.0 if taken as 2% or 3 if taken as 3%. The accuracy of the predicted hydroxylapatite densities is presented in these terms in the following sections.

4.4.2 Trabecular core

Spectra were recorded, and density predictions made for each of the 9 test phantoms for each scanning time. Figure 4.10 shows the accuracy in terms of FBML for different scanning times. The points plotted are the mean accuracy for the 9 predictions made, with error bars showing ± 2 standard deviations of the mean i.e. it
can be assumed with a 95% confidence level that the accuracy is within the error bar limits.

Figure 4.11 shows an estimation of the precision of the predicted density (as described in section 4.3.2). The phantom used for this estimation was the 20% bone mass loss phantom with hydroxylapatite density of 0.4777 g cm\(^{-3}\) which is approximately mid range of the test phantoms. The mean and standard deviation of the 10 predictions for a given scanning time were calculated and the precision represented as 2 standard deviations expressed as a percentage of the mean.

![Figure 4.11: Estimation of the precision of the predicted density.](image)

*Figure 4.11: Estimation of the precision of the predicted density.*

From these figures a minimum scanning time can be estimated which gives the required accuracy and precision. For an accuracy with FBML being 1.0 or less it would seem to be necessary to have a minimum scanning time of at least 20 seconds whereas if a FBML of 2.0 were acceptable then a minimum scanning time of 5 seconds may be acceptable. Figure 4.12 shows a scatter plot of the actual loss of peak mass against predicted loss for data obtained from a scanning time of 20 seconds (not all 9 phantoms are shown). The error bars show the estimated precision for the scanning time. Figure 4.13 shows a similar plot for a 5 second scan. It can be seen from the graphs that for an accuracy of FBML=1 then a scanning time of 20 seconds or more is needed, and for a FBML of 2, a scanning time of between 5 and 10 seconds would be necessary.
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Simulation of In-Vivo Measurements

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![Graph 1](image1.png)

- Nominal density of phantom = 0.4777 gcm\(^{-3}\)
- 1% loss of peak mass density
- 2% loss of peak mass density

**Figure 4.11**: Estimated precision of predictions for each scanning time.

![Graph 2](image2.png)

**Figure 4.12**: Scatter plot of actual and predicted loss for a scanning time of 20 seconds for the 5 test phantoms representing 3, 5, 7, 9, and 12% loss of peak mass.

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*page 110*
4.4.3 Calcaneus

The calcaneus data was analysed in a similar way to that of the trabecular core data for the three models available. Figure 4.14 shows the average accuracy as a function of scanning time and it can be seen that using the full four variable model the accuracy is outside the least stringent requirement of less than 2% FBML. If a fixed tissue thickness of 10 mm is assumed and the three variable model used, a scanning time between 20 and 50 seconds would be acceptable for a FBML=2. However, the precision estimates (see figure 4.15) show that a scanning time of as much as 250 seconds still gives a precision outside an FBML of 2. If a further assumption is made, i.e. that the cortex around the calcaneus is very thin and does not vary significantly, then the two variable model can be used. The scanning time for an accuracy of FBML=2 is between 5 and 10 seconds whereas for the corresponding precision it increases to between 20 and 50 seconds.
Figure 4.14: Average accuracy of the 9 test phantoms for the calcaneus using the three variable model.
4.4.3.1 Grouped data

A method of reducing the number of variables in the spectra was carried out to try to increase the accuracy and precision of the predicted data. The spectra that are used in the calibration set have 100 x-variables (channels) from which the Unscrambler has to extract suitable principle components which then have to be related to the appropriate number of y-variables to create a model. Information in the spectra relating to the y-variables may be spread over a number of channels e.g. the momentum transfer spread of the animal fat peak, which could be incorporated into fewer channels without losing information with the possibility of increasing the statistical significance of it by integration of the counts. The 100 x-variables were compressed into 20 by summing every consecutive 5 channels and remodelled with the appropriate y-variables for the three and two variable models.

Figure 4.16 shows the predicted average accuracy for scanning times up to 20 seconds for the grouped data and if this is compared to figure 4.14 it can be seen that there is no significant difference in the accuracy. However comparing figure 4.17 with figure 4.15 it can be seen that there is an improvement in the precision of approximately 12% in the three variable model and approximately 3% in the two variable model. Figures 4.18 and 4.19 show the scatter plots of actual and predicted loss of peak bone mass for the scanning time of 20 seconds using the grouped data for the three and two variable models.

