A clinical and economic evaluation of contact laser surgery in the prostate

Stephen Richard Keoghane MBBS FRCS

A thesis submitted to The University of London for the degree of Master of Surgery

Department of Urology, the Churchill Hospital Oxford
Health Services Research Unit, University of Oxford
January 1993 - January 1995
Abstract

Contact laser prostatectomy is an exciting new surgical technique, that in theory, can produce clinical results comparable to those obtainable with standard transurethral resection. This thesis has rigorously evaluated this technology in the context of a pragmatic, double blind randomised controlled clinical trial looking at traditional physiological outcome parameters, more subjective measures, as well as the increasingly important economic side of new technology.

One hundred and forty eight patients with lower urinary tract symptoms attributable to benign prostatic enlargement were randomised to either transurethral resection (TURP) or contact laser prostatectomy; one year data were available on 126.

Symptom score was the defined primary outcome measure, which statistically favoured the TURP arm throughout. However, when considering the clinically more important absolute change in symptoms, there was no difference between the two treatment arms of the study.

Rigorous economic analysis has shown TURP to be less expensive, unless length of hospital stay following laser surgery is reduced to one night.

Little change in quality of life as measured by the Short Form 36 generic health questionnaire between baseline and one year.

In conclusion, contact laser vaporisation of the prostate can produce similar results to TURP in terms of symptomatic improvement, with less primary and reactionary haemorrhage but in this study, at a cost of a higher rate of failing trial without catheter and an increased re-operation rate. Interestingly, prostatectomy by whichever method has led to little improvement in general health status one year following surgery.
Statement of the problem

With an increasingly ageing population, benign prostatic enlargement as a cause of lower urinary tract symptoms is a major point of clinical and economic interest.

In recent years there has been enormous interest in the development of new methods to remove the prostate, but what is most worrying about this new influx of technology, is the delayed appearance or even absence of methodologically sound, prospective, randomised controlled trials.

Contact vaporisation laser prostatectomy is one such innovation. This study was designed to evaluate this new technique using traditional physiological outcome measures, more subjective measures such as quality of life, as well as the increasingly important parameter of economics.

Ethical approval for this study was granted from the Central Oxford Ethics Committee COREC number 93:183.
Contents

Chapter 1 - Introduction Benign Prostatic Hypertrophy - epidemiology, history and treatment.

1.1 History
1.2 Epidemiology
1.3 History of treatment
1.4 Surgical Alternatives in the treatment of BPH
   1.41 Transurethral balloon dilatation
   1.42 Transrectal and transurethral hyperthermia
   1.43 Transurethral incision of the prostate
   1.44 Transurethral needle ablation
   1.45 High intensity focused ultrasound
   1.46 Transurethral electrocautery vaporisation
1.5 History of laser
1.6 Long term studies and more recent work
1.7 Wavelengths other than Nd:YAG
1.8 Generic and disease specific questionnaires
1.9 Principles of randomised controlled trials

Chapter 2 - Patients and Methods

2.1 Statistical Power
2.2 Operative procedure and data collection
2.3 Cardiac comormidity
2.4 Economic considerations
Chapter 3 - Results

3.1 Primary outcome measure

3.2 Secondary outcome measure

3.3 Complications

3.4 Quality of life data

3.5 Sexual function data

3.6 Economic data

3.7 Use of community services

3.8 Cardiac comorbidity

Chapter 4 - Conclusions

References

Appendices: Examples of trial questionnaires
            Consent form

Published papers on Nd:YAG laser surgery
Plates Figures and Tables

Plate 1 23.5 F cystoscope
Plate 2 Pictorial representation of contact laser prostatectomy
Plate 3 Haemocue photometer

Table 1 Exclusion criteria

Table 2a AUA symptom scores at baseline, one, three and 12 months
Table 2b AUA scores - medians and interquartile ranges
Table 2c Degree of change in the AUA symptom score between baseline and one and three months
Table 2d Degree of change in AUA symptom score between baseline and one year
Table 3 Peak urinary flow rates at baseline, three and 12 months
Table 4 Pre-and peri-operative data
Table 5 Haematological and biochemical data
Table 6 Irrigation fluid, length of catheterisation and length of stay
Table 7 Complications
Table 8 SF-36 data at baseline, one, three and 12 months
Table 9 Effect sizes in SF-36 data between baseline and one, three and 12 months
Table 9 Effect sizes for SF-36 values between baseline and one, three and 12 months
Table 10 Effect sizes for AUA symptom scores, bothersome scores and peak urinary flow rate
Table 11 Bothersome scores at baseline, one, three and 12 months in laser patients
Table 12 Bothersome scores at baseline, one, three and 12 months in TURP patients
Table 13 Response to the question: Over the past month have you been able to have an erection when sexually stimulated?
Table 14 Have you had difficulty maintaining an erection that has prevented sexual intercourse over the past month?

Table 15 Response to question: To what extent do you feel your sex life has been spoilt by your prostate problem?

Table 16 Mean costs per case, mean difference in costs per case and associated 95% confidence intervals for laser and TURP.

Table 17 Baseline data on cardiac monitored patients

Graph 1 Baseline, one, three and 12 month SF-36 data in the laser patients

Graph 2 Baseline, one, three and 12 month SF-36 data in the TURP patients

Graph 3 Effect size changes for various outcome measures between baseline and one month.

Graph 4a Effect size changes for various outcome measures between baseline and three months.

Graph 4b Effect size changes for various outcome measures between baseline and one year.

Graph 5 Mean difference in costs plotted against re-operation rates

Graph 6 Mean difference in costs plotted against varying laser consumable costs.

Graph 7 Mean difference in costs plotted against laser re-operation rates based on one night hospital stay.
Introduction
Benign Prostatic Hypertrophy - history, epidemiology and treatment.

1.1 History of Benign Prostatic Hypertrophy (BPH).

The condition of bladder neck obstruction has been known since ancient times; “retention of urine” being described by the Egyptians as early as 1550 BC.

Primitive urological surgery is also known to have been carried out by ancient Hindus as described in the work of Charaka and later in that of Susruta. Hessler in his translations described the use of instrumenta tubulata multiplictur adhibenda in the case of retention of urine with swelling of the abdomen.

Traditional Chinese medicine taught of retention occurring when “urine could not be expelled owing to lack of vapors or because of heating of the blood, which reddens the urine, or because of a fit of anger, a chill or an obstruction in the urethra.”

The term “prostate” is accredited to Herophilus of Alexandria in the 4th Century BC, who is said to have referred to the seminal vesicles as adenoieides prostatai and to the ampulla of the vas as kirsoides prostatai, referring to the position of these structures at the bladder neck. However Herophilus referred to the gland itself as “spongy tissue lying at the side of the bladder neck traversed by the ejaculatory ducts” and although Oribasius (325-403 AD) described an induration of the bladder neck, probably one of the earliest descriptions of an enlarged prostate, it was not until 1668 that Bartholin coined the term prostate for the gland.

The great war surgeon Ambrose Pare’ described the prostate as being distinct from the bladder neck, together with details of its shape, its relation to the ejaculatory ducts and its role in ejaculation. However, the first definite statement on the relationship of the enlarged prostate to bladder neck obstruction was made in 1649, when Jean Riolan
said "the neck of the bladder may be obstructed by a tumour of the prostate gland."

Nineteen years later, Reignier de Graaf made an accurate description of the gland’s anatomy, but the credit for understanding and demonstrating enlargement of the prostate goes to Morgagni (1682-1771). He made a distinction between abscess of the prostate and prostatic hyperplasia, and described "morbid excrescences" including a middle lobe the size of a grape, which he thought must be either a tumour or a growth of the prostate, although he favoured the latter.

In 1788 John Hunter noted the obstruction caused by lateral-lobe and middle lobe enlargement and their effect on the bladder musculature, as well as dilatation of the upper tracts, work years ahead of its time, but as often is the case, largely ignored. Everard Home in 1806 emphasised the importance of what he termed the middle lobe, in causing obstruction, although this work was largely plagiarised from Hunter’s unpublished manuscripts. Later, in 1834, Guthrie described obstructive changes at the bladder neck, which may be an early description of bladder neck stenosis.

Mercier, in 1841 then published his "Les Recherches sur les Maladies des Organes Urinaires et Genitaux considérés spécialement chez les Hommes Âgés." He was the first to use the term "hypertrophy" and he realised the role of vascular congestion in causing complications, also describing retention and overflow.

Following this publication, there was much debate between Mercier and Civiale; the former claiming that Civiale had plagiarised his work. However, it must be said that Civiale’s work was more thorough in its description of symptomatology, pathology and complications.

Despite this work, and that of Hunter, the idea of prostatic disease affecting the entire
urinary tract was still prevalent, and continued to hinder progress.

At the turn of the century, in 1902, Cuthbert Wallace was the first to demonstrate the presence of prostatic glandular tissue in the false capsule of the gland; findings confirmed by William Thompson in the same year. However, perhaps the two definitive texts on the subject of prostatic enlargement are those of Randall in 1931, and Rubin Flock’s work on the blood supply to the gland (1937), the name of Flock being all too familiar to all trainee Urologists!

**Aetiology.**

The realization of the surgical importance of prostatic hyperplasia was followed by a spate of theories concerning the aetiology. The wide diversity of ideas included inflammation due to gonorrhoea and non-specific prostatitis (Hunter 1786, Petit 1774) or chronic prostatitis resulting in scarring of the prostatic ducts (Ciechanowski 1901). The local effects of a generalised arteriosclerosis was considered the cause by Launois in 1885 while venous congestion of the prostate (Home 1818) is one of the oldest theories, with the thought that *strict celibacy and a life of excess exacerbated the condition*, reflecting the moral overtones of the time.

While Velpeau (1841) first considered the possibility of neoplasia within the prostate, John Hunter noticed the endocrine link to BPH, with his observation that hyperplasia of the prostate does not occur in castrates. Besides the rather indefinite hormonal factor, age is accepted as the chief agent in the development of prostatic enlargement, and in fact, little has been added since the statement of Sir Astley Cooper in 1831, that "the enlarged prostate is the consequence of age and not disease."
1.2 Epidemiology of Benign Prostatic Hyperplasia.

BPH has been termed one of the major health hazards of men in modern society (Denis 1989). The differences in precise definition of the condition make the available studies of incidence and prevalence hard to interpret, although it is nevertheless clear that it is a common condition, with significant economic implications.

Berry et al. studied the results of 1075 post-mortem examinations, relating the prevalence of BPH to age. This prevalence begins in the fourth decade, and approaches 90% by the ninth decade. Isaacs and Coffey then separated out the prevalence on the basis of histology, dividing the patients into those with macroscopic or microscopic evidence of disease. Their results revealed that the percentage of BPH recognised macroscopically is almost doubled when the prostate is examined microscopically.

The occurrence of clinical BPH in defined populations has been looked at in a number of studies, although the comparability of these reports is open to question, due to the differing approaches to the diagnosis of clinical BPH.

A study by Lytton et al. between 1958 and 1963 counted the number of prostatectomies performed in Connecticut area hospitals, and related these counts to the male population of the city. This data was used to estimate a cumulative incidence of prostatectomy for a man age 80 years of about 10%.

The Veterans Administration Normative Ageing Study (VANAS), is a cohort study of over 2000 initially healthy men enrolled in the Boston area of the United States from
1961 to 1970, and followed up prospectively. VANAS defined clinical BPH as a "physical finding of an enlarged or abnormally firm prostate, or by a history of symptoms if the symptoms cannot be attributable to another cause such as prostatitis or cancer of the prostate."

The incidence, based on a clinical diagnosis, ranged from 9.4 per 1000 cases for men in their forties, to 59.2 per 1000 cases for men in their seventies and eighties.

Arrighi et al published the Baltimore Longitudinal Study of Ageing in 1990, which began in 1958, and was similar in design to the VANAS study, except that patients leaving the study were replaced, maintaining the population of about 1300 men. An expected increase in prevalence with age was noted, ranging from over 50 per cent of men in their sixties, to over 80 per cent of men in their eighties. Furthermore the investigators found a high correlation between clinical BPH, although the precise definition of clinical BPH was not identified, and BPH as identified by previous post-mortem studies.

Diokono et al investigated a sample of men in the community aged 60 or over, in Michigan USA, and found that the presence of one of more symptoms of hesitancy, straining, poor stream, intermittency or use of a catheter was 35% in previously untreated men. They also noted that 23% of men with 'severe' symptoms at the initial survey were asymptomatic one year later.

Probably one of the best published reports on the age specific prevalence of BPH was produced by Garraway et al in 1991, which looked at 5500 men in Bridge of Allan, a community in central Scotland, aged between 40 and 79. Clinical BPH was defined as "a prostate weight > 20g, in the presence of symptoms of urinary dysfunction and/or a peak urinary flow rate < 15 ml/s, without evidence of prostate cancer."
Of the eligible men who participated in the initial survey, 86% of men with an elevated symptom score (11 or more on a scale of 0-48), a reduced peak flow rate, or who were unable to void at least 150ml, accepted an invitation for further urological evaluation.

Based on the clinical definition given, the prevalence of BPH ranged from about:

- 14% for men in their 40s
- 23% for men in their 50s
- 43% for men in their 60s
- 40% for men in their 70s.

Two years after the publication of his original report, Garraway extended his survey to take into account the effects of clinical BPH on everyday life in a second Scottish community. Using the same definition of clinical BPH, it was found that 51% of men with BPH, reported interference with at least one daily activity, and 25% of this group reported interference most of the time. These findings have stimulated an increased interest in patient-centred outcome following prostatectomy (Doll et al 1994, Emberton et al 1994, Thorpe et al 1994).

Chute et al (1993) have looked at an age-stratified random sample of men in the community aged 40-79 who were invited to complete a questionnaire and undertake uroflowmetry. The percentage of men with an “International Prostate Symptom score” of greater than 7, and therefore moderately symptomatic were:

- 12% for men in their 40’s
- 17% for men in their 50’s
- 23% for men in their 60’s
29% for men in their 70's

Bosch et al have produced similar data to that of Garraway, based on a community based sample of 502 men between 55 and 74 years of age. Overall, six and 24% of the men surveyed were severely and moderately symptomatic, however, 82% claimed to have no 'voiding complaints'
1.3 History of Treatment

The history of the treatment of bladder outflow obstruction dates as far back as early Persian literature, when Ibn Cherif talked about the insertion into the urethra of polished twigs of the plant "Tham teres."

Celsus, who lived in Rome at the beginning of the Christian era described the use of bronze catheters for the relief of retention, and effectively, this form of rigid catheterisation changed very little over the centuries.

A variety of unusual and interesting techniques were tried to counter prostatic disease, including ergot and strychnine (Stafford 1845), fresh bull’s prostate (Reinert 1895), intraprostatic injection of sclerosing agents (Iverson and Heine 1874), electrolysis (Tripier 1859) and x-ray therapy (Robarts 1902). Surgically, other than castration first described by Hunter as a potential treatment for the enlarged prostate, numerous procedures were tried on the urological organs, which more often than not, were barbaric in nature and usually ended in failure.

The first attempt at open division of the bladder neck was by Sir William Blizzard in 1806, and this was built upon by Guthrie who designed a sound with a concealed knife. Variations of this instrument then achieved some popularity over the next 40 years.

At the turn of the century, enucleative prostatectomy by the suprapubic route was introduced, first recorded at St. Bartholomew’s Hospital in 1884 (St Bartholomew’s Reports) and built upon by Proust and Gosset in 1901.

Freyer first described a series of routine transvesical prostatectomies in 1901 although
this method was improved by Harris, with the partial closing of the bladder neck.

Retropubic rather than transvesical prostatectomy is usually accredited to Terence Millin, although van Stockum had actually performed this some 37 years previously.

A somewhat barbaric form of transurethral instrumentation had been practised in the early 19th century and it was not until 1876 that major advances began to appear, when Enrico Bottini of Pavia designed a galvanocautery incisor. Bottini’s contemporaries; Fenwick (1895), Chetwood (1901) and Wishard (1925) all attempted to improve this instrument, but the results were unimpressive.

Freudenberg eventually managed to provide a more efficient cooling system and eventually a telescope was added.

Hugh Hampton Young then went on to develop a transurethral “cold punch”, or “prostatic excisor”, which at first, was a very simple device without any means of haemostasis. At the same time as the development of this technique, Beer described the use of very high frequency alternating current in cauterising “bladder warts” which led to the routine use of diathermy in prostate resection. However the actual techniques differed dramatically; Stevens in New York, preferred a series of ‘Bottini’ burns at the bladder neck, while Young’s approach involved cutting away tissue with the ‘punch’, followed by diathermy haemostasis.

Although as early as 1895, Fenwick had designed a ‘galvanic ecraseur’ which was a heated wire snare to cut through the median lobe, this particular technique was not a practical possibility until 1926 when Stern utilised the powerful new radio-frequency valve diathermy invented by Wappler. However, although this more powerful current cut well, it did not prevent haemorrhage.

It may be argued that Georges Luys of Paris first pioneered minimally invasive
prostate surgery in 1913, when he achieved massive coagulation of the prostate under local anaesthetic but the major advance came with Maximillian Stern’s invention of the resectoscope in 1926. McCarthy’s addition of the panendoscope and Walker’s bakelite sheath.

However, the mortality and morbidity associated with the opening phase of endoscopic surgery was high and at this time, the popularity of the technique was much lower in Europe.

By the 1930s, transurethral resection had become firmly established in the United States and now, constitutes more than a third of the major operations performed by Urologists. Mortality for the procedure has been reduced to less than one percent over the last thirty years, but the incidence of immediate post-operative morbidity has remained unchanged at eighteen percent (Mebust et al.).

The potential advantages of ‘minimally invasive therapy’ over conventional TURP are in terms of postoperative morbidity and economic cost. It is anticipated that reduced bleeding may lead to reduced requirement for transfusion; that there may also be fewer cardiovascular risks, particularly in high risk patients; reduced clot formation with a subsequent reduction in clot retention and length of stay.
1.4 Surgical alternatives to transurethral resection of the prostate in the management of BPH:

1.4.1 Transurethral balloon dilatation.

Dilatation of the prostatic urethra using metal sounds has been used for centuries, but although these techniques were successful in relieving obstruction, they were associated with significant morbidity, and soon fell into disuse.

Transurethral balloon dilatation of the prostate is a recently developed procedure, where a balloon is precisely positioned in the prostatic urethra and inflated to a predetermined size in order to cause an anterior commissurotomy, or widen the prostatic urethral lumen and thereby relieve prostatic obstruction. The exact mechanism by which dilatation was thought to improve voiding is still not understood, but may include ischaemic atrophy, stretching of the prostatic capsule or rupture of the anterior / posterior commisures.

Several studies have reported a successful outcome in 50-70% of the patients treated (Castaneda 1987, Reddy 1988, Goldenburg 1993). Wasserman et al reported that patient selection results in a much better outcome, finding that transurethral dilatation of the prostate was most effective in younger men with moderate obstructive voiding symptoms who have no median lobe enlargement, and have residual volumes less than 150cc. However, high relapse rates have been reported by Khoury.

Lepor et al have reported on a small randomised blinded trial comparing balloon dilatation to cystoscopy in 33 patients. Both groups had a significant improvement in
their symptom scores at one and three months, and neither group showed any significant change in their peak flow rates. They concluded that the efficacy previously described by some authors was really a placebo effect, findings now agreed with by the majority of Urologists.

1.42 Transrectal and transurethral microwave hyperthermia.

The term hyperthermia has become associated with the current trend of heat treatment of the prostate. Electromagnetic radiation heats via kinetic energy causing displacement or drift of free charge, the polarisation of atoms and molecules [mostly water], and the polarisation of existing dipoles.

Hyperthermia is subdivided into two categories based on the temperature utilised:

Hyperthermia per se, implies the lowest temperatures used to treat BPH - up to 45 degrees centigrade whereas thermotherapy utilises temperatures as high as 60 - 80 degrees centigrade.

Yerushalmi et al followed 89 patients who were treated for symptomatic BPH for up to eight years. Immediately after completing treatment, 80% of patients had symptomatic improvement. However, during the 6 month to 8 year follow up, 13% required prostatic surgery, and a further 13% underwent additional hyperthermia.

It must be said that not all transrectal hyperthermia trials have demonstrated the same degree of clinical efficacy. Saranja et al treated 83 severely obstructed patients and 31 in urinary retention. They found that only 21% had a >40% increase in symptom score following treatment, and when objective and subjective parameters were taken together, they concluded that 54% were treatment failures.

Abbou et al have carried out a well designed double blind randomised study on 226
patients with accurate data being available on 200 patients. Three different devices were used for transrectal treatment which consisted of six sessions over three weeks, and three for transurethral treatment - one session only.

Fewer patients had peri-operative complications in the transurethral group compared with the transrectal group, although nearly all post-operative complications (within four weeks of treatment) were statistically higher.

At three, six and twelve months, no significant differences emerged between the sham and hyperthermia groups in terms of peak urinary flow rate. Madsen symptom scores were significantly better in the transurethral group, although no significant differences were found with regard to change in symptom score from baseline.

One criticism that could be levelled against this trial relates to the inequality in size of the treatment groups, which will lead to a reduction in statistical power. However, this trial is one of the better conducted with this form of therapeutic energy, and the authors' conclusions that hyperthermia is not an effective treatment are certainly valid.

Perhaps the two definitive trials on the subject of thermotheapy were reported in 1994. Firstly, Nawrocki et al described an elegant double blind randomised controlled trial of 120 patients who were randomised to one of three groups. These groups were, placebo with no heat emission, placebo with heat and finally transurethral therapy itself. The standard and simulated microwave treatment groups showed little difference in clinical improvement, American Urological Association (AUA) symptom scores changing from a median of 19 to 9.5, and 17.5 to 9.5 respectively. Similar changes were seen with regard to peak urinary flow rate, whilst the untreated group showed no clinically relevant deterioration or improvement.

Similar results have been reported by Venn et al in a randomised trial of 96 patients
with urodynamically proven outflow obstruction. At six months, there were no statistically significant differences between treatment and sham treatment in either subjective or objective outcome measures.

Recently however, third generation thermotherapy machines (T3) have been proposed as being more efficacious. Miller et al. has reported on 112 patients treated with such a device resulting in a complication rate of 9%, an 11% retention rate and a greater than 63% improvement in symptoms at one year. However, changes in peak urinary flow rate were modest, with overall a 57% improvement and 'a majority of patients having an improvement better than 3ml/s.'

This study had no control arm, which once again brings into question the placebo effect, and really only demonstrated that high intraprostatic temperatures are possible with this device, leading to some tissue destruction.

Javle et al. have produced some unusual results with the same device. Fifty men were studied as part of a non-randomised, non-controlled clinical trial, and all underwent pre- and post-operative videourodynamic assessment.

While relief of obstruction was poor (44% of the patients showed no urodynamic change), a striking and consistent feature was an improvement in the efficiency of detrusor contraction.

The authors suggested that thermotherapy may relieve features of urinary outflow obstruction by a neurologically mediated mechanism improving the efficiency of detrusor contraction, although with no controls in this series, the validity of this statement is open to question.
1.43 Transurethral incision of the prostate [TUIP]:

TUIP was initially reported by Orandi in 1973 and although this procedure did not enjoy widespread popularity after its introduction, the recent interest in less invasive surgical techniques has lead to a resurgence of interest in TUIP.

The technique is performed with a resectoscope that utilises an electric knife. Normally two incisions are made at five and seven o’clock beginning at the level of the ureteric orifices, and extending back to the verumtananum in the groove between lateral and median lobes. The incisions should be carried down to the prostatic capsule. Since no prostatic tissue is resected, the procedure is technically straightforward, and carries less morbidity than conventional transurethral resection.

There have been multiple reports in the literature (Orandi 1985, Mebust 1987, Edwards 1982 and 1985) regarding the efficacy and safety of TUIP. All series report symptomatic relief in > 80 - 90% of patients in the short term (less than 6 months), with long term results (greater than one year) of between 68 and 88%.

Riehmann et al have published results from a randomised controlled long term outcome study of TURP and TUIP. A very small prostate was necessary for inclusion in this study, and all patients were proven obstructed on pre-operative urodynamics. 82% of the TUIP and TURP patients reached one year follow up while 67% and 71% respectively reached two year follow up.

Operating time, peri-operative blood loss and length of catheterisation all statistically and clinically favoured the TUIP group, although there was no significant difference between the groups with regard to symptomatic outcome.

The data on uroflowrometry raises some questions: The TURP patients had statistically significantly higher peak urinary flow rates pre-operatively despite ‘ formal
At 3 and 24 month follow up the TURP patients again had better flow rates.

The re-operation rate in this study was higher on the TUIP group at 23% versus 16% and was quoted as not being statistically significant at the 5% level. However the reason for this may be because there is insufficient statistical power to detect changes in this particular end-point.

The technique of TUIP is still under used in those patients with a small gland, where the results in terms of symptomatic improvement, are identical to those from TURP, although these patients do represent a small percentage of those requiring surgery.

**1.44 Transurethral needle ablation of the prostate (TUNA).**

TUNA is a method of delivering low-level radiofrequency power through a catheter device fitted with adjustable needles placed in a selected area of the prostate. TUNA ablation produces very localised necrotic lesions, both macroscopically and microscopically by attaining central lesion temperatures around 110 degrees centigrade. First described in the canine model by Goldwasser et al, and then in ex-vivo human prostate (Ramon et al), the first clinical trials of this interesting technique are now appearing.