From the data presented it would seem that the minimum scanning time for measurements to be made on the calcaneus would be between 10 and 20 seconds using the two variable model, and between 20 and 50 seconds if the fixed cortical thickness assumption could not be made and a FBML of 2.0 was acceptable.
Figure 4.15: Estimated precision of predictions for each scanning time for the calcaneus.
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Figure 4.16: Average accuracy for the 9 test phantoms for 4 scanning times using grouped data.

Figure 4.17: Estimated precision for the 4 scanning times using grouped data (the top graph is for the three variable model and the lower graph is the two variable model).
Scanning Time 20 seconds
Three variable model
Grouped data

Figure 4.18: Scatter plot of actual and predicted loss for a scanning time of 20 seconds for 5 test phantoms using the three variable model and grouped data.

Scanning Time 20 seconds
Two Variable Model
Grouped data

Figure 4.19: Similar graph as 4.18 but using the two variable model.
4.4.4 Radius

Figure 4.20: Average accuracy for a range of scanning times using the four variable model.
The range of measurements that represent the radius are soft tissue thicknesses of 10, 20 and 30 mm with each one having cortical thicknesses of 0.5, 1.0 and 1.5 mm. Figure 4.20 shows the average accuracy as a function of scanning time for this range using the four variable model. It can be seen that to achieve sufficient accuracy, scanning times in excess of 250 seconds will be necessary. Figure 4.21 shows the same plot for the three variable model with a constant tissue thickness of 20 mm. In general the thicker the cortex is the poorer the accuracy of the prediction for a given scanning time and it would appear that a minimum is of the order 250 seconds. Figure 4.22 shows the estimated precision and shows scanning times of up to 750 seconds necessary. To improve the precision a grouped data three variable model was made and figure 4.23 is the scatter plot of actual loss of peak mass against predicted for a scanning time of 250 seconds, which would be the minimum for the set criterion.

![Graph showing average accuracy as a function of scanning time for three variable model.](image)

*Figure 4.21: Average accuracy for scanning times using the three variable model.*
Three Variable Model

![Graph showing predicted HA density over Scanning Time](image)

**Figure 4.22**: Estimated precision for scanning times up to 750 seconds using the three variable model.

![Graph showing scatter plot of actual and predicted loss](image)

**Figure 4.23**: Scatter plot of actual and predicted loss for a 250 second scanning time using grouped data in the three variable model.
4.4.5 Femur

The dimensions of the soft tissue thicknesses do not cover the range expected in an average femur but for the sake of completeness figure 4.24 shows the results of the three variable model for the average accuracy of the scanning times for the maximum thickness of soft tissue available. To obtain the required accuracy a scanning time in excess of 750 seconds would be needed and would become increasingly larger as the soft tissue thickness increased.

![Figure 4.24: Average accuracy of test phantoms for scanning times from 50 seconds to 750 seconds using the three variable model.](image)

**Figure 4.24**: Average accuracy of test phantoms for scanning times from 50 seconds to 750 seconds using the three variable model.

4.5 Cortical thinning

The spectra measured on the EDXRD contain information regarding the dimension of the cortical thickness i.e. a particular spectrum will undergo a certain amount of beam hardening depending on the amount of cortex it has to pass through. This of course is also true of soft tissue but to a lesser extent for a given thickness e.g. the linear attenuation coefficients of soft tissue and bone at 30 keV have the ratio of approximately 1:12. In the four variable model dimensions of both soft tissue and cortex are modelled with both of these variables having the same effect on the
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spectrum i.e. beam hardening which may cause the calibration procedure problems because for a given amount of beam hardening the causes need to be distinguished as it is the spectral variation in beam hardening that is important. In the three variable model this problem does not occur as the soft tissue thickness is assumed to be constant so any beam hardening can be attributed to variations in cortical thickness.

4.5.1 Results

Cortical thinning was examined over the region representing the radius site and figure 4.25 shows the predicted thickness of dural using the four variable model for soft tissue thicknesses of 10 and 30 mm. For each scanning time the dural thicknesses from all nine test phantoms was averaged which was plotted with error bars of ±2 standard deviations. The predictions were made for 0.5 and 1.5 mm dural thickness and if it is assumed 30 mm thickness of soft tissue is present, a 0.25 mm accuracy could be attained if a scanning time in excess of 250 seconds was used. Figure 4.26 shows a similar plot for the three variable model with predictions made for the three dural thicknesses. The 0.5 mm predictions seem consistently high by approximately 0.1 mm (the error in the actual thickness of dural is estimated to be ±0.05 mm), and the 1.0 mm predictions consistently 0.15 mm low. From inspection of the figure it can be seen that a 50 seconds scanning time should be sufficient to be able to predict with an accuracy of 0.25 mm. Figure 4.27 shows the predicted thickness for a scanning time of 50 seconds for each of the test phantoms up to a 12% peak loss, with error bars showing the estimated precision and figure 4.28 is the same plot for 250 seconds. The precision for 50 second predictions is approximately ±0.1 mm and for 250 seconds this improves to approximately ±0.05 mm.