Schulman et al have reported on 25 patients who received TUNA therapy. The authors described an improvement in flow rate from a mean of 9.7ml/s, to a mean of 15.8 ml/s at six months. However, 11 patients were lost from the study at three months, and data on only 7 patients was available at 6 months. These small numbers coupled with the non-randomised, non-controlled nature of this small series makes the results uninterpretable.
In 1995, Rosario et al. reported on the treatment of 70 patients mean age (70 years), 64 of these under local anaesthesia. The results from this study were disappointing: The complication rate was 23%, and although a decrease in the International Prostate Symptom score from a mean of 22 to 13, was noted, the change in peak urinary flow rate was negligible.

Urodynamics showed all patients remained obstructed at one month. These data are very early, at one month post-op.

At the same meeting, Lynch et al. also reported preliminary data from a multi-centre, non-randomised case series with flow rates of a similar magnitude, although much improved symptom scores (21.4 to 5.6 at three months).

It appears from these early results, that TUNA cannot match TURP in terms of urinary flow rate and if the reported trend continues, TUNA will be rapidly removed from the urological armamentarium.

1.45 High intensity focused ultrasound.

Fry et al. described the ability of focused ultrasound to destroy nervous tissue in 1954, but applications to urology had to wait until the development of a transducer that was small enough to be introduced into body cavities (Sanghvi et al. 1992).

Foster et al. reported on the results of a formal canine study to determine the safety and efficacy of high intensity ultrasound to ablate the prostate. The technique works due to the fact that ultrasound can be tightly focused in a small volume, which can create temperatures in the focal zone of 80-90°C leading to coagulative necrosis. A small pilot study has been conducted by Bihrlle and colleagues in Indianapolis, on 15 patients with clinical BPH. The combined imaging/therapy probe is placed per rectum and treatment
is aimed at the transition zone.

Results were poor, with an average improvement of only 48.4% in AUA symptom score at 90 days, and with only 4 of the patients achieving a greater than 6 ml/s change in mean flow rate. Furthermore 73.3% developed transient urinary retention. Madersbacher et al have also described their phase one and two results with this technique. The mean prostate volume treated was 44.7 ml with a mean post-operative hospitalisation of 1.2 days although 92% developed transient urinary retention, anticipated by the pre-operative placement of a supra-pubic catheter.

Post-operatively, however, the length of catheterisation was as high as 42 days (mean six days), with 5 ‘minor’ infective and one ‘major’ complication (colonic perforation) resulting. Only 12 patients were followed up for twelve months. The authors state that statistically highly significant changes in urinary flow rate were achieved, although it is questionable if a mean change of 4 is clinically significant. Perhaps more importantly, the treatment for four of the patients failed, necessitating transurethral resection.

Once again the question must be asked as to whether technology is being used simply because it is available, must be asked, although Bihrle et al must be congratulated on their proposed randomised trial which should give some “meaningful” data.

1.46 Electrocautery vaporisation

Transurethral vaporisation prostatectomy (TUVP) is currently proposed as an alternative to both laser and TURP. A standard diathermy machine delivers a large amount of power (in excess of 200W), via a grooved or spherical electrode that is said
to concentrate the energy leading to a high local current density. The grooved electrode is considered superior to the traditional roller ball, because 'the current is concentrated at the edge of the grooves, thereby increasing the temperature and reducing carbonisation'.

The original clinical work was first reported from New York, where Te et al now have data on 76 patients. Mean length of catheterisation was short at one day and 68% of patients were discharged after one night stay. Mean follow-up is only 6.7 months so far, producing results very similar to many of the laser forms of prostatectomy. The recatheterisation rate is 5%, all due to clot retention.

The results from this group’s randomised study are eagerly awaited.

Cornaby et al reported on an initial UK series of 55 patients treated by this method with the vaportrode device (Circon ACMI USA). In this small pilot study, the mean operating time was similar to that of a TURP, 35 minutes (range 20-65) and the majority of the patients were discharged on the second post-operative day. However the morbidity was high; three patients were converted to TURP, three needed catheter re-insertion and one was re-admitted with clot retention at ten days.

Although this technique shows promise, there is great concern over the depth of penetration with such a high current and the associated risk of impotence and incontinence.
1.5 History of LASER.

The principles that now form the basis of laser technology were firmly established as early as the nineteenth century, with the advent of the Bohr theory of the atom and optical resonators. The work of Einstein, Schwalow and Townes [1958], and Prokhorov Vasov in the early 20th century led to the discovery of "Maser" [microwave amplification by the stimulated emission of radiation]. However, the first successful application of stimulated emission of microwaves had to wait until the theory was put into practice by Gordon in 1955.

In 1960, Maimen first observed stimulated emission in the visible portion of the electromagnetic spectrum by exciting a ruby rod with intense pulses of light from a flash lamp, generating the first laser beam.

Johnson in 1961 used a neodymium doped yttrium-aluminium-garnet [Nd: YAG] rod to emit energy in the near infrared portion of the electromagnetic spectrum [1064nm]. The beam from the Nd:YAG laser is invisible, but the point of contact is defined by an aiming beam produced by a low dose helium-neon laser [<5mW at 632.8nm]. In clinical use, light at 1064nm wavelength can be passed through a flexible fibre and is not absorbed by fluids such as blood or irrigation solution. Thus, a deeper tissue effect occurs, with penetration up to a depth of 3 - 5 mm.

Tissue-laser interaction results in the beam being altered with 20-30% of the laser energy undergoing forward scattering, and 39-40% back scattering. Heating of the tissue occurs with coagulation and evaporation including sealing of blood vessels up to 3mm in diameter.

At temperatures above 100 degrees centigrade, tissue liquids and some solids are
turned into vapours of water and hydrocarbons.

Laser prostatectomy appears to show great promise, in terms of both post-operative morbidity and hospital stay via decreased blood loss, and perhaps economic cost.

The use of the Nd:YAG laser in prostatic disease was initially described in 1984 to ablate residual tissue after debulking TURP for localised prostatic cancer [Sander and Breisland]. Subsequently, in 1985, Shanberg and Tansey described the use of an end-fire Nd:YAG laser in a contact mode allowing vaporisation of the tissue.

Ten patients with small glands, were treated although direct contact resulted in damage to the fibre tip so that several fibres had to be used to complete the procedure. All achieved improvement in their urinary symptoms and preserved antegrade ejaculation; however, four had significant postoperative bleeding.

Kandel and Harrison in 1985 then reported on the use of an Nd:YAG laser to treat BPH in dogs. They described contact vaporisation via a perineal urethrostomy, using power outputs of up to 80 watts with good results: there was no significant bleeding following treatment, no urinary retention, incontinence or urethral or bladder neck stricturing.

The development of the transurethral ultrasound guided laser induced prostatectomy [TULIP] system by Roth and Aretz in 1991, led to promising results in 21 dogs, using a non-contact laser under real time ultrasound guidance, producing sloughing of tissue by coagulative necrosis. A range of depth of necrosis from 0.45-1.1cm was produced, with a power setting of between 20 and 55W.

McCullough and Roth then described TULIP in humans: the overall preoperative prostate volume treated was 40cc and patients were assessed up to one year post-
Operatively. Only 63 patients were followed up for 6 months, and although 81% of the patients achieved an improvement in symptom score following treatment, only 56% achieved an increase in urinary flow rate.

A significant problem with the TULIP procedure is the delayed improvements in symptoms and peak flow rates, due probably to acute inflammation resulting from the burn.

Moreover, the accurate location of anatomical landmarks with ultrasound may be more difficult than with a cystoscope. This has led to the development of laser fibres which can be endoscopically located through a cystoscope.

Costello et al used an Nd:YAG laser [1064 nm Surgilase] to treat four patients with symptomatic bladder neck obstruction; three secondary to BPH and one with prostatic carcinoma. A 600 micron quartz fibre was used to deliver laser energy via the gold plated alloy tip containing a hollow deflecting device [Lateralase Trimedyne Inc.], the beam being directed onto the prostatic adenoma in four quadrants in continuous mode for one minute per quadrant. Post-operatively, urinary flow rates showed an improvement of between 4-10 ml/s, no incontinence was demonstrated, all patients remained potent, and no episodes of secondary haemorrhage occurred.

This initial work, although on small numbers of patients, showed the Nd:YAG laser to be a simple and safe way of dealing with BPH.

Kabalin in 1993 described a slightly larger series of 13 non contact laser prostatectomies, entered into a prospective randomised controlled trial, comparing with TURP. Follow up was only as far as six months, two patients in each group experiencing no improvement in symptoms post operatively, but of those treated with
the laser, a 120% and 141% improvement in AUA symptom score was noted at three and six months respectively.

In 1993, Norris et al described a larger series of 108 visual laser ablations of the prostate performed on an outpatient basis. Some aspects of this study showed promise, notably the significant improvement in AUA symptom score, which decreased by an average of 12.59, \( p < 0.001 \). However, follow up data was incomplete on 35 patients, a 7.5% failure of trial without catheter was noted, even with a post operative course of an alpha adrenoceptor antagonist, and a urethral catheter left in situ for 5-7 days. Perhaps more importantly, there was no significant blood loss reported, although no quantitative method was described, no sepsis nor fluid or electrolyte disturbances.

Marks has performed one of the few endoscopic follow up studies on patients undergoing non contact laser prostatectomy, with post operative views of the prostate being achieved between 2 and 19 weeks. Tissue sloughing was prominent in the early weeks following treatment, the superficial vaporisation cavities noted at the time of treatment expanding and coalescing into adjacent areas of coagulative necrosis. Healing was judged incomplete in those patients who underwent follow up video imaging at 6 weeks or earlier. Even at 19 weeks, the longest video follow up in the series, healing did not appear complete, results at variance with Costello et al, who noted re-epithelialisation by 6 weeks.

Muschter et al have built upon the work of McNicholas et al, in using an alternative method of ablating prostatic tissue, utilising a percutaneous route and low power interstitial laser coagulation. Eleven beagles were treated, via 200-600 micron fibres.
transmitting low power laser energy [1-2W], with exposures between 400 and 1500 s.

At 6 weeks, the canine prostates had healed by necrosis surrounding an area of cystic degeneration. Multiple fibre experiments produced larger volume lesions which may be of relevance in the treatment of BPH.

Orovan et al have utilised this interstitial technique via a transurethral route in 16 patients using 7 watts for 10 minutes in each lateral lobe, and 5 minutes in the median lobe. Fourteen of the sixteen patients studied were catheter free on the first post operative day, and all were without a catheter at one week.

A decrease in AUA symptom score and post void residual, together with an increase in the mean peak flow rate was observed.

This technique has the theoretical advantage of producing no urothelial defect during ablation of the prostate, although the relevance of this hypothesis is uncertain.

However, this procedure, or a trans perineal route, under local anaesthesia may show promise in the unfit population, although again, a randomised prospective trial will be needed before widespread uptake of this procedure.

Using the contact laser technique, the laser probe directly touches and immediately vaporises the prostatic tissue. The net result is an immediate removal of obstructing tissue in a manner similar to standard electrosurgical TURP. The energy density of a neodymium YAG laser can be increased by placing the fibre in contact with tissue. The high concentration of the energy in a small target area increases tissue vaporisation and the cutting effect of the laser. Sapphire tips for neodymium YAG laser fibres have been developed in various configurations (Joffe 1986), but were not available in sufficient diameter until 1994 with the advent of the SLT (Surgical Laser Technologies, Oaks,
Daughtry and Rodan first described contact laser prostatectomy in a series of 25 elderly high risk, poor surgical candidates. Laser resection was performed using the SLT contact laser system with the MTRL 3 and 6mm tip probes. The average prostatic size in this series was small at 26 g, with an average operating time of 33 minutes. Follow up was up to 11 months in this series, although symptomatic outcome was rather subjective, classed as “failures”, “fair” or “good.” However, 15 good results were obtained, with peak flow rates improving from a range of 14cc/s to 40cc/s for patients in whom surgery was successful.

No significant bleeding was reported in this series, although no objective data was obtained, both in terms of peri operative blood loss and change in haematocrit. This small series showed promise for the technique of contact laser ablation of the prostate.

Watson et al have produced results from a pilot randomised trial comparing contact laser vaporisation with TURP. Difficulty was reported with glands over 40-50cc, but with smaller prostates, a good decrease in AUA symptom score together with an improvement in flow rates were noted.

More recently, Muschter et al have reported on the heating patterns and coagulation volumes created by both right-angle non-contact coagulation, and contact vaporisation. Nine beagles were treated with the Ultraline fiber (Heraeus Lasersonics, Milpitas, CA; CIRCON / ACMI .CT) and the MTRL 10 sapphire tipped contact probe.

Results painting with the Ultraline fibre at a speed of 1mm/second at 40W, showed that during fibre motion a target point receives irradiation before and after the centre.
of the fibre passes. Painting resulted in a greater coagulated depth than pulling, but fell short of the depths obtained during fixed lasings. Microscopic and thermometric analysis showed that with the contact technique no coagulation defect occurred beyond 1-2 mm from the vaporised area.

1.6 Long Term follow up studies and more recent work.

Recently, longer term follow up on a number of methods of laser prostatectomy have been reported. McCullogh et al reported on two year follow up for the TULIP technique, although only 40 out of the 230 were followed for the 2 years. The mean operative time for this technique was 21 minutes, with minimal intraoperative blood loss. Complications included 1.5% of the patients requiring postoperative endoscopic removal of bladder clot, a rate of impotence of 5%, together with a 4.1% failure rate and a 5% stricture rate, although an improvement in AUA symptom score of 73% at 1 year and flow rate of 60% were noted at one year. However this study was non randomised, contained incomplete follow up on the complete cohort, and the 70% improvement may be expected with placebo.

Schulze et al have reported on a prospective randomised trial of TULIP versus TURP. Forty patients were randomised to one of the two treatment modalities, 13 in each group being in urinary retention. The mean energy used in the TULIP group was 14500 J, mean blood loss being 51ml compared to 515 ml in the TURP group. The mean post operative stay was reduced in the TULIP group at 2.6 versus 6.7 days, but patients had a catheter in situ for up to 90 days, the mean being 34 days, and at three
weeks, 30% of the TULIP patients were in retention.

Turning to non-contact laser prostatectomy, a multi centre study has recently been published describing the use of the right angle Urolase fibre (C.R.Bard inc.) in the treatment of 117 patients with BPH [Leach et al]. AUA-6 symptom scores, flow rates and post void residual showed a trend to improvement at both 6 and 12 months, although it must be said that less than half the original cohort were followed for the full 12 months.

Cowles et al have reported on one year follow up of 115 patients enrolled into a prospective randomised trial comparing TURP with VLAP using the Bard fibre. The two treatment arms were well balanced at baseline other than in AUA symptom score, which was higher in the TURP group. The mean prostate volume treated was small, but wide ranges were quoted (7.7 - 93.9cc for the laser and 11.2-108.2cc for the TURP), and median values would have been more helpful.

A comparison between the two groups at one year revealed a statistically significant difference in post void residual and AUA-6 symptom score favouring the TURP patients. There was no significant difference between the two groups with regard to improvement in mean peak urinary flow. The authors concluded that although based on treatment regimens that are now out dated, the study demonstrated side fire coagulation prostatectomy with the Bard fibre to be safe and efficacious. However the re-operation rate in the laser arm at one year was 10.7% and the re-catheterisation rate 30.4% although this may well reflect the learning curve.

Dixon and Lepor have produced one of the very few prospective randomised blinded studies comparing the Bard Urolase right angle fibre with standard electrocautery resection. The numbers were small at the outset, with 66 patients being
randomised, although the study co-ordinators must be congratulated on attempting to fully blind the patients and the study nurse to the treatment received. Furthermore patients with an enlarged median lobe were excluded from this study.

At 6 and 12 months, the TURP group showed a significantly greater improvement in AUA symptom score compared to the laser group, although there was no statistically significant difference when considering urinary flow rate or post-void residual.

The reoperation rate at 12 months was higher in the laser group (16%) compared to 4% in the resected patients. Global assessment at both 6 and 12 months also favoured the TURP group as did the safety of the procedure.

This data clashes with the results of Kabalin, who took part in the multi centre study but published the results on 25 patients early. He showed no statistical or clinical significance between the laser or TURP groups, but with such small numbers, the relevance of the statistical data is questionable. In 1994, Kabalin published 18 month results on these 25 patients. Two patients from each arm failed to achieve a significant improvement in voiding, and a further two patients in the laser arm were lost to follow up beyond six months. Thus data was available on only 19 patients. The mean length of post-operative catheterisation was 2.7 days for electrocautery resection compared to 4.7 days for laser prostatectomy. Although there was no statistically or clinically significant difference in peak urinary flow rates, AUA symptom scores or post-void residuals, the value of these results is of little significance with data on only 19 patients.

At the 1995 AUA meeting, Kabalin this time reported the long term follow up on 225 patients treated with the Urolase system. Although long term complications
were low (1.3% urethral stricture, 3.5% bladder neck contracture, 4% re-operation).

This series was non-randomised, and contained incomplete follow up with only 25 patients at three years!

Anson et al. have recently reported on six month follow up on 151 patients randomised to sidefire coagulation using the Bard fibre, or TURP. The patients for this trial were highly selected, in that anyone ASA 3 or above, or with renal impairment were excluded. The mean resected weight of tissue was small in the TURP group at 19 grams, suggesting that only small prostates were included. An overall transfusion rate of 16% was reported in this group, whilst no laser patients received a transfusion.

The mean duration of catheterisation post operatively was 2.7 days in the resected patients, but rather more prolonged at 12.2 in the laser arm (the majority having suprapubic catheters). At four weeks the results in terms of change in AUA score, significantly favoured the TURP group, with 41% of the VLAP patients experiencing significant dysuria.

In summary, this elegant paper has shown that sidefire coagulation prostatectomy was associated with significantly less haemorrhage and need for transfusion, and a shorter inpatient stay than TURP. However, with respect to all other outcome measures (symptomatic improvement, time to removal of catheter, post-operative infection, reoperation, maximum urinary flow rate and residual urine) the laser patients fared significantly worse than TURP patients.

At the time of writing, no large randomised controlled trials of the contact technique have been published.

Narayan et al published their results of a rather "hybrid" technique utilising the sidefiring Ultraline fibre in the contact mode. These clinical results followed experimental
work using this fibre coupled to a continuous wave 100 W laser to create lesions in human prostate (Fournier et al). Five human prostate specimens were used; the internal reflector tip being placed in contact with the prostatic urethra producing a single spot with a 60 W beam. The mean crater depth produced was impressive at 9.7 mm (range 5-20 mm), while the thickness of the coagulated tissue below did not exceed 2-3 mm.

The authors proposed the concept of the ‘accelerated evaporation phenomenon’, during which tissue evaporation is enhanced by contact with the fibre tip because of trapping of evaporation gas between the fibre tip and evaporation crater, a situation that excludes the liquid medium and prevents cooling of the walls of the cavity.

It was concluded that significant lesions can be produced in the prostate by employing the Nd: YAG laser in the contact mode. However, despite the authors’ convictions that the problem of fibre deterioration can be overcome by fibre movement, increasing amounts of joules need to be used with power outputs up to 80 W and the problem of single use reflective fibres remains.

61 patients were recruited into a prospective non randomised, non controlled trial, tissue evaporation being achieved by holding the fibre in contact with the area to be treated, and by dragging at a rate of “1 cm/20 seconds”.

The treated glands (21.4 - 97.4 g) received a mean laser energy of 42024 J. The operating time varied from 21-110 minutes.

A good improvement in AUA score was noted up to 12 months post-operatively, although yet again, as has been the case in many published series, follow-up was poor at greater than three months post-operatively (only 43% of the patients getting greater than 3 month, and 11% getting one year follow up).

However, although this study does have some design faults, it has a number of
interesting points.

Firstly, in the 12 patients in urinary retention pre-operatively, all were voiding satisfactorily following laser therapy. Perhaps what is of more interest is the maximum improvement in AUA score seen at 6 months both in those patients who were and were not voiding pre-operatively. This may of course reflect an improvement in detrusor function, but sequential videocystoscopy performed in 16 patients revealed tissue slough up to three months post-operatively which may account for the delay before maximum symptomatic improvement.

Further human experimental work is now appearing from a number of authors: although it must be said that this work should have appeared before this technology was accepted into clinical practice.

Shanberg et al treated twelve men with the Prolase II fibre (Cytocare, Irvine CA), immediately prior to radical prostatectomy. Varying dosimetry was used, and after completion of treatment, prostates were surgically removed. The first group received treatment to a single spot area of 60W for 60 seconds and 40W for 90 seconds. Thermal necrosis was variable, even with the same amount of laser energy.

The second, third and fourth groups had the entire lobe irradiated with 60W for 60 seconds, 50W for 60 seconds and 40W for 90 seconds respectively. Clearly demarcated areas of thermal necrosis were seen in each of these three groups, with a mean depth of penetration of 1.75cm to 0.53cm. In all patients, no laser effect could be detected near the true prostatic capsule.

Muschter and Perlmutter have performed some elegant experimental work, in looking at the heating patterns and coagulation volumes produced by various fibres in the
potato and canine model.

‘Pulling’ lasing was performed with the fibre pulled straight past a set of thermocouples set in a grid, at a speed of 1 mm/s, while ‘painting’ with the sidefire technique was performed in the same way as pulling but with constant oscillation of the fibre.

Painting created larger volume lesions than pulling but although this method of tissue destruction leads to coagulation of a greater volume of canine prostate than the same duration of fixed lasing, the coagulated zone is not as deep.

With regard to contact tips, in the canine model, microscopic pathology and thermometry revealed no coagulation effect beyond 1-2 mm from the vaporised area, although this data is refuted by others (K. Anson personal communication, SLT personal communication), who claim up to 6 mm effects.

The largest coagulation cavities obtained in this series, were with the Interstitial Thermotherapy (ITT) Lightguide S-6190-1 (Dornier, Germering, Germany): the coagulated zone volume in the canine prostate using a 2cm lightguide was more than twice the maximally obtainable free beam sidefire lesion.

Anson et al have carried out an elegant series of experiments to look at the optical properties of laser side firing devices. The intensity profiles, angle of exit and beam divergence of a number of side-firing Nd:YAG devices were measured in vitro and in a mathematical model. The results showed that each fibre had its own distinct profile, but broadly they could be divided into two patterns. The Myriadlase, Ultraline and Angled Delivery Device (Laserscope UK Ltd.), produced tight beams with narrow divergence and high peak intensities, compared with both the Urolase and Prolase which produced wider more divergent beams, with lower peak intensities.
The nature of the tissue irradiated was also found to be important, in that backscatter of photons was greater from coagulated tissue (37%), compared to native tissue (22%).

The authors concluded that although the power density is only one of a number of variables that influence laser tissue interaction (Babayan et al), if strict treatment protocols are adhered to, the differences in optical properties of the fibres will have a major effect on the type of photodermal effect that will occur.

As stated earlier, this sort of experimental work should have been available long before the rapid world-wide diffusion of this technology.

1.7 Wavelengths other than Nd: YAG

The wavelength of the Nd:YAG laser can be changed by using a potassium-titanyl-phosphate (KTP) frequency-doubling crystal. The output from this source, at 532nm emits light in the green range and can be delivered by fibre-optics and used under irrigating fluids. KTP energy is highly absorbed in vascular tissue, resulting in increased superficial vaporisation and good haemostasis. Data on the use of this wavelength, either alone or in combination with Nd:YAG is scarce.

The Holmium: YAG laser (2100 nm wavelength) is a pulsed solid-state laser which is highly absorbed in vascular tissue, resulting in increased superficial haemostasis. It has many of the safety and efficacy advantages of the carbon-dioxide laser and is a precise cutting and vaporising tool. Unlike the CO\textsubscript{2} laser, however, its energy can be delivered down an optical fibre.

Gilling et al have reported on a non-randomised series of 110 patients who were
treated by a combined approach of side-fire coagulation using the Nd:YAG, and contact vaporisation using the Holmium wavelength.

These patients however received a somewhat ‘mixed’ treatment regimen due to the use of three different fibres, each with different lasing properties.

A further 32 patients were then treated solely with the Holmium wavelength. The mean operating time for the combined treatment group was 48 minutes (range 10-100), and the mean hospital stay was 0.9 days (0.1 - 5), although catheterisation was longer; mean 1.6 days and 3.6 days for urethral and suprapubic catheters respectively with a recatheterisation rate of 8.2%.

A similar mean operating time was seen in the pure Holmium group, although these patients had their urethral catheters removed within 24 hours.

Kabalin has also reported on the successful use of the Holmium laser in a tiny sample of ten men with no significant bleeding and minimal catheterisation times.

Semi-conductor diode lasers have recently become available for prostatic irradiation and due to their size and cost, have the potential to increase the convenience and affordability of laser prostatectomy.

Anson et al first described their use in urology in 1994, and also in conjunction with Perlmutter et al, have looked at three systems in the canine prostate (805nm Diomed, Cambridge, 980nm Dornier, Munich and 1000nm Cynosure, Bedford MA, USA). Using the Sidefocus fibre at 25W irradiation at 805nm, smaller lesions and lower temperatures were obtained than at 980 and 1000nm using the Angled Firing Device.

Alsudani and McNicholas have compared the Cytocare Diolase with the Nd:YAG
wavelength in a non-randomised prospective study. No significant differences between
the two groups with regard to outcome or complications were observed at three
months, although it must be said that this may have been due to the small sample of
men studied (n=30).

The current devices are able to produce power outputs up to 60W, but will require
rigorous evaluation to ensure reproducibility of results and outcomes.
1.8 Generic and disease specific symptom scores

In recent years, there has been a shift in emphasis in health care evaluation to measurement of health from the patient's perspective (Spilker 1990). These so-called generic measures are designed to be of general applicability, rather than specific to a single condition, and include the Functional Limitations Profile “FLP” (McDowell and Newell 1987), and the Nottingham Health Profile (Hunt and McEwan 1980, Hunt et al 1985, 1986).

The FLP is a measure of the effect of sickness on behavioural function as assessed by the individual's perception of the effects of ill health on daily tasks. The profile contains 12 dimensions that ill health may adversely affect, which are, ambulation, bodycare, mobility, household management, recreation and pastimes, social interaction, emotion, alertness, sleep and rest, eating, communication and work.

In total, there are 136 items and respondents can score from 0-100 on each of the dimensions except work where the score range is from 0-70.

This questionnaire has been used in a number of studies reflecting a variety of medical conditions (Patrick and Peach 1989, Hart and Evans 1987, Fletcher et al 1988), but despite its popularity, it has a number of important limitations. Its length makes it somewhat cumbersome, it contains no dimension specifically aimed at pain, and further research is required to elucidate particularly its sensitivity to change.

The Nottingham Health Profile (NHP) is the most widely known British designed instrument, consisting of 2 sections. The first containing 38 items is intended to measure perceptions of health in six different areas. The items included are pain, physical mobility, emotional reactions, sleep disturbance, social isolation and energy.
These items were generated from mass public screening exercises, and are weighted according to the perceived seriousness of the dimension.

The second section asks respondents to indicate whether or not their state of health affects activity in seven areas of everyday life: employment, looking after the house, social life, home life, sex life, interests and hobbies and holidays.

Responses are coded as simple yes/no, there is no weighting of replies nor are any of the items summed together. This part of the questionnaire is used less extensively.

The NHP has been widely used, and has had its validity in terms of *face* (the need for a questionnaire to tap simply by item content, an underlying dimension), *content* (the extent to which items on a questionnaire tap all the relevant aspects of the attribute they are intending to measure) and *criterion* (the extent to which a measure correlates with a pre-existing one, preferably a "gold standard") tested to ensure its reliability over time.

However, the fact that attention is paid to only the severe end of the health spectrum means that the data gained from the questionnaire tends to be highly skewed, with most respondents at the "normal" end of the spectrum scoring very low, if at all.

Hence the NHP may not be the most sensitive tool to measure change in general health status over a period of time, a particularly important aspect of assessing outcome after any form of surgery.

The SF-36 standing for Short Form 36 is perhaps one of the most widely known questionnaires to be generated as a product of two large studies from the USA. Firstly the Health Insurance Experiment (Ware and Brook et al.), which was a research project undertaken to determine the best possible methods for measuring health status,
and to compare the outcomes of different methods of delivering care.

The second study from which the SF36 was derived, was that of Tarlov et al, 1989 and Ware et al 1992. The ‘Medical Outcomes Study’ (MOS) was a large scale test of the feasibility of self administered questionnaires and generic scales in the assessment of the outcomes of medical care.

The patient centred approach of these two large studies which led to the development of the SF-36 was seen as quite a new approach to assessing the results of treatment, and is being seen as an increasingly important feature in assessing patients’ management, alongside physiological outcome parameters.

The SF-36 contains eight dimensions, which are transformed into a scale from 0 (for poor health), to 100 (good health), which is in fact the opposite of the NHP where a high score indicates poor health.

These dimensions include the following:

1. physical functioning
2. social functioning
3. role limitation due to physical problems
4. role limitation due to emotional problems
5. mental health
6. energy/vitality
7. pain
8. general health perception.

Minor alterations in the wording of the original SF-36 have been made to make it more acceptable to British patients.

The SF-36 is included in patient pre-operative questionnaire in appendix 1.
The work of Brazier (1992) and Jenkinson (1993) reporting on the internal reliability of the SF-36 has shown the response rates in a random population to be high.

The Oxford Healthy Life survey (Wright et al. 1992) analysed SF-36 data from two large groups; those with long-standing illness, and from those reporting a recent medical consultation. The results showed that those who had consulted a doctor in the past two weeks or admitted to long-standing illness, gained significantly lower scores on the SF-36 in all dimensions.

These results, together with Brazier's work support the format and validity of the questionnaire.
The clinical symptoms that are associated with BPH historically have been termed 'prostatism' or 'symptoms of BPH', and have been categorised as **obstructive** with decreased force and calibre of the urinary stream together with terminal dribbling, and **irritative** which include nocturia, frequency and urgency. These symptoms are certainly not specific for BPH (Chancellor 1993 and 1994), and can be seen in unrelated conditions such as urinary tract infection, neurogenic bladder and urethral stricture. In 1994, Abrams suggested that the above mentioned terms should be rejected and replaced by 'lower urinary tract symptoms', which describes patients' complaints without implying their cause. Abrams further suggested that **voiding** symptoms should replace the term obstructive symptoms, and the term **filling** symptoms would be better than irritative symptoms which suggest a pathological finding. These last two alterations to the already confusing nomenclature on the subject have not yet however been widely accepted.

The recently validated American Urological Association (AUA) symptom score [Barry et al], has been shown to be a reliable and accurate method of evaluating disease severity and outcome in BPH although it is certainly not disease specific. First described in 1992, the validation studies of this seven item scale (see appendix) involved 210 patients with a clinical diagnosis of BPH, and 108 controls, although no standard diagnostic evaluation was imposed. The test was found to be internally consistent, and scores were highly correlated with subject's global ratings of the magnitude of their urinary problem, powerfully discriminating between BPH and control subjects.

Barry et al then correlated this symptom index with other self-administered indices (Boyarsky 1977, Madsen 1983, Fowler 1988), that have been used to measure symptoms for BPH, and compared their psychometric properties. A questionnaire
containing the above scoring systems was administered to 76 patients with 'clinical BPH' although no precise definition was made, as well as 59 control subjects and 27 patients who underwent prostatectomy.

The scores from the four indices were strongly correlated, and all four had good internal consistency and test-retest reliability. All tests were predictive of the patient's global rating of the degree of bother from the urinary condition, although the AUA index discriminated BPH patients from controls significantly better than the Maine Medical Assessment Program, and equivalently to the Madsen-Iverson and Boyarsky indices.

Barry and associates then went on to further this masterful series of papers by comparing the AUA symptom index to commonly used physiological and anatomical measures of the severity of BPH.

198 recruited patients showed no correlation at baseline with uroflowmetry, post-void residual, prostate size or degree of bladder trabeculation; surprisingly, symptom severity was much more strongly related to overall health. Reductions in symptoms following treatment did however correlate with improvements in peak and average flow rate, although this correlation was modest.

Barry has looked at the "bothersomeness" and effect on quality of life of BPH symptoms in developing the 'BPH Impact Index', and although this is being used (Emberton et al), it has not yet received formal approval from the 'International Consultation on BPH', who favour the one question condition specific, quality of life evaluation:

"If you were to spend the rest of your life with your urinary condition just the way it is now, how would you feel about that?"
Despite its established popularity, the AUA index has nevertheless been the subject of criticism and controversy. A series of studies have reported disappointing results when assessing its performance. Chancellor et al, Chai et al, and Lepor et al have all reported on its inability to distinguish between men with BPH and women with urinary symptoms.

Lawrence has looked at the AUA symptom score from a methodological point of view (personal communication), trying to explain the apparent discrepancies in results between authors. The point made was that although the AUA score performs well in the area for which it was designed, that is, in evaluative studies, the measure should not be used as a discriminative tool.

At the 1995 AUA meeting Barry et al presented what is probably one of the most important unanswered questions regarding the AUA symptom score; that is, how much change is perceptible to patients. Analyses were based on data from 1218 men reaching 13 week follow-up. A marked improvement (mean 54% improvement) was associated with a mean change of 8.7 in the AUA symptom score, a moderate improvement (mean 29%) was associated with a mean change of 5.0 and a slight improvement with a 3.09 point change.
1.9 The principles of randomised controlled trials.

Numerous examples of ineffective health care already exist, and history has shown the dangers of introducing new treatments and procedures without critical evaluation of their outcome (Ruffin 1969, EC/IC Bypass Study 1985). With medical practice in the current economic environment, the delivery of health care and the need to address the recognised variations in medical practice have become paramount. The randomised controlled trial (RCT) has become the “gold standard” in such evaluation. McPeek et al defined the RCT as “a planned experiment to assess the effectiveness of treatments by comparing the outcomes in subjects drawn from the same population and allocated to two or more treatment groups by a random method.” Randomly allocating patients between treatments not only balances known prognostic factors, but also unrecognised and unmeasurable factors. These factors are one of the primary reasons why much of the data from observational studies, no matter how elaborate the statistical analysis, is often of little use.

Randomised controlled trials exist in two forms (Schwartz and Lellouch 1967), “explanatory” and “pragmatic.” Explanatory trials test a particular hypothesis in a tightly controlled situation and are concerned with efficacy, the efficacy being defined as the outcome obtained when the treatment is given under optimal conditions. Pragmatic trials, as described in this work, are designed to be generalisable to everyday practice, and are concerned with effectiveness. The only difference between the trial and routine care being the act of randomisation.

The crucial principle of randomisation, is that it is non-deterministic, i.e. someone
randomising a patient will have no insight into which treatment arm he/she will enter. This "blind allocation" avoids selection bias, and may be achieved by a number of ways, such as computer generated lists or random number tables.

Although randomised trials have successfully been carried out to assess the efficacy of surgery (Miller et al 1989), their use in this area remains rare compared to trials involving historical controls, (Sacks et al 1982) and also compared to their use in other specialities. If physicians would not dream of using a drug in clinical practice that had not been properly validated, then why do surgeons persist in "dabbling" in an uncontrolled manner with new technologies.

The optimal point at which minimal access interventions should be evaluated remains a debate. Those in favour of delayed evaluation suggest that if the evaluation is undertaken too early, the technique will be at the stage of development and any comparison to established procedures would be unfair, and would stifle innovation. Those in favour of early evaluation suggest that if this is delayed, the window of opportunity may be lost and it may be too late to prevent widespread diffusion of a technique of uncertain efficacy.

Of particular importance is the selection and combination of outcome measures - when there are multiple measures of outcome in a clinical trial, the chances of one of these being statistically significant, rises. If secondary measures of outcome are to be used, then these should be predetermined, with suitable correction for multiple simultaneous inferences (Smythe et al).
1.10 Economic Issues surrounding the use of minimally invasive techniques

There are significant implications for health service resource use, coming from the expansion of minimally invasive techniques (MIT) and indeed, economic evaluation should play an integral part in the analysis of any new technology in surgery.

In a recent review and look to the future by Bosanquet, the implications of MIT on future resource needs was examined. Drawing on Department of Health and Health Policy Unit estimates, a 48% change in case load has been projected for urological surgery between 1991 and 2000. The development of MIT centres is proposed, with pressures to reduce cost, as more centres become active in the field but perhaps one of the most practical proposals coming from this paper was the increased multidisciplinary approach to assessment of this technology.

Sculpher has argued that a reduction in the demand for hospital beds brought about by MIT, may not necessarily result in a realisation of cash savings, as it is unlikely that this therapy option will actually result in a decrease in the number of surgical beds, or the redeployment of nursing staff. The possibility of decreasing the threshold for treating patients with milder symptoms must also be considered, that is, one must take account of the ‘baseline therapy,’ which may be watchful waiting or medical treatment.

It may also be argued however, that minimally invasive surgery is arriving into a system where daycase surgery is flourishing, and that the reported benefits and additional savings may not be as significant as was once thought.

The learning curve with these procedures is not insignificant, and hence there are economic issues arising from trainees and training in the “new surgery” (Wickham).
While these questions arise from the uncertainty of the short term effects of MAS, these concerns are amplified in the longer term.

The importance of a rigorous evaluation of the economics of laser prostatectomy is therefore clear, as there is not an automatic link between the arrival and diffusion of new MIT techniques and an increase in the cost-effectiveness of health care provision.
Chapter 2 - Patients and Methods

The central work of this thesis was carried out in the setting of a pragmatic randomised controlled clinical trial of contact vaporisation of the prostate in comparison with standard transurethral resection.

The study population included all patients referred to the Churchill Hospital, Oxford who were in need of surgical treatment for benign prostatic hypertrophy. All patients considered suitable for TURP were eligible for entry into the study, unless:

a) they had undergone previous surgery or instrumentation for BPH
b) they had known prostatic malignancy
c) they could not speak or understand sufficient English to answer the questionnaires
d) consent was refused.

Patients were recruited both in the out-patient department and on the ward, and given a written explanation as to the design and aims of the study. Carcinoma of the prostate was excluded using digital rectal examination and prostate specific antigen levels. Informed consent was obtained from all patients, using the standard Royal College of Physicians clinical trial consent form (corec number 93-183 - see appendix).

2.1 Statistical Power

The sample size for this trial was calculated using POWER software, assuming a clinical significance of five AUA points, and the following data (M.J.Barry personal communication), based on six month AUA symptom scores from the TURP arm of a randomised controlled trial of Terazosin versus TURP. At the time of trial design, no published clinical data existed other than the initial evaluation by Barry et al, on AUA score validation.
Subsequent work by Barry et al, presented for the first time at the 1995 AUA meeting calculated that a 5.05 point change in the AUA symptom score was associated with a moderate improvement in global assessment whereas an 8.71 point change was associated with a marked improvement.

**Power Calculation**

Case mean : 6.9  
control mean : 11.9  
standard deviation : 5.5  
number of cases in each arm : 65  
controls per case : 1  
significance level : 0.0001  
power : 90%.

Pre-operative data was obtained using a self directed patient questionnaire, that contained the following as detailed in appendix 1:

1. AUA -7 symptom score  
2. Bothersome score and questionnaires relating to sexual function  
3. The SF-36
The majority of Urologists would probably agree with the choice of AUA symptom score as a primary outcome measure, but the recurring question of the use of pressure-flow studies as an outcome measure needs to be addressed.

Firstly, this study was not designed to look at urodynamic outcome parameters, but rather to assess contact laser technology using patient centred outcomes.

It is certainly true that pressure-flow analyses represent the current gold standard in establishing a *urodynamic* diagnosis of urinary outflow obstruction, but the crucial question is whether these complex investigations improve outcome sufficiently to justify their routine use?

Although the performance of these tests is relatively straightforward, problems arise with standardisation in the analysis and interpretation of pressure-flow plots.

Abrams et al have demonstrated that inclusion of pressure-flow urodynamic data as a pre-operative investigation reduced the subjective failure of TURP from 28% to 12%. These results in terms of symptomatic improvement are similar to the data quoted from the AUA BPH guidelines of 88% (Confidence intervals 75% to 96%) when the overwhelming majority of patients in this world literature review did not have pre-operative urodynamic studies.

The proof that pressure-flow data can accurately predict outcome following prostatectomy will ultimately need a large randomised controlled trial with adequate statistical power. Until these data are available it would appear prudent to take heed of the AUA and International Consultation on BPH guidelines on the routine use of pressure-flow studies prior to prostatectomy.

In addition to subjective data, the data in appendix 2 were collected prior to surgery. Peak urinary flow rates were measured using a Dantec 2000 flow meter using
a voided volume greater than 150 ml. Planimetric prostate volume measurements were assessed with a Bruel and Kjaer 1846 transrectal ultrasound machine using a Type 1850 7Mhz probe with a focal length of between 2 and 5 cm.

Restricted randomisation was achieved using random number tables in a 1:1 ratio balanced to ten, and sealed envelopes were available in the operating theatre containing the treatment option. Details of those patients lost prior to randomisation were collected.

2.2 Operative Procedure.

Being a pragmatic trial, the type of anaesthesia was not specified pre-operatively, and therefore patients received the anaesthetic most appropriate to their medical condition. Surgery was carried out by five experienced surgeons throughout the study and all patients received pre-operative oral 500mg ciprofloxacin antibiotic prophylaxis.

Following randomisation, a urethrocystoscopy was carried out using a zero degree and 70 degree Storz cystoscope, assessing the length of the prostatic urethra, the macroscopic, pathological state of the bladder and residual urine within the bladder.

Operating time was measured from the start of endoscopic prostate removal, to the time of placement of the 22F three way urethral catheter. Irrigant fluid effluent was collected and weighed using electronic scales to allow an estimate of its haemoglobin concentration. In addition to the above data, the data as outlined in appendix 3 was also collected:

At the time of writing, a purpose built contact laser “resectoscope” is in the prototype stage only, and a number of different instruments were tried with the laser apparatus,
the technology utilised for manipulating the fibre and tip being far from perfect.

A side viewing nephroscope as described by Bartsch et al was first employed, but found to be unsatisfactory due to image size, and difficulty manipulating the fiber. A single instrument port cystoscope was found to be unsatisfactory, a double lumen channel instrument proving most "user-friendly", due to its increased calibre.

Plate 1 - 23.5 F cystoscope and laser delivery system

Laser ablation utilising an SLT MD 60 Nd:YAG machine, a 600 micron fibre with a semi-rigid distal end incorporating a 6 millimetre large sapphire tipped round probe
MTRL 10 allowed complete vaporisation, starting with the median, and progressing to the lateral lobes. The probe was brought back to the verumontanum, and “furrows” produced by forward pressure, until the bladder neck was reached. The procedure was considered complete when a cavity was seen with the bladder empty with the cystoscope at the level of the verumontanum.

Plate 2 - Pictorial representation of contact laser prostatectomy

Standard TURP a procedure which does not require further description (Blandy1971) was carried out as the control arm of the trial.

The Haemocue photometer [Haemocue AB Angelholm Sweden] has recently been
verified by Ekengren et al as a method of estimating haemoglobin concentration in the irrigant fluid following transurethral resection. The equipment as described by Be et al is easily portable and gives a rapid result.

Plate 3 - Haemocue photometer

Peri-operative blood loss was assessed by measuring the haemoglobin concentration in the irrigant effluent, which had been anti-coagulated with 1000 units of heparin, using the Haemocue photometer. The following formula was used to determine the volume lost:

\[
\text{photometer value} \times \text{irrigant volume [litres]} \times \frac{\text{patient's haemoglobin (g/litre)}}{5.2}
\]
Post operatively, the 22F balloon catheter was left indwelling, and continuous bladder irrigation with normal saline was commenced regardless of the intra-operative blood loss, to complete the patient's blinding.

The following data was collected on discharge (appendix):

1. hospital stay
2. length of catheterisation
3. post-operative irrigation fluid volume
4. complications
5. transfusion rate
6. haematological and biochemical data

At four weeks all patients were sent a postal questionnaire, which included the patient-centred outcomes as detailed above.

At three months and one year, all patients were reviewed, again receiving patient-centred outcome questionnaires, further data being collected on the use of community services since discharge.

Data was stored in D-base™ in a manner which complied with the data protection act and analysis was performed using SPSS™ software. Items were entered as pre-coded on questionnaires, and scale scoring and item re-coding was performed by SPSS.
Statistics

Statistics are provided in the form of means, standard deviations and 95% confidence intervals (95%CI). To determine whether differences between groups were statistically significant, a grouped t-test or Mann-Whitney test was used according to the shape of the distribution.

'Effect sizes' are used to indicate the extent of change detected by the measures. Kazis has demonstrated the use of effect sizes in identifying changes which are clinically meaningful, in preference to the rather less discriminating criteria of statistical significance. An effect size of 1.0 is equivalent to a change of one standard deviation in the sample, and is a measure of the within subject change, adjusted for the between subject variation. As a benchmark for assessing the relative magnitude of a change, Cohen identified an effect size of 0.2 as small, 0.5 as moderate and 0.8 as large. Siu et al have cited effect size statistics as being appropriate for multi-scale items as well as single item measures.

2.3 Cardiac Comorbidity

The debate surrounding cardiac morbidity and TURP is an on-going one, and as part of this study, a sub-set of patients underwent cardiac monitoring to address the question of 'silent myocardial ischaemia' (SMI).

The incidence of SMI in patients undergoing non-vascular surgery has been infrequently addressed, and varies between 7.6% and 20% (Muir et al, Allman et al). Pasternack et al have shown that ambulatory monitoring of (electrocardiogram) ECG can non-invasively identify those patients undergoing peripheral vascular surgery who are at significantly increased risk for peri-operative myocardial ischaemia.
All patients were monitored overnight pre-operatively for a mean of 15 hours and for two nights post-operatively for a mean of 31 hours.

Evidence of ECG interventricular conduction defects, abnormal resting ST segments, digoxin therapy or left ventricular strain pattern excluded patients from the study due to difficulty in analysing their ECGs. 12 lead ECGs were coded for evidence of ischaemia according to the Minnesota classification. Ambulatory ECG monitoring was undertaken using a Kontron Micro K1 5100, solid state, digital data recorder. Using high quality silver electrodes, leads III and CMV 5 were recorded and subsequently analysed using dedicated Kontron software.

ST depression greater than 1mm on the electrocardiogram lasting more than 1 minute and terminated only by a return to baseline for more than 1 minute was regarded as significant.

2.4 Economic Considerations

Resources used

The economic analysis was based upon 102 patients over a three month follow up period. The evaluation adopted the perspective of the health care system. All resource items associated with the interventions, with post operative stay and community care received over the follow-up period were identified, and the volumes of these resources used by each patient were recorded.

The resources used fell into three broad categories:

1. Theatre costs - these consisted of capital equipment, theatre overheads including variations for operating time and consumables.
2. Hotel costs - taking into account ward overheads and ward capital costs, length of stay and post-operative consumables and morbidity.

3. Community costs - including visits to the GP, practice nurse and hospital outpatients, and home visits from the district nurse.

**Valuation of resources**

Once the volume of resources used by each patient had been calculated, the opportunity cost of these resources (that is, the opportunity forgone to commit these resources to some other alternative use) was measured in terms of the unit costs of each resource item based on 1994/1995 market prices including (where chargeable) value added tax (VAT). These unit costs were then applied to the resource volumes to obtain a total cost per patient. Because the time from randomisation to follow-up was only three months, it was necessary to apply a discount rate to costs. However, the costs of capital equipment were computed in present value terms, as described below.

All cost data are reported as mean values, differences in means and associated 95% confidence intervals.

The cost of laser consumables was based on the usage of the SLT MD60 Neodymium:YAG contact laser with an estimated ten year lifespan (personal communication Kontron Instruments, Watford, Herts., UK), and the MTRL 10 6 mm sapphire tipped probe. Fibres were used a maximum of three times, and tips a maximum of 6 times.

The equivalent annual cost of the laser equipment was calculated by depreciating the capital cost over a ten year period, and assuming an opportunity cost of 5% per annum, which represents the real return which could have been obtained had the
capital funds been invested in some other way. This 'opportunity cost' of the capital cost is effectively the discount rate which is applied in all the economic evaluations when costs or benefits are spread over time. The cost of twice yearly servicing of the laser has also been included.

Health service facilities used by the patients, capital costs of building space, and overheads for both operating theatre facilities and ward or 'hotel' stay were valued using costs generated by the 'SAPPS' (Speciality and Procedures Pricing System) at the Churchill Hospital. Included in these overheads for both ward and operating theatre, were building and staff costs as well as a proportion of the costs for portering, catering, training etc.; that is, all the facilities necessary to run the clinical service. These overheads were allocated to patients on the basis of length of stay or theatre operating time. Theatre staff costs were attained using the mid-point on the relevant salary scale with an additional 13% added for employers' costs.

The costs of practice nurse attendance following discharge were obtained by assuming a ten minute consultation with an F grade nurse, taking the mid point on the salary scale, and the employers costs. This is in accordance with the current practice of the Oxfordshire Family Health Service Authority. The cost of a consultation with a general practitioner was costed from government expenditure plans for 1992/1993 as documented in a Department of Health report, and updated to 1994/1995 prices using the Health Specific Price Index.

The cost of retreating patients with a repeat prostatectomy was estimated using the mean values for resource use in the relevant arm of the trial. It is assumed that the variation about the mean in terms of resource use in each group is the same in retreated patients as in patients undergoing treatment on the first occasion.
Indirect costs such as loss of income borne by the patients were not an important factor in this age group, supporting the decision to adopt a health care system perspective in the economic evaluation.

**Sensitivity Analysis**

The cost of consumable equipment for contact laser prostatectomy may vary in the future as may the recurrence of benign prostatic enlargement in both trial arms. A sensitivity analysis has therefore been performed to examine the implications of making different assumptions about laser consumable costs, and re-operation rates.

The mean difference in cost between laser and TURP plotted against varying laser re-operation rates, using different assumptions on TURP re-operation rate at one year. The mean difference in the cost between the two procedures was also plotted against a percentage decrease in the cost of laser consumables (100% being the current list price). For each assumption of variation in laser consumable price, the mean cost for the procedure was re-calculated from the initial stages of the financial analysis.

Finally, the relationship between laser re-operation rate and mean difference in cost between the two procedures was examined assuming a hospital stay of one night and two district nurse visits. This assumption allows for catheter removal at home if the initial trial without catheter fails.
Chapter 3 - Results

Accurate data were available on 148 patients that were randomised; losses prior to randomisation being shown in table 1.

<table>
<thead>
<tr>
<th>Exclusion criteria</th>
<th>Numbers</th>
</tr>
</thead>
<tbody>
<tr>
<td>Previous prostate surgery</td>
<td>22</td>
</tr>
<tr>
<td>Known prostatic carcinoma</td>
<td>21</td>
</tr>
<tr>
<td>Refusal of consent</td>
<td>5</td>
</tr>
<tr>
<td>Poor English / dementia</td>
<td>7</td>
</tr>
<tr>
<td>Other</td>
<td>21</td>
</tr>
</tbody>
</table>

Table 1 - Losses prior to randomisation

Losses included under the title 'other' included those with neurological conditions but predominantly reflected a period when the laser was not available, or malfunctioned requiring repair, or when the trial co-ordinator was not available.