4.6 Measurements on excised femoral heads

The work in this chapter has described a calibration model and predictions made using that model. All of the measurements have been made on the phantoms described. In a clinical situation, it is probable that the calibration model would be made from a phantom such as the one described in this chapter, and the clinical measurements
obtained from patients would have to be based on such a calibration model. To assess the suitability of using such a model for a clinical situation, EDXRD measurements were made on recently excised femoral heads and predictions made of the bone mineral density.

![Four Variable Model Diagram]

Figure 4.25: Predicted thickness of dural using the four variable model for scanning times between 10 and 250 seconds. (\(X\) is nominal 0.5 mm thickness and \(\bullet\) is nominal 1.5 mm thickness).
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Figure 4.26: Predicted thickness of dural using the three variable model for scanning times between 5 and 250 seconds. (• is nominal 0.5 mm thickness and • is nominal 1.0 mm thickness and ■ nominal 1.5 mm thickness).

Figure 4.27: Predicted thickness of dural for individual test phantoms for a scanning time of 50 seconds using the three variable model. (• is nominal 0.5 mm thickness and • is nominal 1.0 mm thickness and ■ nominal 1.5 mm thickness)
4.6.1 Method

EDXRD spectra were recorded from 16 recently excised femoral heads obtained from total hip replacement operations. The bones were collected by Alex Melia of the medical physics department, UCL, as part of a study investigating the use of Compton Scatter Densitometry (CSD) as a bone density measuring technique. The bones were stored in a deep freeze within hours of removal from the patient. Before the EDXRD measurements were made the bones were allowed to defrost over night, and were then placed in the same position as the phantom with regard to the irradiation geometry (see figure 4.7). The neck of the femur could not be measured as the bone had been cut very close to the base of the head. Measurements were made on the head of the femur such that the measurement volume was in the centre of the head. The experimental set up was otherwise the same as that of the phantom measurements with 5 cm of soft tissue equivalent material placed in front of the excised head. The scanning procedure that was employed in measuring the phantoms was not used for measurements on the femoral heads. This was because the heads did not fit onto the jig used to hold the
phantoms on the scanner so the heads had to be held stationary using a retort clamp, also the measurement volume of the QCT measurements to which the predictions were to be compared was cylindrical in shape, (see next section). Each of the femoral heads was measured for a live time of 750 seconds.

Figure 4.29 shows a spectrum from one of the femoral heads and compares it to a spectrum from a phantom that makes up part of the calibration set. It can be seen that the spectra are similar, and differences are due to the fact that the bone mineral in the excised heads does not consist of purely hydroxylapatite, and the marrow is not identical to animal fat.

![Figure 4.29: A comparison of the spectra recorded from the bone phantom and an excised femoral head.](image)

The data recorded from the 16 femoral heads was read into the Unscramber. The model used consisted of 40 objects i.e. the phantom spectra recorded using 5 cm of soft tissue equivalent material and each of the four dural ring dimensions i.e. this is a three variable model. Predictions were made of the bone mineral density (hydroxylapatite density) of the femoral heads. An estimation of the precision of the predictions was made by recording 10 spectra for one of the femoral heads and obtaining 10 predictions. The mean and standard deviation were calculated with the
precision expressed as 2 standard deviations of the mean which was estimated to be approximately 10%.

4.6.2 Comparison of predicted bone mineral density with QCT data

The trabecular bone mineral density of the excised femoral heads was estimated using QCT measurements. This work was carried out by Alex Melia, Medical Physics Department, UCL. The CT number obtained for the femoral heads was for a cylindrical volume located in the centre of the head as shown in figure 4.30. It can be seen that the measurement volumes of the EDXRD and QCT differ which may lead to inaccuracies if the trabecular structure is not of uniform density throughout the femoral head. A QCT number for each of the heads has an estimated error of approximately 1%, found by measurements on a homogenous calibration phantom (Melia 1996).

![Figure 4.30: The measurement volume in the femoral heads for the QCT data (Melia 1996)](image)

4.6.3 Results

Figure 4.31 shows a scatter plot of the CT number against the predicted bone mineral density. The error bars are for each method as described above. The line is the linear
regression of the data. The calculated correlation coefficient is 0.95 which is significant at the 0.1% level.

![Graph showing correlation between CT number and bone mineral density](image)

*Figure 4.31: Scatter plot of CT number and predicted bone mineral density for the excised femoral heads.*

There are some problems with these predictions using the model i.e. the site modelled is the femoral neck which tends to have thicker dimensions of cortical bone than the femoral head, and is smaller in diameter than the neck. As already discussed the measurement volume differs between the two measuring techniques. Despite these problems it can be seen from figure 4.31 that the bone mineral density of the excised femoral heads as predicted using the model made from the phantoms, correlates well with the density represented by CT number. These results show that it would be possible to make predictions on a clinical site using a model made from phantom measurements. Improvements to the phantom to achieve better results are discussed in chapter six.
4.7 Discussion

The results presented in this chapter show that energy dispersive diffraction measurements can be used to detect small changes in hydroxylapatite content of the bone phantoms. Measurements of the trabecular core only show a predicted accuracy in terms of fractional bone mass loss (FBML) of less than 1, for scanning times as low as 20 seconds and are approximately equal to 1 for scanning times of 5 and 10 seconds. Even for a scanning time of 2 seconds the accuracy is less than a fractional bone mass loss of 2.

In the in-vivo environment problems arise because of the attenuation caused by surrounding material, which results in longer scanning times becoming necessary to obtain the required accuracy and precision.

The calcaneus is the simplest clinical site to work on, however when trying to make predictions from the full, comprehensive set of data i.e. the four variable model, the accuracy and precision is poor for the shorter scanning times, and would need to be in excess of 250 seconds for an accuracy of FBML to be less than 1. However, a fixed soft tissue thickness could easily be achieved for this site and the variation of the cortical thickness is small which may enable a three or two variable model to be used which would give an operating scanning time of approximately 20 seconds.

The radius as a clinical site is more complex in that although a constant soft tissue thickness could easily be achieved, the variation in cortical thickness cannot be ignored meaning the minimum number of variables to be used in the model would be three. Using such a model an operating scanning time of approximately 250 seconds would be required for an accuracy and precision to fall within a FBML of less than 2. The cortical thickness predictions for this scanning time using the three variable model were accurate to within approximately ±0.05 mm.

For the femur, scanning times greater than 750 seconds (which was the maximum scanning times used on the test objects) would be necessary.

The predictions for minimum scanning times made above are made assuming the patient can be subjected to radiation for those times. This may not be the case and an estimation of the radiation dose to the patient is discussed in the following chapter.
In this chapter a description is given of the method carried out to obtain an estimated dose for the general measurements illustrated in chapter four. Precise dose measurements for each of the possible clinical sites was not attempted because the phantom designed for the measurements was a general one which could represent several possible sites. Instead, a dose estimate was made using one set of parameters to establish if the order of magnitude was such that it would render the procedure unacceptable or if it fell within a range comparable with other diagnostic procedures.

5.1 Method of measuring absorbed dose.

In chapter four, figure 4.3 shows the construction of the phantom used to make measurements of trabecular bone mineral density using the energy dispersive diffractometer. To obtain an estimate of dose typical of the measurements taken, a 1.0 mm dural ring was chosen and 20 mm of the tissue equivalent material used. Three sites were chosen for the measurement of absorbed dose, the skin entrance dose, the dose at the cortical surface and the dose in the trabecular core.

The technique used to measure the dose was thermoluminescent dosimetry (TLD). The TLD material used in this study was lithium fluoride (LiF) which has an effective atomic number of 8.31 which is a value close to tissue. The advantage of TLDs is that they can be manufactured in small chips or cylinders etc that can be located useful places in a phantom e.g. the trabecular core and cortical bone surface.

Figure 4.7 in chapter four shows how the phantom was scanned during a measurement and should be compared to figure 5.1 which shows how the TLDs were positioned in
the scanning area and also shows the location of the TLDs for each of the sites at which the dose was being measured. The dose measured at each site was carried out independently for an irradiation time of 900 seconds so that an absorbed dose per second could be established and hence the absorbed dose for a given scanning time could be calculated. The readouts for each of the six TLDs at a given site were averaged to obtain the dose at that site.

Some modifications to the trabecular core phantom needed to be carried out for the purposes of measuring dose using TLDs. Placing the TLD chips in the animal fat of the core was not a practical consideration as this would cause surface contamination of the chip which may produce errors in the readout of light and possibly damage the chip in the annealing process used for the devices reuse. To overcome this difficulty, a different trabecular core was used made from an epoxy resin mixture (White et al 1977) which contained 75% Araldite MY 750 and 25% P.V.C. by weight.