72 patients were treated with contact laser prostatectomy, while 76 received TURP.

The mean age in the TURP group was 70 years (standard deviation [SD] 8), compared to 69 years (SD 8) in the laser group.

3.1 Primary Outcome Measure

Symptom scores at baseline, one, three months and 1 year together with the mean change from baseline score, standard deviations and 95% confidence intervals (95%CI) around the mean change are shown below in table two. One and three month
AUA symptom score data were non-normally distributed, and Mann Whitney test (MW) has been used for the analysis. Medians and interquartile ranges are shown in table 2b.

Although mean symptom scores seem to favour the TURP at one and three months, when taking into account the baseline AUA symptom score, there is no statistically significant difference between the two groups with regard to the clinically more relevant mean change in symptom score.

<table>
<thead>
<tr>
<th>AUA Score</th>
<th>Laser</th>
<th>TURP</th>
<th>p-value (MW)</th>
<th>Laser</th>
<th>TURP</th>
<th>p-value (MW)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre-op</td>
<td>19.9  n=54 +/- 7.7</td>
<td>19.4 n=63 +/- 6.5</td>
<td>N/A</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>1 month</td>
<td>12.3  n=46 +/- 9.1</td>
<td>8.5 n=54 +/- 7.0</td>
<td>0.039</td>
<td>7.3 n=39 +/-10.6</td>
<td>95% CI 4 - 10.6</td>
<td>11.9 n=47 +/-7.5</td>
</tr>
<tr>
<td>3 months</td>
<td>9.6   n=55 +/-7.5</td>
<td>6.5 n=62 +/-5.1</td>
<td>0.029</td>
<td>10.1 n=47 +/-9.7</td>
<td>95% CI 7.3 - 12.9</td>
<td>13.6 n=54 +/-6.9</td>
</tr>
<tr>
<td>1 year</td>
<td>8.7   n=53 +/-6.5</td>
<td>5.8 n=60 +/-5.4</td>
<td>0.006</td>
<td>10.9 n=44 +/-8.4</td>
<td>95% CI 8.4 - 13.4</td>
<td>13.3 n=53 +/-7.8</td>
</tr>
</tbody>
</table>

Table 2a - AUA symptom scores

<table>
<thead>
<tr>
<th>Laser AUA score</th>
<th>TURP AUA score</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 Month 11.0 IQ range 4-19</td>
<td>6.5 IQ range 3-13</td>
</tr>
<tr>
<td>3 Months 7.0 IQ range 4-14</td>
<td>5.0 IQ range 2-9</td>
</tr>
<tr>
<td>1 Year 6.0 IQ range 3.3-15</td>
<td>4 IQ range 2-8</td>
</tr>
</tbody>
</table>

Table 2b - AUA scores - medians and interquartile ranges
Based on Barry’s definition of a small, medium or large degree of change, at one and three and 12 months the TURP patients showed a statistically significant tendency for large improvements in the AUA symptom score compared with the laser group (Chi squared p=0.02, 0.01 and 0.03 respectively) (tables 2c and 2d).

<table>
<thead>
<tr>
<th></th>
<th>Laser 1 month</th>
<th>Laser 3 months</th>
<th>TURP 1 month</th>
<th>TURP 3 months</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Small</strong></td>
<td>41% n=16</td>
<td>30% n=14</td>
<td>15% n=7</td>
<td>7% n=4</td>
</tr>
<tr>
<td><strong>Medium</strong></td>
<td>10% n=4</td>
<td>13% n=6</td>
<td>21% n=10</td>
<td>20% n=11</td>
</tr>
<tr>
<td><strong>Large</strong></td>
<td>49% n=19</td>
<td>57% n=27</td>
<td>64% n=30</td>
<td>72% n=39</td>
</tr>
</tbody>
</table>

Table 2c - Degree of change in AUA symptom score between baseline and one and three months.

At one, three and 12 months there was no significant correlation between pre-operative prostate size and symptomatic outcome in terms of change in AUA symptom score for either TURP (Pearson correlation coefficients 0.04, 0.006 and -0.08), or for laser (-0.09, 0.09 and -0.05).

<table>
<thead>
<tr>
<th></th>
<th>Laser</th>
<th>TURP</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Small</strong></td>
<td>25% n=11</td>
<td>11% n=6</td>
</tr>
<tr>
<td><strong>Medium</strong></td>
<td>21% n=9</td>
<td>9% n=5</td>
</tr>
<tr>
<td><strong>Large</strong></td>
<td>55% n=24</td>
<td>79% n=42</td>
</tr>
</tbody>
</table>

Table 2d - Degree of change in AUA symptom score between baseline and one year.
3.2 Secondary Outcome Measures

Mean maximum flow rates ($Q_{\text{max}}$) at baseline, three months and one year are shown below in table 3. Mean voided volumes at baseline and three months were: At baseline, 281 ml ($n=47$) in the laser arm (SD 123), compared to 263 ($n=52$) in the TURP arm (SD 117), and at three months 318 ml in the laser arm ($n=44$ SD 144) and 325 ml ($n=52$ SD 175) in the TURP arm.

<table>
<thead>
<tr>
<th>Qmax</th>
<th>Laser</th>
<th>TURP</th>
<th>p-value</th>
<th>Mean Change Laser</th>
<th>Mean Change TURP</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pre-op</td>
<td>11.8 ±4.5</td>
<td>11.4 ±5.0</td>
<td>N/A</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>n=48</td>
<td>n=54</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3 months</td>
<td>21.3±11.6</td>
<td>21.8±12.2</td>
<td>ns</td>
<td>10.7±1.4</td>
<td>9.6±2.4</td>
<td>ns</td>
</tr>
<tr>
<td>n=46</td>
<td>n=52</td>
<td></td>
<td>10.2-11.2</td>
<td>8.8-10.4</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 year</td>
<td>17.1±13.2</td>
<td>21.2±12.4</td>
<td>&lt;0.05</td>
<td>6.2±15.0</td>
<td>9.4±12.5</td>
<td>ns</td>
</tr>
<tr>
<td>n=42</td>
<td>n=45</td>
<td></td>
<td>0.79-11.6</td>
<td>5.2-13.6</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Table 3 - Peak urinary flow rates

At three months, there was no significant difference in peak urinary flow rate between the two treatment arms.
Pre- and peri-operative data are shown below in table 4.

<table>
<thead>
<tr>
<th></th>
<th>Laser (SD)</th>
<th>TURP (SD)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean prostate volume (cc)</td>
<td>54.2 26.3</td>
<td>51.9 24.1</td>
<td>ns</td>
</tr>
<tr>
<td></td>
<td>n= 44</td>
<td>n=48</td>
<td></td>
</tr>
<tr>
<td>Mean prostatic urethral length (cm)</td>
<td>2.7 0.8</td>
<td>2.9 1.0</td>
<td>ns</td>
</tr>
<tr>
<td></td>
<td>n=63</td>
<td>n=67</td>
<td></td>
</tr>
<tr>
<td>Mean operating time (minutes)</td>
<td>36 15</td>
<td>39 20.0</td>
<td>ns</td>
</tr>
<tr>
<td></td>
<td>n=69</td>
<td>n=69</td>
<td></td>
</tr>
<tr>
<td>Median peri-operative blood loss ml</td>
<td>39 (0-200)</td>
<td>200 (12-1600)</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td></td>
<td>n=68</td>
<td>n=69</td>
<td></td>
</tr>
</tbody>
</table>

Table 4 - pre and peri-operative data

The ranges for the peri-operative blood loss were wide, (0-200 ml for the laser patients) and (12 - 1600 ml for those receiving TURP), and four laser patients were converted to TURP peri-operatively due to profuse haemorrhage obscuring the view.

The median amount of energy delivered in the laser arm was 31052 joules (range 8542 - 108318).

No laser patient required a peri- or post-operative blood transfusion, whereas 13 TURP patients (20%) were transfused (Chi squared p < 0.001). There was one death in each arm of the study within three months in the case of the TURP arm.
Table 5 shows the mean changes in the relevant haematological and biochemical parameters for both arms of the trial, excluding those patients that received a blood transfusion.

<table>
<thead>
<tr>
<th></th>
<th>Laser</th>
<th>SD</th>
<th>TURP</th>
<th>SD</th>
<th>p-value</th>
<th>Mann-Witney test</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median change in haemoglobin g/dl</td>
<td>-0.42</td>
<td>0.73</td>
<td>-1.19</td>
<td>1.28</td>
<td>N/A</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td></td>
<td>n=50</td>
<td></td>
<td>n=52</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean change in haematocrit</td>
<td>-0.009</td>
<td>0.03</td>
<td>-0.03</td>
<td>0.04</td>
<td>&lt; 0.01</td>
<td>N/A</td>
</tr>
<tr>
<td></td>
<td>n=38</td>
<td></td>
<td>n=41</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Change in serum sodium mmol/l</td>
<td>1.7</td>
<td>3.2</td>
<td>2.1</td>
<td>3.6</td>
<td>ns</td>
<td>ns</td>
</tr>
<tr>
<td></td>
<td>n=46</td>
<td></td>
<td>n=47</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Table 5

The changes in haemoglobin and haematocrit favoured the laser arm, but there was no statistically significant difference in change in serum sodium.
Data on the volume of post-operative irrigation fluid used, length of catheterisation and length of hospital stay is shown in table 6.

<table>
<thead>
<tr>
<th></th>
<th>Laser</th>
<th>TURP</th>
<th>Mann-Witney p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median length of catheterisation (nights)</td>
<td>1 (0-9)</td>
<td>2 (1-20)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td></td>
<td>n=44</td>
<td>n=59</td>
<td></td>
</tr>
<tr>
<td>Median hospital stay (nights)</td>
<td>3 (1-10)</td>
<td>4 (1-8)</td>
<td>&lt;0.005</td>
</tr>
<tr>
<td></td>
<td>n=60</td>
<td>n=64</td>
<td></td>
</tr>
<tr>
<td>Median post-op. irrigation volume (litres)</td>
<td>6 (0-33)</td>
<td>12 (1.5-168)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td></td>
<td>n=46</td>
<td>n=57</td>
<td></td>
</tr>
</tbody>
</table>

Table 6

The ranges for length of stay were wide in both groups, due predominantly to social factors and medical comorbidity, although both hospital stay and length of catheterisation significantly favoured the laser arm.

The use of post-operative continuous bladder irrigation fluid significantly favoured the laser arm both statistically and clinically.
3.3 Complications

Seventeen patients in the laser arm failed to void once the urethral catheter was removed (28%) , compared to eight in the TURP arm (12%) - Chi squared test p < 0.05 .

Three patients who underwent TURP were subsequently found to have urethral strictures and two a bladder neck contracture (6.6% re-operation rate). Two cases of carcinoma of the prostate and one of lymphoma of the prostate were diagnosed in the TURP arm.

10 (13.9 %) laser patients required a cystoscopy for symptoms that were not improved by their original procedure , and subsequently underwent TURP , while one developed a false passage from an attempted cystoscopy by a non-urologist when admitted to another hospital with a secondary haemorrhage.

The mean prostate volume in these patients was 45.7cc (range 20-70) , and the mean amount of energy delivered was 33466 Joules (range 18735 - 44958).

These cases that required re-operation were excluded from the analysis , after their re-operation. Losses after randomisation , were due to the decision to perform three retropubic prostatectomies and one urethrotomy after the initial cystoscopy ; these were all from the laser arm.
Complications that occurred in the first three months are shown in table 7.

<table>
<thead>
<tr>
<th>Complication</th>
<th>TURP</th>
<th>Laser</th>
</tr>
</thead>
<tbody>
<tr>
<td>Haemorrhage requiring re-catheterisation</td>
<td>7 (9.2%)</td>
<td>3 (4.1%)</td>
</tr>
<tr>
<td>Haematuria for &gt; 2 weeks</td>
<td>-</td>
<td>1 (1.4%)</td>
</tr>
<tr>
<td>Proven urinary tract infection</td>
<td>3 (3.9%)</td>
<td>1 (1.3%)</td>
</tr>
<tr>
<td>Scrotal abcess</td>
<td>-</td>
<td>1 (1.3%)</td>
</tr>
<tr>
<td>Incontinence</td>
<td>1 (1.3%)</td>
<td>-</td>
</tr>
<tr>
<td>Prostatitis</td>
<td>-</td>
<td>1 (1.3%)</td>
</tr>
</tbody>
</table>

Table 7 Complications

Urinary tract infection was defined as a significant growth in a mid-stream specimen.

The diagnosis of prostatitis was clinical, based on the symptoms of fever, dysuria and a tender prostate. The one incontinent patient had proven sphincter damage at cystoscopy.
3.4 Quality of Life Data.

Baseline, one, three and 12 month SF-36 data together with standard deviations are shown in table 8 and graphs one and two.

<table>
<thead>
<tr>
<th></th>
<th>Pre-operative</th>
<th>1 month</th>
<th>3 months</th>
<th>1 year</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Laser TURP</td>
<td>Laser TURP</td>
<td>Laser TURP</td>
<td>Laser TURP</td>
</tr>
<tr>
<td>PF</td>
<td>68.4±26.6</td>
<td>72.7±26.5</td>
<td>72.3±25.0</td>
<td>72.1±26.5</td>
</tr>
<tr>
<td></td>
<td>n=59</td>
<td>n=63</td>
<td>n=56</td>
<td>n=52</td>
</tr>
<tr>
<td></td>
<td>66.4±25.9</td>
<td>72.9±25.2</td>
<td>71.8±26.7</td>
<td>76.7±22.8</td>
</tr>
<tr>
<td></td>
<td>n=49</td>
<td>n=54</td>
<td>n=63</td>
<td>n=59</td>
</tr>
<tr>
<td></td>
<td>51.7±41.1</td>
<td>62.9±41.7</td>
<td>57.5±43.2</td>
<td>61.4±42.3</td>
</tr>
<tr>
<td></td>
<td>n=57</td>
<td>n=54</td>
<td>n=63</td>
<td>n=59</td>
</tr>
<tr>
<td></td>
<td>60.6±41.1</td>
<td>71.6±40.6</td>
<td>68.2±42.8</td>
<td>67.8±39.4</td>
</tr>
<tr>
<td></td>
<td>n=48</td>
<td>n=54</td>
<td>n=62</td>
<td>n=58</td>
</tr>
<tr>
<td></td>
<td>70.8±34.3</td>
<td>72.9±32.1</td>
<td>83.9±23.8</td>
<td>80.4±29.7</td>
</tr>
<tr>
<td></td>
<td>n=59</td>
<td>n=63</td>
<td>n=61</td>
<td>n=56</td>
</tr>
<tr>
<td></td>
<td>70.5±32.5</td>
<td>79.7±25.0</td>
<td>77.7±27.6</td>
<td>75.8±19.7</td>
</tr>
<tr>
<td></td>
<td>n=50</td>
<td>n=57</td>
<td>n=52</td>
<td>n=57</td>
</tr>
<tr>
<td>RP</td>
<td>64.3±42.4</td>
<td>72.7±27.5</td>
<td>79.4±19.4</td>
<td>62.4±22.2</td>
</tr>
<tr>
<td></td>
<td>n=61</td>
<td>n=49</td>
<td>n=54</td>
<td>n=62</td>
</tr>
<tr>
<td></td>
<td>69.2±40.9</td>
<td>79.7±25.0</td>
<td>67.1±18.7</td>
<td>62.1±22.5</td>
</tr>
<tr>
<td></td>
<td>n=69</td>
<td>n=57</td>
<td>n=61</td>
<td>n=57</td>
</tr>
<tr>
<td></td>
<td>50.7±33.1</td>
<td>64.2±19.4</td>
<td>62.3±22.2</td>
<td>62.5±22.5</td>
</tr>
<tr>
<td></td>
<td>n=48</td>
<td>n=57</td>
<td>n=54</td>
<td>n=57</td>
</tr>
<tr>
<td>RM</td>
<td>65.5±38.1</td>
<td>70.8±34.3</td>
<td>79.4±32.1</td>
<td>79.0±32.1</td>
</tr>
<tr>
<td></td>
<td>n=59</td>
<td>n=64</td>
<td>n=57</td>
<td>n=62</td>
</tr>
<tr>
<td></td>
<td>70.5±32.5</td>
<td>79.7±25.0</td>
<td>67.1±18.7</td>
<td>62.4±22.2</td>
</tr>
<tr>
<td></td>
<td>n=50</td>
<td>n=57</td>
<td>n=61</td>
<td>n=57</td>
</tr>
<tr>
<td></td>
<td>70.3±22.2</td>
<td>64.2±19.4</td>
<td>62.3±22.2</td>
<td>62.5±22.5</td>
</tr>
<tr>
<td></td>
<td>n=48</td>
<td>n=57</td>
<td>n=54</td>
<td>n=57</td>
</tr>
<tr>
<td>SF</td>
<td>76.1±27.2</td>
<td>72.7±27.5</td>
<td>79.4±19.4</td>
<td>62.4±22.2</td>
</tr>
<tr>
<td></td>
<td>n=62</td>
<td>n=68</td>
<td>n=61</td>
<td>n=56</td>
</tr>
<tr>
<td></td>
<td>82.0±23.4</td>
<td>79.7±25.0</td>
<td>77.7±27.6</td>
<td>80.4±29.7</td>
</tr>
<tr>
<td></td>
<td>n=64</td>
<td>n=57</td>
<td>n=52</td>
<td>n=56</td>
</tr>
<tr>
<td></td>
<td>79.7±25.0</td>
<td>83.9±23.8</td>
<td>80.3±17.8</td>
<td>75.8±19.7</td>
</tr>
<tr>
<td></td>
<td>n=57</td>
<td>n=61</td>
<td>n=52</td>
<td>n=57</td>
</tr>
<tr>
<td>MH</td>
<td>74.8±17.3</td>
<td>78.0±16.0</td>
<td>79.4±19.4</td>
<td>62.4±22.2</td>
</tr>
<tr>
<td></td>
<td>n=62</td>
<td>n=67</td>
<td>n=57</td>
<td>n=61</td>
</tr>
<tr>
<td></td>
<td>78.1±14.3</td>
<td>79.4±17.5</td>
<td>79.0±17.2</td>
<td>80.3±17.8</td>
</tr>
<tr>
<td></td>
<td>n=49</td>
<td>n=57</td>
<td>n=54</td>
<td>n=52</td>
</tr>
<tr>
<td></td>
<td>64.2±19.4</td>
<td>76.6±15.3</td>
<td>79.0±17.2</td>
<td>80.3±17.8</td>
</tr>
<tr>
<td></td>
<td>n=48</td>
<td>n=57</td>
<td>n=54</td>
<td>n=52</td>
</tr>
<tr>
<td></td>
<td>62.3±22.2</td>
<td>79.4±17.5</td>
<td>79.0±17.2</td>
<td>80.3±17.8</td>
</tr>
<tr>
<td></td>
<td>n=54</td>
<td>n=61</td>
<td>n=52</td>
<td>n=57</td>
</tr>
<tr>
<td>VT</td>
<td>59.2±22.3</td>
<td>65.6±18.5</td>
<td>64.2±19.4</td>
<td>62.3±22.2</td>
</tr>
<tr>
<td></td>
<td>n=62</td>
<td>n=67</td>
<td>n=57</td>
<td>n=61</td>
</tr>
<tr>
<td></td>
<td>55.5±19.6</td>
<td>62.3±22.2</td>
<td>67.1±18.7</td>
<td>80.8±24.0</td>
</tr>
<tr>
<td></td>
<td>n=48</td>
<td>n=54</td>
<td>n=61</td>
<td>n=53</td>
</tr>
<tr>
<td></td>
<td>77.5±25.4</td>
<td>57.5±16.4</td>
<td>81.4±24.1</td>
<td>80.8±24.0</td>
</tr>
<tr>
<td></td>
<td>n=50</td>
<td>n=54</td>
<td>n=64</td>
<td>n=59</td>
</tr>
<tr>
<td></td>
<td>51.7±13.9</td>
<td>52.0±15.8</td>
<td>81.4±24.1</td>
<td>80.8±24.0</td>
</tr>
<tr>
<td></td>
<td>n=49</td>
<td>n=63</td>
<td>n=53</td>
<td>n=59</td>
</tr>
<tr>
<td>BP</td>
<td>72.3±28.0</td>
<td>68.4±26.1</td>
<td>78.3±21.6</td>
<td>78.6±25.2</td>
</tr>
<tr>
<td></td>
<td>n=63</td>
<td>n=50</td>
<td>n=54</td>
<td>n=53</td>
</tr>
<tr>
<td></td>
<td>70.5±17.7</td>
<td>77.5±25.4</td>
<td>81.4±24.1</td>
<td>80.8±24.0</td>
</tr>
<tr>
<td></td>
<td>n=67</td>
<td>n=57</td>
<td>n=64</td>
<td>n=59</td>
</tr>
<tr>
<td></td>
<td>54.7±16.0</td>
<td>57.5±16.4</td>
<td>81.4±24.1</td>
<td>80.8±24.0</td>
</tr>
<tr>
<td></td>
<td>n=49</td>
<td>n=54</td>
<td>n=65</td>
<td>n=59</td>
</tr>
<tr>
<td></td>
<td>76.7±22.8</td>
<td>81.4±24.1</td>
<td>81.4±24.1</td>
<td>80.8±24.0</td>
</tr>
<tr>
<td>HP</td>
<td>64.8±22.4</td>
<td>68.4±26.1</td>
<td>78.3±21.6</td>
<td>78.6±25.2</td>
</tr>
<tr>
<td></td>
<td>n=61</td>
<td>n=50</td>
<td>n=54</td>
<td>n=53</td>
</tr>
<tr>
<td></td>
<td>70.5±17.7</td>
<td>57.5±16.4</td>
<td>52.0±15.8</td>
<td>62.0±22.6</td>
</tr>
<tr>
<td></td>
<td>n=67</td>
<td>n=56</td>
<td>n=63</td>
<td>n=52</td>
</tr>
<tr>
<td></td>
<td>90.5±13.9</td>
<td>57.5±16.4</td>
<td>52.0±15.8</td>
<td>62.0±22.6</td>
</tr>
<tr>
<td></td>
<td>n=49</td>
<td>n=54</td>
<td>n=63</td>
<td>n=52</td>
</tr>
</tbody>
</table>

Table 8- SF 36 values

HP = Health Perception
PF = Physical Functioning
SF = Social Functioning
RP = Role limitation due to physical problems
RM = Role limitation due to mental problems
BP = Bodily Pain
MH = Mental Health
VT = Vitality / Energy
Graph 1 - Baseline, one, three and 12 month SF-36 values in laser arm.

Graph 2 - Baseline, one, three and 12 month SF-36 values in TURP arm.
Effect sizes for the eight domains of the SF-36 from baseline to one, three and 12 months are shown in table 9.

<table>
<thead>
<tr>
<th>SF-36 domain</th>
<th>Laser</th>
<th>TURP</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1 month</td>
<td>3 months</td>
</tr>
<tr>
<td>PF</td>
<td>0.52</td>
<td>-0.17</td>
</tr>
<tr>
<td>RP</td>
<td>0.56</td>
<td>0.03</td>
</tr>
<tr>
<td>RM</td>
<td>0.08</td>
<td>0.16</td>
</tr>
<tr>
<td>SF</td>
<td>0.36</td>
<td>-0.20</td>
</tr>
<tr>
<td>MH</td>
<td>-0.09</td>
<td>-0.10</td>
</tr>
<tr>
<td>VT</td>
<td>0.17</td>
<td>-0.14</td>
</tr>
<tr>
<td>BP</td>
<td>0.14</td>
<td>-0.21</td>
</tr>
<tr>
<td>HP</td>
<td>0.45</td>
<td>0.33</td>
</tr>
</tbody>
</table>

Table 9 - Effect sizes for domains of SF-36

Effect sizes from baseline to one, three and 12 months are shown below (table 10) for AUA-7 score, bothersome score and peak urinary flow rate (Q max) changes.

In the case of the SF-36 and urinary flow rate, a negative effect size score represents an improvement in that area; with regard to AUA score and bothersome score, a positive effect size represents a decrease in score and consequently an improvement.

Bothersome scores themselves at baseline, one, three and twelve months are also given for the laser arm (table 11) and for the TURP arm (table 12):

<table>
<thead>
<tr>
<th></th>
<th>Laser</th>
<th>TURP</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td>AUA 7</td>
<td>0.99</td>
<td>1.34</td>
</tr>
<tr>
<td>Bothersome score</td>
<td>0.43</td>
<td>0.97</td>
</tr>
<tr>
<td>Q max</td>
<td>n/a</td>
<td>-2.11</td>
</tr>
</tbody>
</table>

Table 10 - Effect sizes for primary and secondary outcome measures
<table>
<thead>
<tr>
<th>Baseline</th>
<th>5.9 n=59</th>
<th>3.0</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 month</td>
<td>4.6 n=45</td>
<td>3.5</td>
</tr>
<tr>
<td>3 months</td>
<td>2.9 n=54</td>
<td>3.0</td>
</tr>
<tr>
<td>1 year</td>
<td>2.5 n=52</td>
<td>3.0</td>
</tr>
</tbody>
</table>

Table 11- BPH impact index scores in laser arm

<table>
<thead>
<tr>
<th>Baseline</th>
<th>5.9 n=68</th>
<th>2.3</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 month</td>
<td>3.3 n=56</td>
<td>3.3</td>
</tr>
<tr>
<td>3 months</td>
<td>2.4 n=64</td>
<td>3.0</td>
</tr>
<tr>
<td>1 year</td>
<td>1.6 n=59</td>
<td>1.9</td>
</tr>
</tbody>
</table>

Table 12 - BPH impact index scores in TURP arm

At baseline as expected with a randomised sample, there was no significant difference between the two groups (p=0.859). At both one and three months, again there was no statistical difference between the two groups (p=0.069 and 0.371 respectively).
Graphs 3 and 4 show the effect size calculations at one and three months for the AUA -7 symptom score, bothersome score, peak urinary flow rate and representative SF-36 values between baseline and one and three months respectively.
Large changes have occurred in AUA symptom score, bothersome score and peak urinary flow rate.