An advantage of using the epoxy resin trabecular core is that it is easily machined. The core cylinder was cut into two and cavities for the chips machined with a locating pin such that on reassembling with the dural ring in place, the chips were in line perpendicular to the incident ribbon beam of radiation (see figure 5.1).

The diffractometer used to make the measurements has a filtration of 1 mm beryllium and 1 mm aluminium. Dose measurements made on a clinical system should have a minimum of 2.5 mm of aluminium (ICRP publication 33) and consequently two sets of dose measurements were taken, one with the existing filtration and one with an extra 1.5 mm aluminium added. The measurements made with the existing filtration will give the energy absorbed in the phantom to obtain the results quoted in chapter four for a given scanning time. To relate the dose estimates with added filtration to the scanning times in chapter four a correction factor will need to be applied because adding extra filtration will mean increased scanning times become necessary to obtain the required accuracy. This correction procedure is explained in section 5.2.1.
Figure 5.1: Positioning of the TLDs in the phantom with an epoxy resin substitute for the trabecular core.
5.2 Results

Table 5.1 shows the absorbed dose, $D$, at the three sites for both thicknesses of aluminium filtration, and table 5.2 shows the effective dose, $E$. The figures quoted are dose per second of irradiation and have an estimated error of ± 5%. The total effective dose given in table 5.2 is simply the sum of the effective doses for each site which is acceptable for appendicular sites e.g. the calcaneus and forearm where the radiation absorbed can be assumed to be localised. However for a site such as the femur, the effects of the scattered radiation on organs in close proximity to the site would need to be considered.

<table>
<thead>
<tr>
<th>Skin entrance dose</th>
<th>Absorbed dose $D$ per sec. mGy (±5%)</th>
<th>1 mm Al</th>
<th>2.5 mm Al</th>
</tr>
</thead>
<tbody>
<tr>
<td>Skin entrance dose</td>
<td>0.86</td>
<td>0.51</td>
<td></td>
</tr>
<tr>
<td>Cortical surface</td>
<td>0.40</td>
<td>0.20</td>
<td></td>
</tr>
<tr>
<td>Trabecular core</td>
<td>0.10</td>
<td>0.08</td>
<td></td>
</tr>
</tbody>
</table>

Table 5.1: The absorbed dose per second for the three measurement sites for 1.0 mm and 2.5 mm aluminium filtration.

<table>
<thead>
<tr>
<th>Weighting factor (w)</th>
<th>Effective dose $E$ per sec. μSv. (±5%)</th>
<th>1 mm Al</th>
<th>2.5 mm Al</th>
</tr>
</thead>
<tbody>
<tr>
<td>Skin entrance dose</td>
<td>0.01</td>
<td>8.63</td>
<td>5.08</td>
</tr>
<tr>
<td>Cortical surface</td>
<td>0.01</td>
<td>3.97</td>
<td>2.00</td>
</tr>
<tr>
<td>Trabecular core</td>
<td>0.05</td>
<td>5.17</td>
<td>4.18</td>
</tr>
<tr>
<td>Total effective dose</td>
<td></td>
<td>17.8</td>
<td>11.26</td>
</tr>
</tbody>
</table>

Table 5.2: Effective dose per second for both 1.0 mm and 2.5 mm aluminium filtration.
5.2.1 Correction factor for added filtration

It is possible from the tables above to calculate a dose estimate for a given scanning time, e.g. it was concluded in the previous chapter that a minimum scanning time for a measurement on the calcaneus would be approximately 20 seconds. From table 5.1 the skin dose for that time can be calculated i.e. 0.86 x 20 = 17.27 mGy. However a scanning time of 20 seconds with an extra 1.5 mm aluminium would not give the same accuracy of prediction as with 1.0 mm aluminium because in effect the total intensity of the recorded spectrum would be decreased due to attenuation, and hence to obtain the same accuracy an increased scanning time would be necessary. An estimate of how long this increase in time would be is necessary so that the dose figures for the 2.5 mm filtration can be used. A calibration spectrum obtained for the phantom with 1.0 mm dural ring and 20 mm soft tissue was corrected for the attenuation effects of 1.5 mm aluminium channel by channel. Figure 5.2 shows the effect on the spectrum. There is a reduction in the total integrated number of counts of approximately 20%. It is this percentage that is used as a correction factor in the scanning times, for example the 20 second scanning time for the calcaneus quoted above would become 24 seconds with the added filtration in order to obtain the same accuracy, and the corresponding skin entrance dose would be 0.51 x 24 = 12.2 mGy.

![Figure 5.2: The attenuation of a spectrum caused by adding an extra 1.5 mm aluminium to make a total of 2.5 mm aluminium.](image)

Figure 5.2 : The attenuation of a spectrum caused by adding an extra 1.5 mm aluminium to make a total of 2.5 mm aluminium.
Table 5.3 shows the estimated skin doses and total effective dose for a sample of times used in the study. The 2.5 mm filtration doses have been estimated by adding 20% to the scanning times.

<table>
<thead>
<tr>
<th>Scanning times [seconds]</th>
<th>1.0 mm Aluminium filtration</th>
<th>2.5 mm Aluminium filtration</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>5</td>
<td>10</td>
</tr>
<tr>
<td>Skin entrance dose mGy</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>4.3</td>
<td>8.6</td>
</tr>
<tr>
<td>Total effective dose μSv</td>
<td>88.9</td>
<td>177.8</td>
</tr>
</tbody>
</table>

Table 5.3: Skin entrance dose and total effective dose for a range of scanning times. The figures for the 2.5 mm filtration have been estimated by increasing the scanning times by 20%. (All doses quoted are estimated to be accurate to within ±5%).

5.3 Discussion

It can be seen from the doses shown in table 5.3 that the radiation dose to the patient is high using EDXRD. The skin entrance dose is perhaps the easiest to compare with other techniques, e.g. for a QDR-1000 DEXA machine, the skin dose for a vertebra
Chapter Five

Estimation of Radiation Dose

scan is typically 140 μGy and a skin dose using QCT for a vertebral scan is approximately 10 mGy (Kusama et al, 1995). Using EDXRD on the calcaneus a minimum 20 seconds scanning time is required giving a skin entrance dose of approximately 17 mGy, and even allowing for the extra 1.5 mm aluminium filtration will still produce an absorbed skin entrance dose of approximately 12 mGy. For a scan of the radius a minimum scan time was of the order 250 seconds which would give an absorbed skin entrance dose of approximately 152 mGy using 2.5 mm aluminium.

Table 5.4 gives an indication of the effective doses for various radiographic procedures, the data is taken from Huda and Morin (1996) and Kusama et al (1995).

<table>
<thead>
<tr>
<th>Radiographic procedure</th>
<th>Effective Dose [μSv]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chest (PA and lateral)</td>
<td>50-100</td>
</tr>
<tr>
<td>Skull</td>
<td>100-200</td>
</tr>
<tr>
<td>Thoracic spine</td>
<td>500-1100</td>
</tr>
<tr>
<td>Pelvis</td>
<td>700-1400</td>
</tr>
<tr>
<td>Abdomen</td>
<td>600-1700</td>
</tr>
<tr>
<td>Lumbar spine</td>
<td>1300-2700</td>
</tr>
<tr>
<td>Head CT scan</td>
<td>2000-4000</td>
</tr>
<tr>
<td>Body CT scan</td>
<td>2000-10000</td>
</tr>
<tr>
<td>DEXA vertebra</td>
<td>5.8</td>
</tr>
<tr>
<td>QCT vertebra</td>
<td>110</td>
</tr>
</tbody>
</table>

Table 5.4: Typical effective doses for types of radiographic procedures.

Using EDXRD with 2.5 mm aluminium for 20 seconds the estimated effective dose is approximately 270 μSv and for 250 seconds is 3377 μSv. For a procedure that would be used as a routine screening method for determining bone mass loss these figures are unacceptably high, even for a one off measurement the dose is unacceptable.

The following chapter will suggest ways in which the system may be improved such that the scanning time and dose would be reduced.
6

Discussion and Further Work

6.1 General considerations

The work presented in this study has shown that, in principle, energy dispersive x-ray diffraction (EDXRD) is a technique that is capable of determining small changes in the quantity of a material that is present in an object under investigation. However, applying this principle to many practical applications is problematic due to variables that may mask the quantity we are trying to measure, and over which we have little or no control. This is particularly apparent in the simulated in-vivo bone mineral density measurements made where there are physical parameters that degrade the inherent capabilities of the technique i.e. attenuation due to surrounding material. The time of the measurement plays a crucial role in the in-vivo situation with respect to the radiation dose administered to a patient. Despite these problems the results presented have shown that a potential exists for the technique if the problematic variables are handled with multivariate analysis, and in this chapter refinements are suggested to improve on the results obtained in this study.