Little change has been recorded in quality of life as measured by the SF-36, the only domains showing any appreciable changes, being health perception, role limitation due to physical problems and physical functioning. The change in these domains indicates a worsening of health between baseline and follow up.

Graph 4b shows the effect size changes between baseline and 12 months.

Once again, large changes have taken place in AUA symptom score, bothersome score and peak urinary flow rate, whilst little change has occurred in quality of life as measured by the SF-36.
3.5 Sexual function data

Pre-operatively, 55% of the patients claimed to be potent in the year prior to surgery while 76 patients (84%) reported an erection 'a few times or more' within the month prior to surgery (table 13), although 24% (n=9) of the laser patients who replied reported 'difficulty maintaining an erection which prevented sexual intercourse in the past month' compared with 40% n=20 of the TURP patients (table 14).

Table 15 shows the pre-operative replies to the question of how spoilt their sex life had become as a result of perceived prostatic problems. There were no statistically significant associations at baseline between the extent to which patients felt their sex life had been spoilt by their prostate problems and prostate volume, age or whether the patient had been in retention pre-operatively.

Table 13 shows the patients' responses to the question 'over the past month have you been able to have erections when you were sexually stimulated?'

There was no significant difference between the laser and TURP groups with regard to these responses: overall, 35 patients (39%) reported an erection most of the time or 'always' during the past month. When asked whether they had difficulty maintaining an erection, which prevented them from having intercourse, 9 of the laser patients (24%) compared with 20 of the TURP patients (40%) reported this. However, more of the laser patients did not attempt sexual intercourse (34% v 22% (Table 14)).

There were no significant differences between the study groups with respect to how spoilt their sex life had become as a result of their prostate problem (table 15). Overall, 30 patients (33%) reported that their sex life had not been spoilt, while 24 patients (26%) reported that it had been spoilt considerably or completely.
3 month post operative data

Overall 29 patients (40%) said their sex life had improved as a result of surgery. There was no significant difference between the two study groups: 44% (n=14) of the laser patients reported an improvement in their sex life, compared with 38% (n=15) of the TURP group. 44% of the patients reported no change; (laser 50% [n=14], TURP 40% [n=16]).

4% (n=1) of the laser patients who had answered both at baseline and three months and were potent pre-operatively, were impotent, compared with 3% (n=1) of the TURP group (ns).

There was no association between prostate volume, age or pre-operative catheterisation and the degree to which the patient reported his sex life had been spoilt either overall or in the laser or the TURP groups separately.

Overall, there were significant associations between the three SF-36 domains of energy/vitality, mental health and role limitation due to physical problems and the degree to which the patients' sex life remained spoilt (analysis of variance p=0.0001, p=0.015 and p=0.05 respectively). Those patients who reported worse SF-36 scores had poorer sexual function.

With regard to the extent that their 'prostatic problem' had spoilt their sex life, 38% (n=10) of the patients who answered 'not at all' changed their reply to 'slightly', 'somewhat', 'considerably' or 'completely' following prostatectomy. Six of these patients reported only a slight deterioration. Breaking these figures down by operation, 22% of the laser patients who pre-operatively reported that their prostate problem had not spoilt their sex life, said that it had been spoilt at three months, compared with 52% of the TURP group (Chi squared = ns).
Considering sex life and satisfaction with treatment, overall there was a tendency for those patients who were very satisfied to have no sexual problems, and for those who were less satisfied to feel that their sex-life had been spoilt by surgery (Spearman Correlation $r=0.264$, $n=90$, $p=<0.012$).

On breaking these results down by treatment, this trend was evident for both treatments, although it was only statistically significant for the TURP group (Spearman $r=0.263$, $n=46$, $p=<0.03$).

When asked 'Would you recommend this operation to a friend?'; overall 85% of the patients would recommend the operation ($n=108$). 93% ($n=56$) of those patients who reported that their sex life had not been spoilt or only slightly spoilt said they would have the operation, or would recommend it to a friend, compared with 69% ($n=20$) of those who claimed their sex life was somewhat or completely spoilt (Fisher’s exact test $p=0.004$). There was no significant difference between treatment groups with regard to this association.

<table>
<thead>
<tr>
<th>Laser</th>
<th>Pre-op</th>
<th>3 months</th>
<th>TURP</th>
<th>Pre-op</th>
<th>3 months</th>
</tr>
</thead>
<tbody>
<tr>
<td>Never</td>
<td>13.2% n=5</td>
<td>18.4% n=7</td>
<td>17.3% n=9</td>
<td>8.7% n=4</td>
<td></td>
</tr>
<tr>
<td>A few times</td>
<td>39.5% n=15</td>
<td>23.7% n=9</td>
<td>38.5% n=20</td>
<td>32.6% n=15</td>
<td></td>
</tr>
<tr>
<td>About half the time</td>
<td>5.3% n=2</td>
<td>2.6% n=1</td>
<td>7.7% n=4</td>
<td>15.2% n=7</td>
<td></td>
</tr>
<tr>
<td>Most of the time</td>
<td>15.8% n=6</td>
<td>28.9% n=11</td>
<td>21.2% n=11</td>
<td>26.1% n=12</td>
<td></td>
</tr>
<tr>
<td>Always</td>
<td>26.3% n=10</td>
<td>26.3% n=10</td>
<td>15.4% n=8</td>
<td>17.4% n=8</td>
<td></td>
</tr>
</tbody>
</table>

Table13 - Response to the question ‘over the past month have you been able to have erections when you were sexually stimulated?’
<table>
<thead>
<tr>
<th></th>
<th>Laser Pre-op</th>
<th>Laser 3 months</th>
<th>TURP Pre-op</th>
<th>TURP 3 months</th>
</tr>
</thead>
<tbody>
<tr>
<td>Difficulty</td>
<td>24%</td>
<td>19%</td>
<td>40%</td>
<td>27%</td>
</tr>
<tr>
<td></td>
<td>n=9</td>
<td>n=7</td>
<td>n=20</td>
<td>n=12</td>
</tr>
<tr>
<td>No difficulty</td>
<td>42%</td>
<td>46%</td>
<td>38.0%</td>
<td>49%</td>
</tr>
<tr>
<td></td>
<td>n=16</td>
<td>n=17</td>
<td>n=19</td>
<td>n=22</td>
</tr>
<tr>
<td>Not attempted</td>
<td>34%</td>
<td>35%</td>
<td>22.0%</td>
<td>24%</td>
</tr>
<tr>
<td></td>
<td>n=13</td>
<td>n=13</td>
<td>n=11</td>
<td>n=11</td>
</tr>
</tbody>
</table>

Table 14 - Have you had difficulty in maintaining an erection which has prevented you from having sexual intercourse in the past month?

<table>
<thead>
<tr>
<th></th>
<th>Laser Pre-op</th>
<th>Laser 3 months</th>
<th>TURP Pre-op</th>
<th>TURP 3 months</th>
</tr>
</thead>
<tbody>
<tr>
<td>Not at all</td>
<td>31.6%</td>
<td>52.6%</td>
<td>34.0%</td>
<td>23.9%</td>
</tr>
<tr>
<td></td>
<td>n=12</td>
<td>n=20</td>
<td>n=18</td>
<td>n=11</td>
</tr>
<tr>
<td>Slightly</td>
<td>18.4%</td>
<td>10.5%</td>
<td>11.3%</td>
<td>47.8%</td>
</tr>
<tr>
<td></td>
<td>n=7</td>
<td>n=4</td>
<td>n=6</td>
<td>n=22</td>
</tr>
<tr>
<td>Somewhat</td>
<td>26.3%</td>
<td>15.8%</td>
<td>26.4%</td>
<td>10.9%</td>
</tr>
<tr>
<td></td>
<td>n=10</td>
<td>n=6</td>
<td>n=14</td>
<td>n=5</td>
</tr>
<tr>
<td>Considerably</td>
<td>18.4%</td>
<td>10.5%</td>
<td>20.8%</td>
<td>15.2%</td>
</tr>
<tr>
<td></td>
<td>n=7</td>
<td>n=4</td>
<td>n=11</td>
<td>n=7</td>
</tr>
<tr>
<td>Completely</td>
<td>5.3%</td>
<td>10.5%</td>
<td>7.5%</td>
<td>2.2%</td>
</tr>
<tr>
<td></td>
<td>n=2</td>
<td>n=4</td>
<td>n=4</td>
<td>n=1</td>
</tr>
</tbody>
</table>

Table 15 - Response to the question 'to what extent do you feel that your sex life has been spoilt by your prostate problem'?
3.6 Economic Results

Table 16 shows the breakdown of the baseline mean cost of each procedure in £ Sterling (rounded) with associated 95% confidence intervals (CI).

<table>
<thead>
<tr>
<th></th>
<th>Theatre overheads</th>
<th>Theatre Consumables</th>
<th>Total Theatre Costs</th>
<th>Hotel Costs</th>
<th>Community Costs</th>
<th>Total Health Service Costs</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>TURP</strong> (n=49)</td>
<td>376</td>
<td>58</td>
<td>435</td>
<td>417</td>
<td>131</td>
<td>984</td>
</tr>
<tr>
<td><strong>Laser</strong> (n=53)</td>
<td>367</td>
<td>210</td>
<td>640</td>
<td>375</td>
<td>99</td>
<td>1115</td>
</tr>
<tr>
<td><strong>Mean difference (95% CI)</strong></td>
<td>9 (-46, 64)</td>
<td>-152 (-164, -140)</td>
<td>-205 (-263, -148)</td>
<td>42 (-22,107)</td>
<td>33 (-33, 98)</td>
<td>-131 (-248, -13)</td>
</tr>
</tbody>
</table>

Table 16: Mean costs per case, mean difference in costs per case and 95% confidence intervals of laser and TURP groups at 3 months follow-up, £S 1994.

These are the baseline results, making no assumptions about re-operation rates for either group. The main area in which costs are significantly different is theatre costs which are £205 or 47% higher in the laser group (CI £148 to £263), at £640 compared with £435 in the TURP group. The theatre costs difference is attributable entirely to theatre consumables, which averaged £210 in the laser group compared with £58 in the TURP group; a difference of £152 (CI £140-£164).

The other categories of cost (hotel and community costs) are slightly lower in the laser group, but these differences are not significantly different. The mean total health service costs for the laser group are £1115 per patient, compared with £984 in the TURP group, an excess cost of £131 or 13% (CI £13-£248).
Graph five shows the mean difference in cost between laser and TURP plotted against varying laser re-operation rates, using varied assumptions on the TURP re-operation rate at one year. Laser surgery does not become financially viable until the re-operation rate for TURP rises to 20% at one year.

Graph six again shows the mean difference in cost between the two procedures plotted against varying laser consumable costs, assuming a 5% re-operation rate for both types of surgery at five years.

Graph seven sets hotel costs at one night, and adds two district nurse visits allowing for catheter removal in the community if trial without voiding fails.
Mean difference in costs v re-operation rates

TURP Reop Rates
- 1%
- 5%
- 10%
- 15%
- 20%
- 25%
- 30%

Laser Reop Rates

Graph 5
Mean Difference in cost Vs Varying Laser Consumables

Mean Difference £

Graph 6
Mean Difference in costs Vs Laser reoperation rates Reop rate
(Hospital stay = 1 Night + 2 District Nurse Visits)
3.7 Use of community services

The mean number of visits to the general practitioner (GP) in the laser arm within 1 month of discharge was 1.18 (95% CI ± 0.352) compared with 0.90 (95% CI ± 2.88) in the TURP arm (Mann-Whitney p value = ns). The TURP arm data were skewed by one patient who made eighteen visits to his GP. The laser patients were seen more often by a practice nurse (table 17), mean number of visits 1.3 (95% CI ± 0.782) in the laser arm, compared with 0.158 (95% CI ± 1.82) in the TURP arm (Mann Whitney p value = 0.011).

There was no statistically significant difference between the 2 arms with regard to mean number of district nurse visits: 0.34 (95% CI ± 0.23) in the laser arm compared with 0.19 (95% CI ± 1.62) in the TURP arm (p = ns).

3.8 Cardiac morbidity data

Accurate data were available on a total of 62 patients. Baseline data are shown below in table 17.

<table>
<thead>
<tr>
<th></th>
<th>Mean Age and range in years</th>
<th>Pre-op IHD</th>
<th>Pre-op SMI</th>
<th>Anaesthetic time (minutes)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Laser</td>
<td>72 (57-72)</td>
<td>33% n=10</td>
<td>7% n=2</td>
<td>61.5 ±20.5</td>
</tr>
<tr>
<td>n=30</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>TURP</td>
<td>71 (47-83)</td>
<td>22% n=7</td>
<td>25% n=8</td>
<td>62.5 ±31.5</td>
</tr>
<tr>
<td>n=32</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Table 17 - Baseline data on cardiac monitored patients.

There were no statistically significant differences at baseline between the groups with regard to anaesthesia time (non-parametric analysis of variance = ns), incidence of ischaemic heart disease (Chi squared = ns) and the presence of pre-operative SMI.
(Fishers exact test $p=ns$).

Post-operatively, 5 laser patients (17%) and 8 TURP patients (25%) patients had evidence of SMI. However only three patients in the TURP and laser arm showed any change in their SMI status.

One laser patient developed an arrhythmia within three months of his surgery. He had undergone previous coronary artery bypass grafting, but interestingly showed no pre-operative evidence of SMI. One patient with no pre-operative history, or peri-operative cardiac ischaemia, suffered a myocardial infarction within 3 months.
Chapter 4  Conclusions

Primary outcome measure

Based on the AUA symptom score as the pre-defined primary outcome measure a number of conclusions can be confidently drawn in the knowledge that adequate statistical power exists.

The AUA symptom score at one month was certainly worse in the patients who underwent contact laser prostatectomy, and can be explained by the delayed sloughing of necrotic prostate and possibly the depth of burn beyond the sapphire tip of the probe leading to a degree of oedema. Although no cystoscopic follow up has been performed in this study, endoscopic examination of those patients who underwent re-operation following laser prostatectomy, has shown that the ‘tags’ of ischaemic prostate do disappear leaving a smooth cavity.

At three months it has been shown that, with regard to the important outcome measure of absolute change in AUA symptom score, there is no statistical difference between TURP and laser prostatectomy. One year data have shown a similar trend suggesting that in those patients with a successful outcome there, is nothing to choose between the two techniques when the aim is to improve symptoms. However, throughout the study, those patients that underwent traditional endoscopic surgery have shown a trend towards a larger improvement in symptom score.

Little work has been carried out on the important question of how a subjective assessment of change in symptom frequency depends on the baseline score. As has been previously mentioned, Barry et al have looked at the question of what absolute decrease in AUA symptom score is clinically relevant, and have recently addressed
what degree of *mean reduction* in this instrument is clinically relevant and perceived as beneficial by the patient. The mean change in symptom score from baseline to one year in the laser and TURP groups reported in this study (10.9 and 13.3 respectively) equates with a subjective global improvement of 'excellent' to 'very good'.

If prostate surgery is to be offered to the symptomatic patient, then one can state with confidence, based on these data, that contact laser prostatectomy offers a satisfactory outcome at one year in terms of symptom improvement.

Peak urinary flow rates have followed a similar trend to symptom scores, with no statistically significant difference in *absolute change* in flow rate between the two treatment options. However, the question of what magnitude of change in flow rate is perceptible or indeed important to patients still remains unanswered.

Secondary outcome measures of peri-operative blood loss, length of catheterisation and hospital stay also favour the laser patients. However, the high failure of initial voiding in the laser patients, and the re-operation rate of 13.9% at one year, are important factors that must not be overlooked. This re-operation rate must be taken into context with the four patients who were randomised to laser and then underwent TURP due to intra-operative bleeding. The combined 'failure and re-operation rate' then climbs to 18.4%. However, this seemingly very high re-operation rate should be considered in the context of the pragmatic scientific formality of this study, where a definite learning curve was inherent and there was no limit with regard to prostate size. In fact, 50% of the patients in the laser arm that underwent re-operation had an indwelling urethral catheter prior to surgery, and the mean prostate volume of the group undergoing repeat surgery was 47cc. These factors traditionally have always predisposed to a less satisfactory outcome following endoscopic prostatectomy.
Although morbidity rates vary dramatically following TURP, the procedure still retains a risk for the patient in terms of predominantly primary haemorrhage.

Melchior et al reported an incidence of haemorrhage, defined as patients requiring a blood transfusion, of 2.5 per cent intraoperatively, and 3.7 per cent post operatively.

A series of 388 transurethral resections was subsequently reported by Doll et al with significantly higher rate of bleeding [13%], which led to clot retention in 11%, and resulted in the need for immediate transurethral resection in 2 patients. Perhaps the definitive report on post-operative morbidity following TURP has come from the National Prostatectomy Audit (Emberton personal communication), with a 90 day mortality of 2.3%, and a 12% re-operation rate.

Thorpe et al, as part of the Northern Regional Prostate Audit, reviewed the results of 1396 transurethral resections, finding an overall blood transfusion rate of 2.4%, but perhaps more importantly, 2.0% of patients required returning to theatre due to haemorrhage, clot retention or early repeat TURP due to failure to void following catheter removal.

This morbidity must not be forgotten, and the seemingly high complication rates that are associated with contact vaporisation prostatectomy should be contrasted with the reduced life-threatening morbidity resulting from blood loss. The sample size of this study is however far too small to detect and compare a rare complication such as mortality.
Quality of life

The data presented here suggest that at three months, the health state of the patients undergoing either TURP or laser prostatectomy as measured on the SF-36 was broadly similar. Little change had occurred other than 'general health perception' where TURP patients indicated considerable decline in their scores over the period as compared to laser patients. This may suggest that the severity of the operation leads these men to become more concerned about their general health and health state than they had been prior to surgery. However, these general concerns do not reflect any reduction in reported health status on other dimensions. At three months however, scores on the AUA-7 and bothersome score and changes in flow rate have all shown considerable improvement, and suggest similar degrees of improvement for both arms of the trial.

The reduction in scores in 'general health perception' at three months generated the hypothesis that TURP patients may find the procedure affects their assessment of overall health and future well-being. The questions on this dimension ask patients to assess their health in general, in comparison to others, and to assess whether they are likely to become ill in future. All these assessments may be adversely affected by surgery but may not accurately reflect the impact of it upon daily functioning and well being. Indeed, this claim seems borne out by the small impact of the surgery on other aspects of their lives as measured by the SF-36.

However, one year data suggest that the SF-36 is of little use as an outcome measure following prostatic surgery, due to the small degree of change that takes place. It seems logical to imagine that an elderly patient with lower urinary tract symptoms may
be extremely ‘bothered’ by these symptoms without them severely impinging on his general health.

What is clear from this study however, is the importance of disease specific measures of health status. The AUA-7 and BPH impact index gave clear positive indications of the impact of surgery on urological aspects of well-being.

It appears that the decline in ‘general health perception’ on the SF-36 at three months is still simply an immediate response to prostatic surgery, and that as has been reported with side-fire coagulation laser prostatectomy, improvement is delayed until at least three months post-operatively. This finding has important implications when gaining informed consent prior to a contact vaporisation procedure.

**Sexual function data**

Sexual function is a major concern for many patients with benign prostatic enlargement, but the relationship, between potency and BPH is complicated by the fact that BPH occurs mainly in older men, at a time when potency may be declining for other reasons.

The impotence rate in the general population has been addressed infrequently, and moreover, continues to produce different estimates (Kinsey et al, Feldman et al), varying between 5% and 75% depending on age. Jonler et al have recently looked at age-related impotence and quality of life. In a sample size of 1680 men with a mean age of 61.2 years, by the age 70-79 years, only 20% of the men studied claimed to almost always have erections when sexually stimulated. Impotence and quality of life were found to be associated even when the quality of life estimates were adjusted for
Numerous authors have shown that decreased sexual function commonly occurs with ageing (Kaiser, Morley et al), predominantly as a result of vascular disease or hypogonadism. However, the subject of sexual function and quality of life in benign urological disease has been investigated infrequently (Maccione et al).

The overall pre-operative potency described here of 55% within the past year is similar to that described by Hanbury et al in a similar age group of British men, although the reported increase in sexual dysfunction one month prior to admission is surprising, and may in fact reflect more honestly sexual function in this age group.

Pre-operatively we have shown no association between problems with sexual function and prostate volume, age or urinary retention, although there was some association with the quality of life assessed with the SF-36.

Three months post-operatively, approximately 40% of each treatment arm reported an improvement in sexual function, and almost all of those patients whose sex life had not been spoilt would recommend surgery.

The impotence rate post-operatively in those men who were potent prior to surgery of between 3 and 4% in this study is similar to the findings in the above series and others (Fowler et al, Hargreave et al), although much lower than those reported in the National Prostatectomy Audit of 20.3% complete impotence.

With such small numbers in the group of men who were potent one month prior to surgery, and taking into account the response of the majority of these elderly men of "I don't know" when asked about retrograde ejaculation, it becomes impossible to make any sensible comments on the much talked about subject of retrograde ejaculation with this sample size.


Community Resource use

Although as surgeons, there is a tendency to forget the initial period of post-operative recovery following discharge from hospital, the use of community resources does consume Health Service funds, and usually only comes to light when the ‘problematic’ post-TURP patient is referred back to the Urologist.

The increased use of the GP and practice nurse by those patients who underwent contact laser postatectomy is probably a direct consequence of the natural history of the burn injury to the prostate. We have shown that symptom scores are certainly both statistically and clinically worse in the laser arm within four weeks of surgery, and one year results would suggest that the recovery period following contact vaporisation of the prostate is longer than three months. This worsening of urological health, which is also reflected by a decrease in general health as measured by the SF 36 may explain the increased use of community services in the laser patients.

Laser prostatectomy is still a technique in evolution, but the obvious way forward with this form of therapy would be to produce a more efficient laser with less heat-sink, and a probe that could rapidly vaporise a large volume of tissue. Recent advances in the delivery system have included the introduction of rigid fibres, a new side-facing contact probe and a purpose made laser ‘resectoscope’. All these technological advances will facilitate more tissue destruction, shorter operating times, and hopefully a reduced re-operation rate.

The data reported in this thesis should not therefore be treated as the answer to the question of comparability between contact laser and TURP, but merely as a sound
scientific basis upon which results can only improve.

In recent years there has been a strong move towards a more pragmatic attitude in surgical trials with a view to increasing generalisability of trial results away from efficacy and towards ‘effectiveness’, with broad inclusion criteria, non-rigid definition of interventions and the surgeon’s standard practice as the control procedure. This type of trial helps answer the question: How will the technology perform on a routine operating list, with routine anaesthesia, in a district general hospital?

Methodology of surgical intervention studies is urgently in need of further research in the area of pragmatic trial design. In particular the issue of operator experience and its effect on outcome remains little explored, despite its implications for physician training, specialisation and resource use. The shifting relative risk which may arise as a physician moves up the learning curve of a particular technique is often neglected and may lead to a misapplication of trial results. The use of statistical modelling to assess the contribution of such factors to outcome is likely to develop rapidly in future years, given the particular relevance of this issue to the expanding field of minimal access therapy.

It is no longer acceptable to undertake research that does not meet high scientific standards. Neither is it acceptable simply to say that a new urological technology “works”. The scientific quality on which such conclusions are based must be understood, as must, to which study population they apply, in what clinical setting and in whose hands, and at what cost. The trade-offs which may exist between short and long term outcome and the valuations that patients attach to these must also be considered. Finally the technology can be introduced in a manner which will maximise cost-effectiveness if best use of scarce resources is to be achieved. This is most likely
to occur if a multi-disciplinary team is involved at the stage of trial design.

The current influx of new technologies into the field of benign prostatic enlargement presents the urological community with a challenge. Collaborative work between surgeons and researchers will hopefully put an end to the vast amount of meaningless data that continue to appear in the literature and prevent inappropriate 'dabbling' in the field of MIT in Urology.

Postscript

Two year data are now available on 100 patients (laser = 47, TURP = 53). There are no statistically significant changes between the two treatment arms in AUA symptom score, BPH impact index or peak urinary flow rate. Two year data and mean changes from baseline are shown below:

<table>
<thead>
<tr>
<th></th>
<th>2 year mean</th>
<th>Mean change 0-2 years</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Laser</td>
<td>TURP</td>
</tr>
<tr>
<td>AUA score</td>
<td>7.8</td>
<td>5.7</td>
</tr>
<tr>
<td>BPH impact index</td>
<td>2.1</td>
<td>1.8</td>
</tr>
<tr>
<td>Q max</td>
<td>14.2</td>
<td>15.9</td>
</tr>
</tbody>
</table>

However, the re-operation rate has risen again - during the second year the re-operation rate in the laser arm was 4% and 2% in the TURP arm.

Further work in this field should target the reasons behind this high re-operation rate following contact laser prostatectomy, focusing on such factors as prostate volume and pre-operative urodynamic parameters that may or may not predict outcome.
References


Launois PE. 1885. De l’Appareil urinaire des Vieillards. These de Paris.


1995. The treatment of benign prostatic hyperplasia by transurethral needle ablation. BAUS abstract ; 156.


Schwalow AL. 1958. Physical review. 112; 1940.


Te EA. 1995. Transurethral electrovaporisation of the prostate. SMIT Seventh International meeting; PL 44.


Acknowledgements

This study was funded through a grant from Oxfordshire Regional Health Authority.

I am grateful to Mr. G. Fellows and Mr. J.C. Smith in the Department of Urology, the Churchill Hospital Oxford for their constant help and advice throughout the study.

Dr. C.P. Jenkinson’s help in the field of quality of life and Dr. A.M. Gray’s in the field of health economics were invaluable.

Mr. G. Watson, one of the innovators in the field of laser prostatectomy gave freely of his time and advice in the early days of the study.

The graphics included in this thesis were produced from the Department of Medical Illustration at The John Radcliffe Hospital, Oxford.

The data on cardiac comorbidity was a joint project between Dr. Gordon French and Dr. Alastair Windsor from the Nuffield Department of Anaesthetics, Oxford and the Department of Urology.

Dr. K.C Lawrence and Dr. D.B. Chappel were instrumental in setting up some of the theoretical aspects of the study but without Peter Brooks’ computing advice and patience, and Helen Doll’s expertise in data analysis the entire trial would have floundered.

Finally thanks are due to my supervisors Mr. David Cranston in the Department of Urology, Professor Mundy at The Institute of Urology and Dr. Sarah Stewart-Brown for her support in the Health Services Research Unit.
Appendix

1.0 Trial Questionnaires

2.0 Trial Consent form
The following questions ask for your views about your health, how you feel and how well you are able to do your usual activities. If you are unsure about how to answer any questions, please give the best answer you can and make any of your own comments if you like.

(Please tick one)

1. In general, would you say your health is:
   - Excellent □
   - Very good □
   - Good □
   - Fair □
   - Poor □

2. Compared to one year ago, how would you rate your health in general now?
   - Much better now than one year ago □
   - Somewhat better now than one year ago □
   - About the same □
   - Somewhat worse now than one year ago □
   - Much worse now than one year ago □
3. **HEALTH AND DAILY ACTIVITIES**

The following questions are about activities you might do during a typical day. Does your health limit you in these activities? If so, how much?

(Please tick one box on each line)

<table>
<thead>
<tr>
<th>Activities</th>
<th>Yes, limited a lot</th>
<th>Yes, limited a little</th>
<th>No, not limited at all</th>
</tr>
</thead>
<tbody>
<tr>
<td>a) Vigorous activities, such as running, lifting heavy objects, participating in strenuous sports</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>b) Moderate activities, such as moving a table, pushing a vacuum cleaner, bowling or playing golf</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>c) Lifting or carrying groceries</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>d) Climbing several flights of stairs</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>e) Climbing one flight of stairs</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>f) Bending, kneeling or stooping</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>g) Walking more than a mile</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>h) Walking half a mile</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>i) Walking 100 yards</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>j) Bathing and dressing yourself</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

4. During the past 4 weeks, have you had any of the following problems with your work or other regular daily activities as a result of your physical health?

(Answer Yes or No to each question)

<table>
<thead>
<tr>
<th>Problems</th>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td>a) Cut down on the amount of time you spent on work or other activities</td>
<td></td>
<td></td>
</tr>
<tr>
<td>b) Accomplished less than you would like</td>
<td></td>
<td></td>
</tr>
<tr>
<td>c) Were limited in the kind of work or other activities</td>
<td></td>
<td></td>
</tr>
<tr>
<td>d) Had difficulty performing the work or other activities (eg. it took extra effort)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
5. During the **past 4 weeks**, have you had any of the following problems with your work or other regular daily activities as a result of any emotional problems (such as feeling depressed or anxious)?

**(Answer Yes or No to each question)**

<table>
<thead>
<tr>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td>a)</td>
<td></td>
</tr>
<tr>
<td>b)</td>
<td></td>
</tr>
<tr>
<td>c)</td>
<td></td>
</tr>
</tbody>
</table>

6. During the **past 4 weeks**, to what extent has your physical health or emotional problems interfered with your normal social activities with family, friends, neighbours or groups?

**(Please tick one)**

| Not at all |    |
| Slightly   |    |
| Moderately |    |
| Quite a bit|    |
| Extremely  |    |

7. How much **bodily** pain have you had during the **past 4 weeks**?

| None       |    |
| Very mild  |    |
| Mild       |    |
| Moderate   |    |
| Severe     |    |
| Very severe|    |

8. During the **past 4 weeks**, how much did **pain** interfere with your normal work (including work both outside the home and housework)?

| Not at all |    |
| A little bit|    |
| Moderately |    |
| Quite a bit|    |
| Extremely  |    |
These questions are about how you feel and how things have been with you **during the past month**. (For each question, please indicate the one answer that comes closest to the way you have been feeling).

9. How much time during the past month:

<table>
<thead>
<tr>
<th>Item</th>
<th>All of the time</th>
<th>Most of the time</th>
<th>A good bit of the time</th>
<th>Some of the time</th>
<th>A little of the time</th>
<th>None of the time</th>
</tr>
</thead>
<tbody>
<tr>
<td>a)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>b)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>c)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>d)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>e)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>f)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>g)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>h)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>i)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>j)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

(Please tick one box on each line)

10. Please choose the answer that best describes how **true** or **false** each of the following statements is for you.

<table>
<thead>
<tr>
<th>Item</th>
<th>Definitely true</th>
<th>Mostly true</th>
<th>Not sure</th>
<th>Mostly false</th>
<th>Definitely false</th>
</tr>
</thead>
<tbody>
<tr>
<td>a)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>b)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>c)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>d)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Please could you tell us about your symptoms over the past month or so

(Please tick one box on each line)

<table>
<thead>
<tr>
<th>Question</th>
<th>Not at all</th>
<th>Less than 1 time in 5</th>
<th>Less than half the time</th>
<th>About half the time</th>
<th>More than half the time</th>
<th>Almost always</th>
</tr>
</thead>
<tbody>
<tr>
<td>11. How often have you had the sensation of not emptying your bladder after you finished urinating?</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>12. How often have you had to urinate again less than two hours after you finished urinating?</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>13. How often have you found you stopped and started again several times when you urinated?</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>14. How often have you found it difficult to postpone urination?</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>15. How often have you had a weak urinary stream?</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>16. How often have you had to push or strain to begin urination?</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>17. How many times did you usually get up to urinate from the time you went to bed at night until the time you got up in the morning?</td>
<td>None</td>
<td>1 time</td>
<td>2 times</td>
<td>3 times</td>
<td>4 times</td>
<td>5 or more times</td>
</tr>
</tbody>
</table>
### Over the past month:

<table>
<thead>
<tr>
<th>Question</th>
<th>None</th>
<th>Only a little</th>
<th>Some</th>
<th>A lot</th>
</tr>
</thead>
<tbody>
<tr>
<td>Over the past month:</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>18. How much physical discomfort did urinary symptoms cause you?</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>19. How much did you worry about your health because of urinary symptoms?</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>20. Overall, how bothersome has any trouble with urination been?</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>21. How much of the time has any urinary problem kept you from doing the kinds of things you would usually do?</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>22. Have you had any sexual erections in the past year?</td>
<td>Yes</td>
<td>No</td>
<td></td>
<td></td>
</tr>
<tr>
<td>If NO go to Question 26.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>23. Over the past month have you been able to have erections when you were sexually stimulated?</td>
<td>Never</td>
<td>A few times</td>
<td>About half the time</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Most of the time</td>
<td>Always</td>
<td></td>
<td></td>
</tr>
<tr>
<td>24. Have you had difficulty in maintaining an erection which has prevented you from having sexual intercourse in the past month?</td>
<td>Yes</td>
<td>No</td>
<td>Not attempted</td>
<td></td>
</tr>
<tr>
<td>25. To what extent do you feel that your sex life has been spoilt by your prostate problems?</td>
<td>Not at all</td>
<td>Slightly</td>
<td>Somewhat</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Considerably</td>
<td>Completely</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
**Please could you answer some questions about yourself**

**26. Date of birth**
- Day [ ]
- Month [ ]
- Year [ ]

**27. Do you live with other adults?**
- Yes [ ]
- No [ ]

**28. How old were you when you left full time education (school, college, or university)?**
- 16 years or less [ ]
- 17 [ ]
- 18 [ ]
- 19 years or over [ ]

**29. What is your current marital status?**
- Widowed [ ]
- Divorced/separated [ ]
- Married or living as married [ ]
- Single and never been married [ ]

**30. What is your current employment status?**
- Working full time (30 hours or more per week) [ ]
- Working part time (less than 30 hours per week) [ ]
- Caring for home or family (not seeking paid work) [ ]
- Unemployed and looking for work [ ]
- Unable to look for work due to illness or disability [ ]
- Retired and not working [ ]

**31. What is your most recent occupation?**

Please write name of job and brief details of what you actually do or did:

[ ]

Are/were you:
- A manager [ ]
- A foreman or supervisor [ ]
- Self-employed [ ]
- An employee (none of the above) [ ]

**32. Does your job or daily activity normally involve a lot of:**
- Sitting still [ ]
- Walking and standing [ ]
- Strenuous physical activity [ ]
By placing a tick (✓) in one box in each group below, please indicate which statement best describes your own health status today.

33. **Mobility**
   - I have no problems in walking about
   - I have some problems in walking about
   - I am confined to bed

34. **Self-care**
   - I have no problems with self-care
   - I have some problems with washing or dressing myself
   - I am unable to wash or dress myself

35. **Usual Activities**
   - I have no problems with performing my usual activities (eg. work, study, housework, family or leisure activities)
   - I have some problems with performing my usual activities
   - I am unable to perform my usual activities

36. **Pain/Discomfort**
   - I have no pain or discomfort
   - I have moderate pain or discomfort
   - I have extreme pain or discomfort

37. **Anxiety/Depression**
   - I am not anxious or depressed
   - I am moderately anxious or depressed
   - I am extremely anxious or depressed
To help people say how good or bad a health state is, we have drawn a scale (rather like a thermometer) on which the best state you can imagine is marked by 100 and the worst state you can imagine is marked by 0.

We would like you to indicate on this scale how good or bad is your own health today, in your opinion. Please do this by drawing a line starting from the box below (your own health state today) to whichever point on the scale indicates how good or bad your current health state is.
39. Have you had any difficulties with answering these questions? (please feel free to comment)

Yes [ ]
No [ ]

40. Any other comments:
Prostatectomy Study
Doctor's Pre-operative Questionnaire

A. HISTORY
1. Previous prostate surgery other than biopsy? Yes ☐ No ☐
2. Urinary tract infections treated in the past 12 months?
   None ☐ 1 ☐ 2 ☐ 3 ☐ 4 or more episodes ☐
3. Episodes of gross haematuria in the past 12 months?
   None ☐ 1 ☐ 2 ☐ 3 ☐ 4 or more episodes ☐
4. Episodes of clot retention (requiring catheter) in the last 12 months?
   None ☐ 1 or more episodes ☐
5. Episodes of acute retention (not due to clot retention but requiring catheter) in the last 12 months?
   None ☐ 1 ☐ 2 ☐ 3 ☐ 4 or more episodes ☐
6. Episodes of acute retention (not due to clot retention but requiring catheter) prior to one year ago?
   None ☐ 1 ☐ 2 ☐ 3 ☐ 4 or more episodes ☐
7. Currently on indwelling catheter or intermittent (at least daily) programme of catheterisation?
   Yes ☐ No ☐
8. Previous vasectomy?
   Yes ☐ No ☐

B. EXAMINATION
9. Estimate of prostate size on digital rectal examination: ☐ grams
10. Prostate gland suspicious of cancer on palpitation?
    Yes ☐ No ☐

C. INVESTIGATIONS
11. Urinalysis
    Protein ☐ Blood ☐ Glucose ☐ Other ☐
12. MSU or CSU
    RBC ☐ WBC ☐ Organisms ☐ Growth ☐
13. Flow rates

<table>
<thead>
<tr>
<th>Date</th>
<th>Average flow</th>
<th>Peak flow</th>
<th>Volume</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

14. Ultrasound

(a) Renal/Urinary tract

(b) Estimated size: Trans-abdominal

(c) Estimated size: Trans-rectal

15. Blood tests

FBC

Haematocrit

U&Es

Creatinine

Others

Prostate Specific Antigen

16. Others (i.e. not routine, not part of trial)

Urodynamics, others

D. CO-MORBIDITY

17. Does the patient have any of the following problems (if yes, give brief details including dates)?

(a) Myocardial infarction

Yes, within last 6 months

Yes, but not within last 6 months

No

(b) Angina

If Yes:

CCS Class 3

CCS Class 4

Unstable

Other

continued...
17. (continued)
   (c) Pulmonary oedema
       Yes | | No
   (d) Other medical problems
       Yes | | No

18. What medication is the patient taking?

1    2    3    4    5
   6    7    8    9    10

19. Findings on examination
    Height cm
    Weight kg
    Pulse
    Blood pressure mm Hg
Prostatectomy Study
Doctor's Peri-operative Questionnaire

Registration No. □□□□ □□□□ Trial No. □□□□ □□□□

DETAILS OF OPERATION

1. Name of surgeon(s): __________________________________________

2. Name of anaesthetist(s): ______________________________________

3. Type of operation (Laser/Electroresection): ________________________

4. Date: __/__/____

5. Anaesthetic
   a) ECG abnormal?  Yes □ No □
      If Yes, please give details ____________________________________

   b) Evidence of valvular disease?  Yes □ No □
      If Yes, please give details ____________________________________

   c) Poor medical status?  Yes □ No □
      If Yes, please give details ____________________________________

   d) Anaesthetic used
      General □ Spinal □ Epidural □ Other □

6. Time of start of operation: __/__/____

7. Time of finish of operation: __/__/____

8. Length of operation: ______ minutes

9. Number of joules used: ______
### OPERATIVE FINDINGS

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>10. Urethral stricture present?</strong></td>
<td></td>
</tr>
<tr>
<td><strong>Yes (admits No. 24 'scope)</strong></td>
<td></td>
</tr>
<tr>
<td><strong>Yes (does not admit No. 24 'scope)</strong></td>
<td></td>
</tr>
<tr>
<td><strong>No</strong></td>
<td></td>
</tr>
<tr>
<td><strong>11. Estimated length of prostatic urethra</strong></td>
<td>cm</td>
</tr>
<tr>
<td><strong>12. Estimated prostate size</strong></td>
<td>grams</td>
</tr>
<tr>
<td><strong>13. Degree of median lobe hypertrophy</strong></td>
<td></td>
</tr>
<tr>
<td>Small in proportion to rest of prostate</td>
<td></td>
</tr>
<tr>
<td>Proportionate to the rest of the prostate</td>
<td></td>
</tr>
<tr>
<td>Enlarged out of proportion to the rest of the prostate</td>
<td></td>
</tr>
<tr>
<td>Prominent, obstructing <em>ball valve</em> type median lobe</td>
<td></td>
</tr>
<tr>
<td><strong>14. Bladder trabeculation present?</strong></td>
<td></td>
</tr>
<tr>
<td>None</td>
<td></td>
</tr>
<tr>
<td>Mild (subtle trabeculation)</td>
<td></td>
</tr>
<tr>
<td>Moderate (prominent trabeculation)</td>
<td></td>
</tr>
<tr>
<td>Severe (diverticuli and sacculation)</td>
<td></td>
</tr>
<tr>
<td><strong>15. Bladder diverticuli present?</strong></td>
<td></td>
</tr>
<tr>
<td>None</td>
<td></td>
</tr>
<tr>
<td>1-2 small diverticuli</td>
<td></td>
</tr>
<tr>
<td>≥3 small diverticuli, or ≥1 large diverticulum</td>
<td></td>
</tr>
<tr>
<td><strong>16. Bladder stones present?</strong></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td></td>
</tr>
<tr>
<td>No</td>
<td></td>
</tr>
<tr>
<td><strong>17. a) Estimated blood loss</strong></td>
<td>mls</td>
</tr>
<tr>
<td><strong>b) Method used:</strong></td>
<td></td>
</tr>
<tr>
<td>Hemocue</td>
<td></td>
</tr>
<tr>
<td>Other (please specify)</td>
<td></td>
</tr>
</tbody>
</table>
18. Complications or problems (describe)

__________________________________________________________________________

__________________________________________________________________________

__________________________________________________________________________

__________________________________________________________________________

19. Deviations from protocol (with reasons)

__________________________________________________________________________

__________________________________________________________________________

__________________________________________________________________________

__________________________________________________________________________

20. Recovery room (time and problems if any)

__________________________________________________________________________

__________________________________________________________________________

__________________________________________________________________________

__________________________________________________________________________

21. Residual urine, volume in mls: □
Prostatectomy Study
Doctor's Discharge Questionnaire

Registration No.        Trial No.

DISCHARGE FORM

1. Date of admission:   
   Date of operation:   
   Date of discharge:   

2. Length of stay      nights in hospital

3. Number of transfusions
   (a) Pre-op
   (b) Post-op
   (c) Total units

4. Irrigation fluid used (total volume) litres

5. Catheter used?
   Yes  No
   Catheter removed before discharge
     Yes  No
   If YES, number of nights catheter in place:
6. Complications
   (i) DVT/PE
   (ii) UTI
   (iii) "TUR syndrome"
   (iv) MI
   (v) Chest infection
   (vi) Death
   (vii) Clot retention
   (viii) Failed TWOC

7. Flow rates

<table>
<thead>
<tr>
<th>Date</th>
<th>Average flow</th>
<th>Peak flow</th>
<th>Volume</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

INVESTIGATIONS

8. Blood tests
   Hb & Haematocrit
   U&Es
   Creatinine
The following questions ask for your views about your health, how you feel and how well you are able to do your usual activities. If you are unsure about how to answer any questions, please give the best answer you can and make any of your own comments if you like.

1. In general, would you say your health is:
   - Excellent
   - Very good
   - Good
   - Fair
   - Poor

2. Compared to one year ago, how would you rate your health in general now?
   - Much better now than one year ago
   - Somewhat better now than one year ago
   - About the same
   - Somewhat worse now than one year ago
   - Much worse now than one year ago
HEALTH AND DAILY ACTIVITIES

The following questions are about activities you might do during a typical day. Does your health limit you in these activities? If so, how much?

(Please tick one box on each line)

<table>
<thead>
<tr>
<th></th>
<th>Yes, limited a lot</th>
<th>Yes, limited a little</th>
<th>No, not limited at all</th>
</tr>
</thead>
<tbody>
<tr>
<td>a) Vigorous activities, such as running, lifting heavy objects, participating in strenuous sports</td>
<td>[ ]</td>
<td>[ ]</td>
<td>[ ]</td>
</tr>
<tr>
<td>b) Moderate activities, such as moving a table, pushing a vacuum cleaner, bowling or playing golf</td>
<td>[ ]</td>
<td>[ ]</td>
<td>[ ]</td>
</tr>
<tr>
<td>c) Lifting or carrying groceries</td>
<td>[ ]</td>
<td>[ ]</td>
<td>[ ]</td>
</tr>
<tr>
<td>d) Climbing several flights of stairs</td>
<td>[ ]</td>
<td>[ ]</td>
<td>[ ]</td>
</tr>
<tr>
<td>e) Climbing one flight of stairs</td>
<td>[ ]</td>
<td>[ ]</td>
<td>[ ]</td>
</tr>
<tr>
<td>f) Bending, kneeling or stooping</td>
<td>[ ]</td>
<td>[ ]</td>
<td>[ ]</td>
</tr>
<tr>
<td>g) Walking more than a mile</td>
<td>[ ]</td>
<td>[ ]</td>
<td>[ ]</td>
</tr>
<tr>
<td>h) Walking half a mile</td>
<td>[ ]</td>
<td>[ ]</td>
<td>[ ]</td>
</tr>
<tr>
<td>i) Walking 100 yards</td>
<td>[ ]</td>
<td>[ ]</td>
<td>[ ]</td>
</tr>
<tr>
<td>j) Bathing and dressing yourself</td>
<td>[ ]</td>
<td>[ ]</td>
<td>[ ]</td>
</tr>
</tbody>
</table>

4. During the past week, have you had any of the following problems with your work or other regular daily activities as a result of your physical health?

(Answer Yes or No to each question)

<table>
<thead>
<tr>
<th></th>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td>a) Cut down on the amount of time you spent on work or other activities</td>
<td>[ ]</td>
<td>[ ]</td>
</tr>
<tr>
<td>b) Accomplished less than you would like</td>
<td>[ ]</td>
<td>[ ]</td>
</tr>
<tr>
<td>c) Were limited in the kind of work or other activities</td>
<td>[ ]</td>
<td>[ ]</td>
</tr>
<tr>
<td>d) Had difficulty performing the work or other activities (eg. it took extra effort)</td>
<td>[ ]</td>
<td>[ ]</td>
</tr>
</tbody>
</table>
1. During the past week, have you had any of the following problems with your work or other regular daily activities as a result of any emotional problems (such as feeling depressed or anxious)?

(Answer Yes or No to each question)

<table>
<thead>
<tr>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td>a)</td>
<td></td>
</tr>
<tr>
<td>Cut down on the amount of time you spent on work or other activities</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td>b)</td>
<td></td>
</tr>
<tr>
<td>Accomplished less than you would like</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td>c)</td>
<td></td>
</tr>
<tr>
<td>Didn’t do work or other activities as carefully as usual</td>
<td></td>
</tr>
</tbody>
</table>

2. During the past week, to what extent has your physical health or emotional problems interfered with your normal social activities with family, friends, neighbours or groups?

(Please tick one)

<table>
<thead>
<tr>
<th>Not at all</th>
<th>Slightly</th>
<th>Moderately</th>
<th>Quite a bit</th>
<th>Extremely</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

3. How much bodily pain have you had during the past week?

<table>
<thead>
<tr>
<th>None</th>
<th>Very mild</th>
<th>Mild</th>
<th>Moderate</th>
<th>Severe</th>
<th>Very severe</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

4. During the past week, how much did pain interfere with your normal work (including work both outside the home and housework)?

<table>
<thead>
<tr>
<th>Not at all</th>
<th>A little bit</th>
<th>Moderately</th>
<th>Quite a bit</th>
<th>Extremely</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
These questions are about how you feel and how things have been with you during the past week. (For each question, please indicate the one answer that comes closest to the way you have been feeling).

**How much time during the past week:**

- Did you feel full of life?
- Have you been a very nervous person?
- Have you felt so down in the dumps that nothing could cheer you up?
- Have you felt calm and peaceful?
- Did you have a lot of energy?
- Have you felt downhearted and low?
- Did you feel worn out?
- Have you been a happy person?
- Did you feel tired?
- Has your health limited your social activities (like visiting friends or close relatives)?

10. Please choose the answer that best describes how true or false each of the following statements is for you.

(Please tick one box on each line)
Please could you tell us about your symptoms over the past week or so

(Please tick one box on each line)

<table>
<thead>
<tr>
<th></th>
<th>Not at all</th>
<th>Less than 1 time in 5</th>
<th>Less than half the time</th>
<th>About half the time</th>
<th>More than half the time</th>
<th>Almost always</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>6</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>7</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

1. How often have you had the sensation of not emptying your bladder after you finished urinating?

2. How often have you had to urinate again less than two hours after you finished urinating?

3. How often have you found you stopped and started again several times when you urinated?

4. How often have you found it difficult to postpone urination?

5. How often have you had a weak urinary stream?

6. How often have you had to push or strain to begin urination?

7. How many times did you usually get up to urinate from the time you went to bed at night until the time you got up in the morning?
### Over the past week:

<table>
<thead>
<tr>
<th>Question</th>
<th>None</th>
<th>Only a little</th>
<th>Some</th>
<th>A lot</th>
</tr>
</thead>
<tbody>
<tr>
<td>18. How much physical discomfort did urinary symptoms cause you?</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>19. How much did you worry about your health because of urinary symptoms?</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>20. Overall, how bothersome has any trouble with urination been?</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>21. How much of the time has any urinary problem kept you from doing the kinds of things you would usually do?</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Question</th>
<th>Not at all bothersome</th>
<th>Bothers me a little</th>
<th>Bothers me somewhat</th>
<th>Bothers me a lot</th>
</tr>
</thead>
<tbody>
<tr>
<td>18. How much physical discomfort did urinary symptoms cause you?</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>19. How much did you worry about your health because of urinary symptoms?</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>20. Overall, how bothersome has any trouble with urination been?</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Question</th>
<th>None of the time</th>
<th>A little of the time</th>
<th>Some of the time</th>
<th>All of the time</th>
</tr>
</thead>
<tbody>
<tr>
<td>18. How much physical discomfort did urinary symptoms cause you?</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>19. How much did you worry about your health because of urinary symptoms?</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>20. Overall, how bothersome has any trouble with urination been?</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Question</th>
<th>Never</th>
<th>A few times</th>
<th>About half the time</th>
<th>Most of the time</th>
<th>Always</th>
</tr>
</thead>
<tbody>
<tr>
<td>18. How much physical discomfort did urinary symptoms cause you?</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>19. How much did you worry about your health because of urinary symptoms?</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>20. Overall, how bothersome has any trouble with urination been?</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Question</th>
<th>Yes</th>
<th>No</th>
<th>Not attempted</th>
</tr>
</thead>
<tbody>
<tr>
<td>18. How much physical discomfort did urinary symptoms cause you?</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>19. How much did you worry about your health because of urinary symptoms?</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>20. Overall, how bothersome has any trouble with urination been?</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Question</th>
<th>Not at all</th>
<th>Slightly</th>
<th>Somewhat</th>
<th>Considerably</th>
<th>Completely</th>
</tr>
</thead>
<tbody>
<tr>
<td>18. How much physical discomfort did urinary symptoms cause you?</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>19. How much did you worry about your health because of urinary symptoms?</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>20. Overall, how bothersome has any trouble with urination been?</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Question</th>
<th>Yes</th>
<th>No</th>
<th>Not attempted</th>
</tr>
</thead>
<tbody>
<tr>
<td>18. How much physical discomfort did urinary symptoms cause you?</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>19. How much did you worry about your health because of urinary symptoms?</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>20. Overall, how bothersome has any trouble with urination been?</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Question</th>
<th>Not at all</th>
<th>Slightly</th>
<th>Somewhat</th>
<th>Considerably</th>
<th>Completely</th>
</tr>
</thead>
<tbody>
<tr>
<td>18. How much physical discomfort did urinary symptoms cause you?</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>19. How much did you worry about your health because of urinary symptoms?</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>20. Overall, how bothersome has any trouble with urination been?</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

2. Have you had any sexual erections in the past year? Yes No

If NO go to Question 26.