6.2 Dry excised bone samples

The measurements made on the archaeological bone samples show that EDXRD is a useful tool in determining the trabecular bone mass of femurs and vertebrae particularly when a non invasive method is required. The only other non invasive methods of measuring trabecular bone density independently from cortical bone are Quantitative Computerised Tomography (QCT) and Compton scatter densitometry. Further work has been proposed in the area of investigating archaeological bone in two directions.
6.2.1 Densitometry

The first area of proposed work is to improve on the trabecular bone mineral density measurements undertaken in this study. The primary bones of interest to the archaeologist are the femur, radius and ulna, the vertebrae and the iliac crest (Mays 1996). It is proposed that standard geometrical configurations of the system could be established for each of the bone types such that a measurement volume fell within the trabecular region of the bone. In excised bone the amount of radiation applied is not a restriction so the geometry could be finely tuned to obtain the maximum sensitivity concerning changes in the mineral density. Calibration models for each of the bone types could be made, either by the method described in chapter three, or by calibration with QCT measurements on the calibration samples. The calibration model could be univariate or multivariate i.e. the corrections for attenuation could be carried out on the measured spectra before a calibration model is made as carried out in this study, or variations in cortical thickness and physical size of the bone could be modelled using multivariate calibration techniques. Either way, once a calibration model has been established, predictions could be made on further measurements in a relatively straightforward manner. It is proposed that the bones used in the study come from a location that has good documentation of the individuals i.e. the age and sex are known accurately. This information would enable relationships between measured bone mass and age to be determined and also establish if the relative bone densities of different bone samples for an individual had any correlation e.g. does bone loss at certain appendicular sites correlate to bone loss in sites such as the femur and vertebra, and if so what are the relative rates of loss? This information may prove advantageous in determining the usefulness of making measurements in certain sites in a clinical in-vivo environment.

6.2.2 Determination of mineral type

The second area in which further work is proposed is to extend the technique to try to quantify the types of mineral in a given sample. The spectra obtained from the archaeological bones in this study indicate that different amounts of calcium carbonate present in a sample can be detected. Diagenetic change can be a problem to the archaeologist when trying to measure bone density using standard methods because there is no way of determining the types of mineral present in a bone sample non invasively. It is proposed that the common minerals formed due to diagenesis be
established e.g. calcium carbonate and brushite, and the diffraction profiles established either by direct measurement or by using the computer model described in chapter two. The geometry of the system would have to be optimised to obtain the resolution necessary to differentiate between the different minerals, possibly using pencil beam geometry rather than the ribbon beam used in this study. If identification of the different minerals is possible then a further step is proposed to quantify the amount of each mineral present. One way this may be done is to use phantoms made up of varying amounts of the different minerals and use multivariate calibration methods to produce models.

6.3 In-vivo measurements

As stated in chapter five, the results obtained in this study that have the required accuracy and precision, give a radiation dose to the patient that is unacceptably high particularly if the technique is going to be considered as a regular screening procedure. To reduce the radiation dose, the scanning times need to be reduced while keeping the sensitivity, accuracy and precision of the system.

The work presented has shown that the measuring technique possesses good inherent accuracy, despite the influences of variables that alter the characteristics of the diffraction profile that contain the information being looked for. However, this inherent accuracy is only present providing the scanning time is not restricted. The calibration data used in the Unscrambler was collected for a total integrated number of counts in the spectrum of 750 000, and the model formed using this data. While creating the calibration model, the Unscrambler uses a cross validation procedure which tests the accuracy of the model by predicting the quantities required from the spectra by using subsets of the calibration data (see section 1.6.2). This prediction data is saved and can be accessed. Figure 6.1 shows a scatter plot of the actual and predicted density of hydroxylapatite in the calibration phantoms for the four variable model. The error bars are the root mean square error of prediction estimated by the Unscrambler. This plot shows that high accuracy predictions are possible even using the four variable model provided there is no restriction in the counting time. The average accuracy of the ten predictions is approximately 98%. The results shown in chapter four, show that the accuracy was poor using the four variable model at reduced scanning times.
6.3.1 Targeting clinical sites

Instead of a wide ranging set of variables being measured and modelled in a general phantom as used in this study, it is suggested that making phantoms that represent a chosen clinical site would produce an improvement in the results obtained. A more specific calibration set of data could be made with a range of mixtures that have a smaller increment of bone mass loss between measurements, and more cortical thicknesses could be modelled over a given range. If a four variable model was to be used because the soft tissue thickness could not be standardised for a clinical site, then more soft tissue dimensions could be modelled within the range applicable to the site.