23. **Over the past week** have you been able to have erections when you were sexually stimulated?

<table>
<thead>
<tr>
<th>Frequency</th>
<th>Yes</th>
<th>No</th>
<th>Not attempted</th>
</tr>
</thead>
<tbody>
<tr>
<td>Never</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>A few times</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>About half the time</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Most of the time</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Always</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

24. Have you had difficulty in maintaining an erection which has prevented you from having sexual intercourse in the past week?

<table>
<thead>
<tr>
<th>Difficulty Level</th>
<th>Yes</th>
<th>No</th>
<th>Not attempted</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Not attempted</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

25. To what extent do you feel that your sex life has been spoilt by your prostate problems?

<table>
<thead>
<tr>
<th>Extent of Spoilage</th>
<th>Not at all</th>
<th>Slightly</th>
<th>Somewhat</th>
<th>Considerably</th>
<th>Completely</th>
</tr>
</thead>
<tbody>
<tr>
<td>Not at all</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Slightly</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Somewhat</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Considerably</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Completely</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Please could you answer some questions about problems caused by the prostate or operation

26 Have you had to use any of the following services since leaving hospital?

<table>
<thead>
<tr>
<th>Service</th>
<th>No</th>
<th>Yes</th>
<th>If yes, number of occasions</th>
</tr>
</thead>
<tbody>
<tr>
<td>General practitioner</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Practice nurse</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hospital outpatients</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>District nurse</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Physiotherapist</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Other (please specify)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Would you have liked more help from any of these services since you left hospital?

Yes □  No □

If yes, which service?

27 How much extra help from friends, family or neighbours have you had since you left hospital?

A great deal □  Quite a lot □  A little □  None □

28 Would you have liked more help from friends, family or neighbours since you left hospital?

Yes □  No □

29. (a) Do you feel ready to return to your normal activities or work yet?

Yes □  No □

(b) If YES, when was this? □ days after the operation

If NO, go to Question 31

30. Have you returned to your normal activities or work yet?

Yes □  No □

If YES, when was this? □ days after the operation
If **NO**, have you been advised not to?

Yes □  No □

If **YES**, by whom?

GP □  Relative □  Other □

Please specify:

31. Has a relative or friend taken time off work to care for you (including time to collect you from hospital)?

Yes □  No □

If yes, how long?

[ ] days  [ ] hours

32. Have you incurred any other costs as a result of your prostate problem (e.g. increased washing, pads, etc.) yourself?

Yes □  No □

If yes, please specify

_____________________________________________________________________________________________________

33. How would you rate your prostate problem now compared to when you joined the study?

Feeling much worse □
Feeling worse □
Feeling the same □
Feeling better □
Feeling much better □

34. Overall how satisfied have you been with the course of treatment so far?

Very satisfied □
Somewhat satisfied □
Neither satisfied nor dissatisfied □
Somewhat dissatisfied □
Dissatisfied □

35. What would you recommend to a friend in a similar situation as yourself?

Have operation □  Do not have operation □  Not sure □
By placing a tick (√) in one box in each group below, please indicate which statement best describes your own health status today.

36. **Mobility**
   I have no problems in walking about
   I have some problems in walking about
   I am confined to bed

37. **Self-care**
   I have no problems with self-care
   I have some problems with washing or dressing myself
   I am unable to wash or dress myself

38. **Usual Activities**
   I have no problems with performing my usual activities (eg. work, study, housework, family or leisure activities)
   I have some problems with performing my usual activities
   I am unable to perform my usual activities

39. **Pain/Discomfort**
   I have no pain or discomfort
   I have moderate pain or discomfort
   I have extreme pain or discomfort

40. **Anxiety/Depression**
   I am not anxious or depressed
   I am moderately anxious or depressed
   I am extremely anxious or depressed
To help people say how good or bad a health state is, we have drawn a scale (rather like a thermometer) on which the best state you can imagine is marked by 100 and the worst state you can imagine is marked by 0.

We would like you to indicate on this scale how good or bad is your own health today, in your opinion. Please do this by drawing a line starting from the box below (your own health state today) to whichever point on the scale indicates how good or bad your current health state is.
The following questions ask for your views about your health, how you feel and how well you are able to do your usual activities. If you are unsure about how to answer any questions, please give the best answer you can and make any of your own comments if you like.

1. In general, would you say your health is:

   - Excellent □
   - Very good □
   - Good □
   - Fair □
   - Poor □

2. Compared to one year ago, how would you rate your health in general now?

   - Much better now than one year ago □
   - Somewhat better now than one year ago □
   - About the same □
   - Somewhat worse now than one year ago □
   - Much worse now than one year ago □
HEALTH AND DAILY ACTIVITIES

The following questions are about activities you might do during a typical day. Does your health limit you in these activities? If so, how much?

(Please tick one box on each line)

<table>
<thead>
<tr>
<th>Activity</th>
<th>Yes, limited a lot</th>
<th>Yes, limited a little</th>
<th>No, not limited at all</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vigorous activities, such as running, lifting heavy objects, participating in strenuous sports</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Moderate activities, such as moving a table, pushing a vacuum cleaner, bowling or playing golf</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lifting or carrying groceries</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Climbing several flights of stairs</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Climbing one flight of stairs</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bending, kneeling or stooping</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Walking more than a mile</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Walking half a mile</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Walking 100 yards</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bathing and dressing yourself</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

During the past 4 weeks, have you had any of the following problems with your work or other regular daily activities as a result of your physical health?

(Answer Yes or No to each question)

<table>
<thead>
<tr>
<th>Problem</th>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cut down on the amount of time you spent on work or other activities</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Accomplished less than you would like</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Were limited in the kind of work or other activities</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Had difficulty performing the work or other activities (eg. it took extra effort)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
5. During the **past 4 weeks**, have you had any of the following problems with your work or other regular daily activities as a result of any emotional problems (such as feeling depressed or anxious)?

   (Answer Yes or No to each question)

<table>
<thead>
<tr>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td>![ ]</td>
<td>![ ]</td>
</tr>
</tbody>
</table>

   a) Cut down on the **amount of time** you spent on work or other activities

   b) Accomplished **less** than you would like

   c) Didn't do work or other activities as **carefully** as usual

   (Please tick one)

   | Not at all | ![ ] |
   | Slightly   | ![ ] |
   | Moderately | ![ ] |
   | Quite a bit | ![ ] |
   | Extremely  | ![ ] |

6. During the **past 4 weeks**, to what extent has your physical health or emotional problems interfered with your normal social activities with family, friends, neighbours or groups?

7. How much **bodily** pain have you had during the **past 4 weeks**?

   | None | ![ ] |
   | Very mild | ![ ] |
   | Mild | ![ ] |
   | Moderate | ![ ] |
   | Severe | ![ ] |
   | Very severe | ![ ] |

8. During the **past 4 weeks**, how much did **pain** interfere with your normal work (including work both outside the home and housework)?

   | Not at all | ![ ] |
   | A little bit | ![ ] |
   | Moderately | ![ ] |
   | Quite a bit | ![ ] |
   | Extremely | ![ ] |
These questions are about how you feel and how things have been with you during the past month. (For each question, please indicate the one answer that comes closest to the way you have been feeling).

(Please tick one box on each line)

3. How much time during the past month: All of the time Most of the time A good bit of the time Some of the time A little of the time None of the time

a) Did you feel full of life? □ □ □ □ □ □ □

b) Have you been a very nervous person? □ □ □ □ □ □ □

c) Have you felt so down in the dumps that nothing could cheer you up? □ □ □ □ □ □ □

d) Have you felt calm and peaceful? □ □ □ □ □ □ □

e) Did you have a lot of energy? □ □ □ □ □ □ □

f) Have you felt downhearted and low? □ □ □ □ □ □ □

g) Did you feel worn out? □ □ □ □ □ □ □

h) Have you been a happy person? □ □ □ □ □ □ □

i) Did you feel tired? □ □ □ □ □ □ □

j) Has your health limited your social activities (like visiting friends or close relatives)? □ □ □ □ □ □ □

10. Please choose the answer that best describes how true or false each of the following statements is for you. (Please tick one box on each line)

(Please tick one box on each line)

a) I seem to get ill more easily than other people □ □ □ □ □ □ □

b) I am as healthy as anybody I know □ □ □ □ □ □ □

c) I expect my health to get worse □ □ □ □ □ □ □

d) My health is excellent □ □ □ □ □ □ □
Please could you tell us about your symptoms over the past month or so

(Please tick one box on each line)

1. How often have you had the sensation of not emptying your bladder after you finished urinating?

<table>
<thead>
<tr>
<th>Not at all</th>
<th>Less than 1 half the time</th>
<th>Less than 1 half the time</th>
<th>About half the time</th>
<th>More than half the time</th>
<th>Almost always</th>
</tr>
</thead>
</table>

2. How often have you had to urinate again less than two hours after you finished urinating?

<table>
<thead>
<tr>
<th>Not at all</th>
<th>Less than 1 half the time</th>
<th>Less than 1 half the time</th>
<th>About half the time</th>
<th>More than half the time</th>
<th>Almost always</th>
</tr>
</thead>
</table>

3. How often have you found you stopped and started again several times when you urinated?

<table>
<thead>
<tr>
<th>Not at all</th>
<th>Less than 1 half the time</th>
<th>Less than 1 half the time</th>
<th>About half the time</th>
<th>More than half the time</th>
<th>Almost always</th>
</tr>
</thead>
</table>

4. How often have you found it difficult to postpone urination?

<table>
<thead>
<tr>
<th>Not at all</th>
<th>Less than 1 half the time</th>
<th>Less than 1 half the time</th>
<th>About half the time</th>
<th>More than half the time</th>
<th>Almost always</th>
</tr>
</thead>
</table>

5. How often have you had a weak urinary stream?

<table>
<thead>
<tr>
<th>Not at all</th>
<th>Less than 1 half the time</th>
<th>Less than 1 half the time</th>
<th>About half the time</th>
<th>More than half the time</th>
<th>Almost always</th>
</tr>
</thead>
</table>

6. How often have you had to push or strain to begin urination?

<table>
<thead>
<tr>
<th>None</th>
<th>1 time</th>
<th>2 times</th>
<th>3 times</th>
<th>4 times</th>
<th>5 or more times</th>
</tr>
</thead>
</table>

17. How many times did you usually get up to urinate from the time you went to bed at night until the time you got up in the morning?

<table>
<thead>
<tr>
<th>None</th>
<th>1 time</th>
<th>2 times</th>
<th>3 times</th>
<th>4 times</th>
<th>5 or more times</th>
</tr>
</thead>
</table>
**Over the past month:**

<table>
<thead>
<tr>
<th>Question</th>
<th>None</th>
<th>Only a little</th>
<th>Some</th>
<th>A lot</th>
</tr>
</thead>
<tbody>
<tr>
<td>18. How much physical discomfort did urinary symptoms cause you?</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>19. How much did you worry about your health because of urinary symptoms?</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>20. Overall, how bothersome has any trouble with urination been?</td>
<td>Not at all bothersome</td>
<td>Bothers me a little</td>
<td>Bothers me somewhat</td>
<td>Bothers me a lot</td>
</tr>
<tr>
<td>21. How much of the time has any urinary problem kept you from doing the kinds of things you would usually do?</td>
<td>None of the time</td>
<td>A little of the time</td>
<td>Some of the time</td>
<td>All of the time</td>
</tr>
<tr>
<td>22. Have you had any sexual erections in the past year?</td>
<td>Yes</td>
<td>No</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>If NO go to Question 26.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>23. Over the past month have you been able to have erections when you were sexually stimulated?</td>
<td>Never</td>
<td>A few times</td>
<td>About half the time</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Most of the time</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Always</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>24. Have you had difficulty in maintaining an erection which has prevented you from having sexual intercourse in the past month?</td>
<td>Yes</td>
<td>No</td>
<td>Not attempted</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>25. To what extent do you feel that your sex life has been spoilt by your prostate problems?</td>
<td>Not at all</td>
<td>Slightly</td>
<td>Somewhat</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Considerably</td>
<td></td>
<td>Completely</td>
<td></td>
</tr>
</tbody>
</table>
Please could you answer some questions about problems caused by the prostate or operation

26. Have you had to use any of the following services since your last visit to hospital?

<table>
<thead>
<tr>
<th>Service</th>
<th>No</th>
<th>Yes</th>
<th>If yes, number of occasions</th>
</tr>
</thead>
<tbody>
<tr>
<td>General practitioner</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Practice nurse</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hospital outpatients</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>District nurse</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Physiotherapist</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Other (please specify)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Would you have liked more help from any of these services since your last visit to hospital?

Yes [ ] No [ ]

If yes, which service?

27. How much extra help from friends, family or neighbours have you had since your last visit to hospital?

A great deal [ ] Quite a lot [ ] A little [ ] None [ ]

28. Would you have liked more help from friends, family or neighbours since your last visit to hospital?

Yes [ ] No [ ]

29. (a) Do you feel ready to return to your normal activities or work yet?

Yes [ ] No [ ]

(b) If YES, when was this? [ ] days after the operation
   If NO, go to Question 31

30. Have you returned to your normal activities or work yet?

Yes [ ] No [ ]

If YES, when was this? [ ] days after the operation

Question continued on next page
If NO, have you been advised not to?

Yes ☐ No ☐

If YES, by whom?

GP ☐ Relative ☐ Other ☐

Please specify:

31. Has a relative or friend taken time off work to care for you (including time to collect you from hospital)?

Yes ☐ No ☐

If yes, how long?

☐ days ☐ hours

32. Have you incurred any other costs since your last visit to hospital, as a result of your prostate problem (e.g. increased washing, pads, etc.) yourself?

Yes ☐ No ☐

If yes, please specify:

33. How would you rate your prostate problem now compared to when you joined the study?

Feeling much worse ☐ Feeling worse ☐ Feeling the same ☐ Feeling better ☐ Feeling much better ☐

34. Overall how satisfied have you been with the course of treatment so far?

Very satisfied ☐ Somewhat satisfied ☐ Neither satisfied nor dissatisfied ☐ Somewhat dissatisfied ☐ Dissatisfied ☐

35. What would you recommend to a friend in a similar situation as yourself?

Have operation ☐ Do not have operation ☐ Not sure ☐
By placing a tick (✓) in one box in each group below, please indicate which statement best describes your own health status today.

36. Mobility
   I have no problems in walking about
   I have some problems in walking about
   I am confined to bed

37. Self-care
   I have no problems with self-care
   I have some problems with washing or dressing myself
   I am unable to wash or dress myself

38. Usual Activities
   I have no problems with performing my usual activities (e.g. work, study, housework, family or leisure activities)
   I have some problems with performing my usual activities
   I am unable to perform my usual activities

39. Pain/Discomfort
   I have no pain or discomfort
   I have moderate pain or discomfort
   I have extreme pain or discomfort

40. Anxiety/Depression
   I am not anxious or depressed
   I am moderately anxious or depressed
   I am extremely anxious or depressed

41. Flow rates

<table>
<thead>
<tr>
<th>Date</th>
<th>Average flow</th>
<th>Peak flow</th>
<th>Volume</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
To help people say how good or bad a health state is, we have drawn a scale (rather like a thermometer) on which the best state you can imagine is marked by 100 and the worst state you can imagine is marked by 0.

We would like you to indicate on this scale how good or bad is your own health today, in your opinion. Please do this by drawing a line starting from the box below (your own health state today) to whichever point on the scale indicates how good or bad your current health state is.
The following questions ask for your views about your health, how you feel and how well you are able to do your usual activities. If you are unsure about how to answer any questions, please give the best answer you can and make any of your own comments if you like.

1. In general, would you say your health is:
   - Excellent
   - Very good
   - Good
   - Fair
   - Poor

2. Compared to one year ago, how would you rate your health in general now?
   - Much better now than one year ago
   - Somewhat better now than one year ago
   - About the same
   - Somewhat worse now than one year ago
   - Much worse now than one year ago
HEALTH AND DAILY ACTIVITIES

The following questions are about activities you might do during a typical day. Does your health limit you in these activities? If so, how much?

(Please tick one box on each line)

<table>
<thead>
<tr>
<th>Activity</th>
<th>Yes, limited a lot</th>
<th>Yes, limited a little</th>
<th>No, not limited at all</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vigorous activities, such as running, lifting heavy objects, participating in strenuous sports</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Moderate activities, such as moving a table, pushing a vacuum cleaner, bowling or playing golf</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lifting or carrying groceries</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Climbing several flights of stairs</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Climbing one flight of stairs</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bending, kneeling or stooping</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Walking more than a mile</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Walking half a mile</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Walking 100 yards</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bathing and dressing yourself</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

During the past 4 weeks, have you had any of the following problems with your work or other regular daily activities as a result of your physical health?

(Answer Yes or No to each question)

<table>
<thead>
<tr>
<th>Problem</th>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cut down on the amount of time you spent on work or other activities</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Accomplished less than you would like</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Were limited in the kind of work or other activities</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Had difficulty performing the work or other activities (eg. it took extra effort)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
5. During the past 4 weeks, have you had any of the following problems with your work or other regular daily activities as a result of any emotional problems (such as feeling depressed or anxious)?

(Answer Yes or No to each question)

<table>
<thead>
<tr>
<th></th>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td>a) Cut down on the amount of time you spent on work or other activities</td>
<td></td>
<td></td>
</tr>
<tr>
<td>b) Accomplished less than you would like</td>
<td></td>
<td></td>
</tr>
<tr>
<td>c) Didn't do work or other activities as carefully as usual</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

(Please tick one)

6. During the past 4 weeks, to what extent has your physical health or emotional problems interfered with your normal social activities with family, friends, neighbours or groups?

<table>
<thead>
<tr>
<th></th>
<th>Not at all</th>
<th>Slightly</th>
<th>Moderately</th>
<th>Quite a bit</th>
<th>Extremely</th>
</tr>
</thead>
</table>

7. How much bodily pain have you had during the past 4 weeks?

<table>
<thead>
<tr>
<th></th>
<th>None</th>
<th>Very mild</th>
<th>Mild</th>
<th>Moderate</th>
<th>Severe</th>
<th>Very severe</th>
</tr>
</thead>
</table>

8. During the past 4 weeks, how much did pain interfere with your normal work (including work both outside the home and housework)?

<table>
<thead>
<tr>
<th></th>
<th>Not at all</th>
<th>A little bit</th>
<th>Moderately</th>
<th>Quite a bit</th>
<th>Extremely</th>
</tr>
</thead>
</table>
These questions are about how you feel and how things have been with you during the past month. (For each question, please indicate the one answer that comes closest to the way you have been feeling).

9. How much time during the past month:

a) Did you feel full of life?
   - All of the time
   - Most of the time
   - A good bit of the time
   - Some of the time
   - A little of the time
   - None of the time

b) Have you been a very nervous person?
   - All of the time
   - Most of the time
   - A good bit of the time
   - Some of the time
   - A little of the time
   - None of the time

c) Have you felt so down in the dumps that nothing could cheer you up?
   - All of the time
   - Most of the time
   - A good bit of the time
   - Some of the time
   - A little of the time
   - None of the time

d) Have you felt calm and peaceful?
   - All of the time
   - Most of the time
   - A good bit of the time
   - Some of the time
   - A little of the time
   - None of the time

e) Did you have a lot of energy?
   - All of the time
   - Most of the time
   - A good bit of the time
   - Some of the time
   - A little of the time
   - None of the time

f) Have you felt downhearted and low?
   - All of the time
   - Most of the time
   - A good bit of the time
   - Some of the time
   - A little of the time
   - None of the time

g) Did you feel worn out?
   - All of the time
   - Most of the time
   - A good bit of the time
   - Some of the time
   - A little of the time
   - None of the time

h) Have you been a happy person?
   - All of the time
   - Most of the time
   - A good bit of the time
   - Some of the time
   - A little of the time
   - None of the time

i) Did you feel tired?
   - All of the time
   - Most of the time
   - A good bit of the time
   - Some of the time
   - A little of the time
   - None of the time

j) Has your health limited your social activities (like visiting friends or close relatives)?
   - All of the time
   - Most of the time
   - A good bit of the time
   - Some of the time
   - A little of the time
   - None of the time

10. Please choose the answer that best describes how true or false each of the following statements is for you.

   (Please tick one box on each line)

   a) I seem to get ill more easily than other people
      - Definitely true
      - Mostly true
      - Not sure
      - Mostly false
      - Definitely false

   b) I am as healthy as anybody I know
      - Definitely true
      - Mostly true
      - Not sure
      - Mostly false
      - Definitely false

   c) I expect my health to get worse
      - Definitely true
      - Mostly true
      - Not sure
      - Mostly false
      - Definitely false

   d) My health is excellent
      - Definitely true
      - Mostly true
      - Not sure
      - Mostly false
      - Definitely false
Please could you tell us about your symptoms over the past month or so

(Please tick one box on each line)

<table>
<thead>
<tr>
<th>Question</th>
<th>Not at all</th>
<th>Less than 1 time in 5</th>
<th>Less than half the time</th>
<th>About half the time</th>
<th>More than half the time</th>
<th>Almost always</th>
</tr>
</thead>
<tbody>
<tr>
<td>11.</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>12.</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>13.</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>14.</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>15.</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>16.</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>17.</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

11. How often have you had the sensation of not emptying your bladder after you finished urinating?

12. How often have you had to urinate again less than two hours after you finished urinating?

13. How often have you found you stopped and started again several times when you urinated?

14. How often have you found it difficult to postpone urination?

15. How often have you had a weak urinary stream?

16. How often have you had to push or strain to begin urination?

17. How many times did you usually get up to urinate from the time you went to bed at night until the time you got up in the morning?
### Over the past month:

<table>
<thead>
<tr>
<th>Question</th>
<th>None</th>
<th>Only a little</th>
<th>Some</th>
<th>A lot</th>
</tr>
</thead>
<tbody>
<tr>
<td>18. How much physical discomfort did urinary symptoms cause you?</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>19. How much did you worry about your health because of urinary symptoms?</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>20. Overall, how bothersome has any trouble with urination been?</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>21. How much of the time has any urinary problem kept you from doing the kinds of things you would usually do?</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Question</th>
<th>Not at all bothersome</th>
<th>Bothers me a little</th>
<th>Bothers me somewhat</th>
<th>Bothers me a lot</th>
</tr>
</thead>
<tbody>
<tr>
<td>22. Have you had any sexual erections in the past year?</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>If NO go to Question 26.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>23. Over the past month have you been able to have erections when you were sexually stimulated?</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>24. Have you had difficulty in maintaining an erection which has prevented you from having sexual intercourse in the past month?</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>25. To what extent do you feel that your sex life has been spoilt by your prostate problems?</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Question</th>
<th>Not at all</th>
<th>Slightly</th>
<th>Somewhat</th>
</tr>
</thead>
<tbody>
<tr>
<td>26.</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Please could you answer some questions about problems caused by the prostate or operation

26. Have you had to use any of the following services since your last clinic visit?

<table>
<thead>
<tr>
<th>Service</th>
<th>No</th>
<th>Yes</th>
<th>If yes, number of occasions</th>
</tr>
</thead>
<tbody>
<tr>
<td>General practitioner</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Practice nurse</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hospital outpatients</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>District nurse</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Physiotherapist</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Other (please specify)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Would you have liked more help from any of these services since your last clinic visit?

Yes □ No □

If yes, which service?

27. Has a relative or friend taken time off work to care for you (including time to collect you from hospital)?

Yes □ No □

If yes, how long? □ days □ hours

28. Since your last visit to hospital, have you incurred any other costs as a result of your prostate problem (e.g. increased washing, pads, etc.) yourself?

Yes □ No □

If yes, please specify

29. How would you rate your prostate problem now compared to before your operation?

Feeling much worse □
Feeling worse □
Feeling the same □
Feeling better □
Feeling much better □
30. Overall how satisfied have you been with the course of treatment so far?

   Very satisfied
   Somewhat satisfied
   Neither satisfied nor dissatisfied
   Somewhat dissatisfied
   Dissatisfied

31. What would you recommend to a friend in a similar situation as yourself?

   Have operation
   Do not have operation
   Not sure
By placing a tick (3) in one box in each group below, please indicate which statement best describes your own health status today.

32. **Mobility**
   - I have no problems in walking about
   - I have some problems in walking about
   - I am confined to bed

33. **Self-care**
   - I have no problems with self-care
   - I have some problems with washing or dressing myself
   - I am unable to wash or dress myself

34. **Usual Activities**
   - I have no problems with performing my usual activities (eg. work, study, housework, family or leisure activities)
   - I have some problems with performing my usual activities
   - I am unable to perform my usual activities

35. **Pain/Discomfort**
   - I have no pain or discomfort
   - I have moderate pain or discomfort
   - I have extreme pain or discomfort

36. **Anxiety/Depression**
   - I am not anxious or depressed
   - I am moderately anxious or depressed
   - I am extremely anxious or depressed
37.