6.3.2 Improvements to the phantoms

As pointed out in chapter four, the phantom materials are not ideal to simulate their human equivalents, and improvements could be made which may benefit the predicting...
ability of the system. The powder used in the trabecular core is hydroxylapatite, which although the main mineral present in bone, does not constitute the entire make up of bone and the density of hydroxylapatite alone is greater than bone tissue. This will lead to an increase in the total attenuation of the signal compared to that of bone tissue which means longer scanning times are necessary for a given intensity. It may be possible to construct better trabecular cores by making a mixture of minerals that more closely represent the bone or using powdered dry bone, ideally human bone or if not animal bone. Instead of using dural rings to simulate the cortex, it could be made from a material that has attenuation properties closer to those of cortical bone. One possibility is to use an epoxy resin mixture similar to that used in the dosimetry measurements. The problem with the dural is that it attenuates the beam more than cortical bone would, which has the effect of reducing the signal collected from the measurement volume within the trabecular region. A more suitable material would increase the signal for a given scanning time, although it should be noted that the absorbed dose in the trabecular core would be increased.

6.3.3 Detector considerations

The high purity Ge detector used in the study can be assumed to have almost 100% efficiency at the energies used. However, a way of improving the efficiency of collecting the scattered photons for a given scattering time would be to use the scattering angle either side of the incident beam, such that two spectra were collected. Figure 6.2 shows a schematic diagram of such an arrangement. The two collected spectra would be summed and used for the prediction of the required quantities.

6.3.4 Improving the calibration model

There are several ways the calibration model could be improved. It has already been mentioned that each clinical site would be targeted independently, and the calibration data for a given site could be improved in the following ways.

1) The counting statistics of the calibration data could be improved by setting the total integrated number of counts in the spectrum to a higher value. The calibration data set would be made on a sample where the dose considerations were not applicable so the time of the measurement is not a problem. Improvements may also be made by using
repeated measurements in the calibration model i.e. instead of using one recorded spectrum for a given set of parameters, a number of repeated measurements could be used which would help smooth out noise in the data.

2) Take a wider range of calibration data, i.e. ensure that data from which predictions are to be made, fall well inside the range of the calibration data. This would mean modelling a trabecular bone mineral content greater than the peak bone mass, down to a loss greater than would be of interest in prediction.

3) A technique could be used which involves the use of multiple angle measurements. The diffraction profiles at several angles could be recorded at the same time using an arrangement as shown in figure 6.3. If, for example three such angles were used, the resulting profiles could be joined end to end as indicated in figure 6.4. The three spectra shown were derived using the computer model (see chapter 2) for 3, 5, and 7 degrees. The geometry modelled is similar to that used in the phantom measurements and is for a 50% hydroxylapatite 50% polyethylene by weight mixture. The spectra show different characteristics with respect to the peak intensities and will alter with respect to changes in the variables being modelled in different ways which may give the Unscrambler more principle components with which to work. This may be particularly useful when trying to model a large number of variables e.g. the four variable model used in this study. Work is currently being undertaken to investigate the use of multiple detectors in EDXRD work (Malden 1996).
Figure 6.3: Schematic arrangement to make multiple angle measurements.

Figure 6.4: Computer simulation of diffraction profiles taken at 3, 5 and 7 degrees.
6.4 Conclusion

From the work carried out in this study it can be said that the EDXRD technique has the potential to be used in a clinical environment. This preliminary work has been limited to simulating appendicular sites and the technique would need to be extended to some of the more commonly used clinical sites i.e. the femur and spine. It is hoped that by implementing some or all of the above modifications, the technique will become a useful and viable proposition for in-vivo clinical measurement of trabecular bone mineral density and cortical thickness. Being able to measure these two quantities in isolation from each other would be an advantage over current methods in common use such as DEXA which give an overall bone density value.

For the clinical system to operate, an accurate calibration set of data for a given clinical site would be needed from which predictions of patient measurements could be made. This calibration set could be made from a set of phantoms similar to those described in this work, in which case the measurement time for the calibration data set is not limited by dose restrictions. The measurements made on the excised femoral heads are the closest to a clinical system that was attempted in this work, and it was shown that predictions on clinical material could be made from a phantom. By incorporating some of the improvements discussed above the results may be improved on. Assuming the dose of the measurement could be reduced to an acceptable level by implementing the suggestions above, the calibration set could be made from measurements on patients. However to do this the calibration set would have to be modelled using the trabecular bone density, cortical thickness and soft tissue thickness obtained from QCT measurements. The next step in progressing with this work is to move toward a more clinical environment and to ensure that the radiation dose is reduced while maintaining the required accuracy and precision on sites that are clinically relevant.
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