To help people say how good or bad a health state is, we have drawn a scale (rather like a thermometer) on which the best state you can imagine is marked by 100 and the worst state you can imagine is marked by 0.

We would like you to indicate on this scale how good or bad is your own health today, in your opinion. Please do this by drawing a line starting from the box below (your own health state today) to whichever point on the scale indicates how good or bad your current health state is.
LASER versus TURP - a Randomised Controlled Trial

COREC No. 93-183

Have you read the Invitation Letter/Information Sheet? Yes/No

Have you had an opportunity to ask questions and discuss this study? Yes/No

Have you received satisfactory answers to your questions? Yes/No

Have you received enough information about the study? Yes/No

Who have you spoken to? Dr/Mr/Ms

Do you understand that you are free to leave the study:
- at any time
- without having to give a reason for leaving,
- and without affecting your medical care? Yes/No

Signed: ___________________________ Date: ________________

Name (in block letters): ________________________________
Is day-case prostatectomy feasible?

S.R. KEOGHANE, J.M. MILLAR* and D.W. CRANSTON
Departments of Urology and *Anaesthetics, Churchill Hospital, Oxford, UK

Objective To assess the possibility of discharging patients, catheter-free, on the same day that they undergo contact-laser prostatectomy.

Patients and methods Ten patients underwent contact vaporization of the prostate using the SLT (Surgical Laser Technologies, Oaks, PA, USA) Nd:YAG laser with an MTRL10 6 mm tip. Patients were selected in the out-patient clinic for day-case surgery on the basis of their good general health and clinically small glands. All patients had pre-operative urodynamic assessment and were proven obstructed and stable. Contact vaporization was carried out under general anaesthesia. Both intra-operative blood loss and irrigant absorption were assessed. The follow-up at 3 and 6 months included American Urological Association (AUA-7) symptom scores and the measurement of urinary flow rates.

Results The mean operating time was 25.2 min, with a mean application of 43.05 kj of laser energy. The mean absorption of irrigant fluid was 30 ml and the mean intra-operative blood loss was 31 ml. Nine patients were discharged on the day of treatment. Two patients went into clot retention following discharge and had a suprapubic catheter sited, and two failed to void once discharged, necessitating catheterization for 2 weeks. At 3 and 6 months, there was a substantial decrease in the AUA symptom score and an improvement in urinary flow rate.

Conclusion Day-case laser prostatectomy is possible, but the patients must be selected carefully and, perhaps more importantly, a specialist day-case anaesthetist must be available.

Keywords Contact laser prostatectomy, day-case surgery

Introduction

Contact laser prostatectomy causes immediate vaporization of the prostate and removal of obstructing tissue. It was first described by Daughtry and Rodan [1] in a series of 25 elderly, high-risk patients who were poor candidates for surgery. Laser resection was performed using the SLT contact laser system with the MTRL3 and 6 mm tip probes (Surgical Laser Technologies, Oaks, PA, USA). The mean prostatic size in that series was small (26 g), with a mean operating time of 33 min. The follow-up was up to 11 months, although symptomatic outcome was subjective and classed as 'failures', 'fair' or 'good'. However, 15 'good' results were obtained, with peak flow rates improving from 14 mL/s to 40 mL/s for patients in whom surgery was successful. No significant bleeding was reported, although no objective data were obtained for peri-operative blood loss or change in haematocrit. This small series showed promise for the technique of contact laser ablation of the prostate.

Watson et al. [2] have reported results from a pilot randomized trial comparing contact laser vaporization with transurethral resection of the prostate (TURP). Difficulty was reported with glands over 40–50 mL, but with smaller prostates, a substantial decrease in AUA symptom score, together with an improvement in flow rates, were noted.

In a double-blind, randomized, controlled trial of 152 patients, we have recently shown that the symptomatic outcome at 3 months from the contact technique equalled that of TURP [3]. In this study, the mean pre-operative prostate volume in the laser arm of the trial was 51.9 mL, with a median duration of post-operative catheterization of one night (range 0–9 nights) [3]. Following this trial, we have examined the feasibility of performing day-case laser prostatectomy.

Patients and methods

Ten patients (mean age 63 years, range 58–67) were carefully selected in the out-patient clinic on the basis of their good general health, a clinically small prostate gland (mean prostate volume 40.4 mL, range 26–60) and the availability of supervision by a relative at home after treatment. A health-assessment questionnaire, blood pressure check and electrocardiogram were used to ensure the patients' fitness for anaesthesia. Following informed consent, all patients underwent a pre-operative assessment of urodynamics, transrectal ultrasonography (TRUS), American Urological Association (AUA-7)

Accepted for publication 11 July 1995
symptom score, a 'bother' score and information on their sexual function. Pressure flow studies were conducted using the MMS (Medical Measurement Systems) UD 2000 equipment, while planimetric measurements of prostate volume were obtained using a Brueel and Kjaer 1846 transrectal ultrasonography machine with a Type 1850, 7 Mhz probe with a focal length of between 2 and 5 cm.

Ciprofloxacin antibiotic prophylaxis, ranitidine and metoclopramide were administered orally 2 h before treatment. All procedures were performed under general anaesthesia with fentanyl 1.5 μg/kg and propofol 2.5–3 mg/kg for induction, and nitrous oxide in 30% oxygen and a propofol infusion for maintenance. Diclofenac 100 mg was given rectally during the procedure. All patients received gentamicin (80 mg intravenously) and an intravenous infusion of 1 L of Hartmann's solution. Three patients received frusemide (40 mg intravenously) to encourage diuresis.

A cysto-urethroscopy was carried out using a zero-degree and 70-degree Storz cystoscope, to assess the length of the prostatic urethra, the macroscopic pathological state of the bladder, and residual urine within the bladder.

Operating time was measured from the start of endoscopic vaporization to the time of placement of the urethral catheter or removal of the cystoscope. Irrigant fluid effluent was collected and weighed to facilitate the estimation of its haemoglobin content. The amount of energy delivered by the laser was also recorded.

Laser ablation of the prostate was performed using an SLT MD 60 Nd:YAG machine. A 600 μm fibre with a semi-rigid distal end incorporating a 6 mm large, sapphire-tipped, round probe (MTIRL 10) allowed complete vaporization, starting with the median and progressing to the lateral lobes. The probe was brought back to the verumontanum, and 'furrows' produced by forward pressure, until the bladder neck was reached (Fig. 1). Normal saline at 35.8°C was used throughout as the irrigant. Peri-operative blood loss was assessed by measuring the haemoglobin concentration in the irrigant effluent, which had been anti-coagulated with 1000 units of heparin [4] and intra-operative irrigation fluid absorption was assessed by using ethanolic saline (Baxter Medical, UK) [5].
Table 1 AUA-7 symptom scores and maximum urinary flow rates before, 3 and 6 months after laser contact vaporization

<table>
<thead>
<tr>
<th>Patient</th>
<th>Before</th>
<th>3 months</th>
<th>6 months</th>
</tr>
</thead>
<tbody>
<tr>
<td>AUA-7 score</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>25</td>
<td>14</td>
<td>20</td>
</tr>
<tr>
<td>2</td>
<td>19</td>
<td>13</td>
<td>7</td>
</tr>
<tr>
<td>3</td>
<td>22</td>
<td>6</td>
<td>4</td>
</tr>
<tr>
<td>4</td>
<td>25</td>
<td>5</td>
<td>2</td>
</tr>
<tr>
<td>5</td>
<td>17</td>
<td>8</td>
<td>8</td>
</tr>
<tr>
<td>6</td>
<td>22</td>
<td>7</td>
<td>3</td>
</tr>
<tr>
<td>7</td>
<td>32</td>
<td>10</td>
<td>4</td>
</tr>
<tr>
<td>8</td>
<td>23</td>
<td>8</td>
<td>5</td>
</tr>
<tr>
<td>9</td>
<td>24</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>10</td>
<td>23</td>
<td>2</td>
<td>6</td>
</tr>
<tr>
<td>Mean</td>
<td>23.2</td>
<td>7.5</td>
<td>6.2</td>
</tr>
<tr>
<td>Maximum flow rate, mL/s</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>9.0</td>
<td>12.1</td>
<td>9.0</td>
</tr>
<tr>
<td>2</td>
<td>6.1</td>
<td>10.3</td>
<td>12.6</td>
</tr>
<tr>
<td>3</td>
<td>16.0</td>
<td>34.3</td>
<td>20.8</td>
</tr>
<tr>
<td>4</td>
<td>10.0</td>
<td>24.0</td>
<td>18.0</td>
</tr>
<tr>
<td>5</td>
<td>11.9</td>
<td>9.8</td>
<td>10.8</td>
</tr>
<tr>
<td>6</td>
<td>5.9</td>
<td>18.3</td>
<td>17.0</td>
</tr>
<tr>
<td>7</td>
<td>7.1</td>
<td>17.0</td>
<td>13.6</td>
</tr>
<tr>
<td>8</td>
<td>10.0</td>
<td>19.0</td>
<td>19.4</td>
</tr>
<tr>
<td>9</td>
<td>8.5</td>
<td>20.0</td>
<td>39.5</td>
</tr>
<tr>
<td>10</td>
<td>6.5</td>
<td>19.3</td>
<td>24.2</td>
</tr>
<tr>
<td>Mean</td>
<td>9.1</td>
<td>18.4</td>
<td>18.5</td>
</tr>
</tbody>
</table>

The first five cases treated had no urethral catheter placed; the second five received 1 h of continuous bladder irrigation with normal saline on returning to the day-case unit, before catheter removal and discharge. The Day Surgery Unit’s discharge criteria were used to ensure that the patients were fit to be discharged. All patients were given Tylex (paracetamol and codeine) tablets to take for analgesia at home and were contacted the next day by the consultant anaesthetist. Follow-up questionnaires, to be returned after the second post-operative day, were also used. All patients were assessed at 3 and 6 months using urinary flow rates and symptom scores.

Results

Pre-operative urodynamic assessment revealed a mean voiding pressure of 129 cmH2O (range 103–136) and showed all patients to be stable and obstructed. Mean operating time was 25.2 min (range 15–50), with a mean of 43.05 kJ (range 15.7–48.18) of laser energy delivered. The mean irrigant fluid absorption was 30 mL (range 0–90) while the mean intra-operative blood loss was 31 mL (range 5–70). The mean recovery time in the Day Surgery Unit was 4 h 53 min (range 227–405 min). All patients made a good recovery from anaesthesia and pain was minimal unless associated with retention.

Nine patients were discharged, catheter-free, on the same day that they were treated. Two patients went into
clot retention within 2 days of discharge and had a suprapubic catheter sited. Two failed to void once discharged, necessitating catheterization for 2 weeks. Following these initial early complications, however, all patients were voiding satisfactorily. The follow-up questionnaire was returned by nine patients. Despite early problems, eight were happy to be treated as day cases and would recommend this to a friend. Five patients required analgesia at home and nausea, reported as 'mild' by two patients, did not otherwise occur.

All patients claimed to be potent before undergoing surgery, although four said they felt their sex life had been spoilt by their urinary symptoms. At 6 months, all patients again said they were fully potent, with only two claiming their sex life had been spoilt by their urinary symptoms; only one patient had definite retrograde ejaculation. The results at 3 and 6 months are shown in Table 1, and an example of the results of uroflowmetry is shown in Fig. 2.

Discussion

The aim of all new minimally invasive methods of producing a prostatectomy should be to reduce both morbidity and cost; safe day-case surgery would fulfil these aims. Sapphire tips for Nd:YAG laser fibres have been developed in various configurations [6], but were not available in a sufficient diameter for prostatectomy until 1994, with the advent of the SLT MTRL6 10 mm tip. Although in recent years there has been a move towards early post-operative removal of the urethral catheter and/or early discharge after TURP [7,8], the aim of every urologist to discharge patients, catheter-free, on the same day following prostatectomy, has not yet been realized. While discharge on the same day is indeed possible with the side-fire laser technique [9], a catheter is left in situ for at least a week and often longer, due to laser-related oedema in the majority of cases. The results of the present small pilot study demonstrate that this goal can be achieved, but the selection of patients is paramount and morbidity is not insignificant; telephone follow-up on the next day is also essential. With increasingly sophisticated technology and careful selection of patients, day-case prostatectomy will become a reality in the near future.

References

3 Keoghane SR, Cranston DW, Lawrence KC, Doll HA, Fellows GJ, Smith JC. The Oxford laser prostate trial: a randomised controlled trial of contact vaporisation of the prostate versus TURP. J Urol 1995; Abs 230

Authors

S.R. Keoghane, FRCS, Research Fellow in Urology.
J.M. Millar, FRCA, Consultant Anaesthetist.
D.W. Cranston, DPhil, FRCS, Consultant Urologist.
Correspondence: Mr S.R. Keoghane, Department of Urology, The Churchill Hospital, Headington, Oxford OX3 7LJ, UK.

© 1995 British Journal of Urology 76, 600–603
The Oxford Laser Prostate Trial: a double-blind randomized controlled trial of contact vaporization of the prostate against transurethral resection; preliminary results

S. R. KEOGHANE*†, D. W. CRANSTON*, K. C. LAWRENCE†, H. A. DOLL†, G. J. FELLOWS* and J. C. SMITH*

*Department of Urology, The Churchill Hospital, and †Health Services Research Unit, Department of Public Health and Primary Care, University of Oxford, Oxford, UK

**Objective** To compare the results of contact laser vaporization and transurethral resection of the prostate (TURP) in a double-blind randomized controlled clinical trial.

**Patients and methods** The study comprised 148 patients with clinical benign prostatic hypertrophy (BPH) who were recruited and allocated randomly to undergo either TURP (72 patients) or laser ablation of the prostate (76 patients). The outcome was assessed using the American Urological Association (AUA — 7) symptom score after 1 and 3 months as the primary measure and by urinary flow rates, haematological factors and the duration of hospital stay and length of catheterization.

**Results** With 90% statistical power, the results at 3 months showed no clinical or statistical difference between the treatments in change in AUA symptom score. A lower blood loss, hospital stay and duration of catheterization significantly favoured the laser treatment, although the failure rate of trial without catheter and the rate of re-operation were higher after laser treatment.

**Conclusions** These early data are encouraging for this technique, although the outcome after one year requires evaluation before advocating the widespread uptake of this method.

**Keywords** Contact laser prostatectomy, randomized controlled trial

**Introduction**

Benign prostatic enlargement (BPE) remains one of the most prevalent diseases affecting an increasingly aged male population [1] and in recent years enormous effort has been focused on developing treatment regimens that have a similar efficacy to TURP and minimum morbidity [2].

The development and early results of both side-fire and contact laser prostatectomy have been described in detail [3,4]. Contact laser prostatectomy appears to show great promise in both reduced post-operative morbidity and hospital stay because blood loss and the duration of post-operative catheterization are decreased. Encouraging results have been reported by Watson et al. [5], from a small pilot randomized trial comparing contact laser vaporization with TURP.

Difficulty was reported with glands >40–50 mL but with smaller prostates there was a substantive decrease in symptom score and an improvement in flow rates.

The recently validated AUA symptom score [6] has been shown to have the measurement properties necessary for evaluating disease severity and outcome in patients with BPE. It has the necessary construct validity and excellent responsiveness which are required of an evaluative instrument.

However, what is missing in the fast-moving field of minimally invasive therapy of the prostate are methodologically sound results upon which treatment decisions can be based.

**Patients and methods**

The study population included all patients referred to the Churchill Hospital, Oxford who needed surgical treatment for BPE. Patients were excluded if they had undergone previous surgery or instrumentation for BPE, had prostatic malignancy, were unable to speak or understand sufficient English to answer the questionnaires or if they refused consent.

The sample size required for the trial was calculated using 'POWER™' software; the chosen sample size of 150 would detect a difference of 5 in the AUA symptom score with a double-sided α of 0.05 (5% significance), and β of 0.1 (90% power). Restricted randomization was used, from random-number tables in a 1:1 ratio, balanced to 10. Sealed envelopes containing the treatment option were kept in the operating theatre.
Operative procedure

Patients received the anaesthetic most appropriate to their medical condition and surgery was carried out by one of the same five surgeons (Consultant or experienced Registrar and Senior Registrar grade) throughout the study. All patients received oral ciprofloxacin antibiotic prophylaxis 2 h before surgery. After randomization, cysto-urethroscopy was carried out using a 0° and 70° Storz cystoscope, assessing the length of the prostatic urethra, the macroscopic pathological state of the bladder and residual urine volume within the bladder.

At the time of writing, a purpose-built contact-laser 'resectoscope' is only a prototype and several different instruments were tried with the laser apparatus. A side-viewing nephroscope was used initially but had too small an image and the fibre was difficult to manipulate. A single instrument-port cystoscope was also unsatisfactory and a double-lumen channel instrument proved the most 'user-friendly' because it had a larger calibre.

Complete vaporization was achieved using an SLT MD60 Nd:YAG machine (Surgical Laser Technologies, Oaks, PA, USA) and a 600 mm fibre with a semi-rigid distal end incorporating a 6 µm, sapphire-tipped, round probe (MTRL 10), starting with the median and progressing to the lateral lobes. The probe was brought back to the verumontanum and 'furrows' produced by forward pressure until the bladder neck was reached.

Conventional TURP was carried out as the control procedure of the trial. The irrigant fluid effluent was collected, anti-coagulated with 1000 units of heparin, weighed and the peri-operative blood loss estimated from the haemoglobin concentration in the irrigant effluent, using the Haemocue photometer [7]. The volume of blood lost was calculated as:

\[
\frac{\text{photometer value} \times \text{irrigant volume [L]}}{\text{patient's haemoglobin [g/L] \times 5.2}}
\]

Post-operatively, a 22 F three-way balloon catheter was left indwelling and continuous bladder irrigation with normal saline was commenced regardless of the intra-operative blood loss, to ensure that the patient was unaware of which treatment he had received.

The patient, ward and medical staff, other than the operating surgeon, were also kept unaware of which treatment was received and the urinary catheter was removed when indicated clinically.

The outcome was assessed using the AUA-7 symptom score as the primary measure, the peak urinary flow rate \(Q_{\text{max}}\), the duration of hospital stay and catheterization, the post-operative irrigation fluid volume, the incidence of complications, the transfusion rate, haematological and biochemical data and the costs to the health service.

After 4 weeks, the patients were sent a postal questionnaire which included questions about the patient's perspective of the outcomes detailed above. A follow-up at 3 months in out-patients by an observer unaware of the treatment included a similar questionnaire, details of complications since discharge and a measurement of urinary flow rate.

The difference between the groups for primary and secondary outcome measures was assessed using a grouped t-test or a Mann-Whitney test as appropriate to the distribution. Patients who transferred between the laser and TURP arms were excluded from the analysis of efficacy.

Results

A total of 152 patients were randomized, with losses before randomization caused by a variety of medical conditions, laser malfunction and periods when the trial co-ordinators were not available.

The losses in theatre after randomization were a consequence of the decision to perform three retropubic prostatectomies and one urethrotomy after the initial cystoscopy; these were all from the laser arm. Thus, 148 patients were randomized and assessed; 72 patients (mean age 69 years) were treated using contact laser prostatectomy and 76 (mean age 70 years) underwent TURP.

The mean \((\text{sn})\) prostate volume and prostatic urethral length for patients receiving the laser treatment were 54.2 (26.3) mL (44 patients) and 2.7 (0.8) cm (63 patients), respectively, and for those undergoing TURP were 51.9 (24.1) mL (48 patients) and 2.9 (1.0) cm (67 patients), respectively.

The median amount of energy delivered in the laser arm was 31 kJ (range 8.5–10.8). Table 1 shows the mean changes in the relevant haematological and biochemical variables or both arms of the trial, excluding those patients who received a blood transfusion. The ranges for the peri-operative blood loss were wide, 0–200 mL for patients undergoing laser treatment and 12–1600 mL for those undergoing TURP: four patients treated by laser were converted to TURP peri-operatively because trauma from the cystoscope caused bleeding from a highly vascular prostate. No patient receiving laser treatment required a peri- or post-operative blood transfusion, whereas 13 patients (20%) undergoing TURP were transfused (chi-squared test, \(P<0.001\)). One patient who underwent TURP died at 2 months from heart disease and one patient with pre-existing severe cardiac disease who received laser treatment suffered a myocardial infarction at 3 months.

© 1996 British Journal of Urology 77, 382–385
Table 1 Peri- and post-operative data for patients undergoing laser treatment or TURP

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Laser</th>
<th>n</th>
<th>range</th>
<th>TURP</th>
<th>n</th>
<th>range</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Peri-operative</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean operating time (min)</td>
<td>36</td>
<td>69</td>
<td>15</td>
<td>39</td>
<td>69</td>
<td>20</td>
<td>NS</td>
</tr>
<tr>
<td>Median blood loss (mL)</td>
<td>39</td>
<td>68</td>
<td>0-200</td>
<td>200</td>
<td>69</td>
<td>12-1600</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Mean change in haemoglobin (g/L)</td>
<td>-4.2</td>
<td>50</td>
<td>7.3</td>
<td>-11.9</td>
<td>52</td>
<td>12.8</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Mean change in haematocrit</td>
<td>-0.009</td>
<td>38</td>
<td>0.03</td>
<td>-0.03</td>
<td>41</td>
<td>0.04</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Mean change in serum sodium (mmol/L)</td>
<td>1.7</td>
<td>46</td>
<td>3.2</td>
<td>2.1</td>
<td>47</td>
<td>3.6</td>
<td>NS</td>
</tr>
<tr>
<td>Post-operative</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Median length of catheterization (nights)</td>
<td>1</td>
<td>44</td>
<td>0-9</td>
<td>2</td>
<td>59</td>
<td>1-20</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Median hospital stay (nights)</td>
<td>3</td>
<td>60</td>
<td>1-10</td>
<td>4</td>
<td>64</td>
<td>1-8</td>
<td>&lt;0.005</td>
</tr>
<tr>
<td>Median irrigation volume (L)</td>
<td>6</td>
<td>46</td>
<td>0-33</td>
<td>12</td>
<td>57</td>
<td>1.5-168</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

The duration of catheterization, hospital stay and the volume of post-operative irrigation fluid used are shown in Table 1. Seventeen patients (28%) treated by laser failed to void once the urethral catheter was removed, compared with eight (12%) treated by TURP (chi-squared test, \( P < 0.05 \)).

Three patients who underwent TURP were subsequently found to have urethral strictures and two had a bladder neck contracture. Three cases of carcinoma of the prostate and one of lymphoma of the prostate were diagnosed histologically from the 'chips' obtained from patients undergoing TURP.

Six (8.3%) patients treated by laser required a subsequent cystoscopy for symptoms that were not improved by their original procedure and they subsequently underwent TURP, while one developed a false passage from an attempted cystoscopy by a non-urologist when admitted to another hospital with a secondary haemorrhage. These patients requiring re-operation were excluded from the analysis after the re-operation.

Complications occurring in the first 3 months are shown in Table 2. The AUA symptom scores at baseline, 1 and 3 months, the flow rates at 3 months and the mean change from the baseline score, sds and 95% CI are shown in Table 3.

Discussion

Randomized controlled trials of surgery techniques are rare and the optimum time at which minimally invasive interventions should be evaluated remains debatable. While some useful information exists about side-fire laser prostatectomy [8,9], no large trials using the contact method have yet been published. Those in favour of a delayed evaluation of minimally invasive technology suggest that if the evaluation is undertaken too early, the technique will still be under development and any comparison with established procedures would be unfair and thus might stifle innovation. Those in favour of early evaluation suggest that if it is delayed, an opportunity may be lost and it may then be too late to prevent the widespread diffusion of a technique of uncertain efficacy [10]; this was certainly the case with TURP. The opportunity of performing a randomized controlled trial of TURP was lost and as a result, questions still remain about the relative treatment efficacy and safety of open versus transurethral prostatectomy [11].

The preliminary 3 month results presented here show promise; with 90% statistical power there appeared to be no clinical or statistical difference between the techniques in AUA symptom score, as a primary measure of
Table 3 AUA symptom scores and flow rates after TURP or laser prostatectomy

<table>
<thead>
<tr>
<th></th>
<th>Laser TURP</th>
<th>Mean change</th>
<th>Laser TURF</th>
<th>Mean change</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean n sd</td>
<td>P-value</td>
<td>Mean n sd</td>
<td>95% CI</td>
</tr>
<tr>
<td>AUA score</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Before</td>
<td>19.9 54 7.7</td>
<td>19.4 63 6.5</td>
<td>N/A</td>
<td></td>
</tr>
<tr>
<td>1 month</td>
<td>12.3 46 9.1</td>
<td>8.5 54 7.0 0.039</td>
<td>7.3 39 10.6</td>
<td>4-10.6 11.9</td>
</tr>
<tr>
<td>3 months</td>
<td>9.6 55 7.5</td>
<td>6.5 62 5.1 0.029</td>
<td>10.1 47 9.7 7.3-12.9</td>
<td>13.6</td>
</tr>
<tr>
<td>Qmax</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Before</td>
<td>11.8 48 4.5</td>
<td>11.4 54 5.0 N/A</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3 months</td>
<td>21.3 46 11.6</td>
<td>21.8 52 12.2 ns</td>
<td>10.7 38 1.4</td>
<td>7.1-14.3 9.6</td>
</tr>
</tbody>
</table>

outcome. However, at 1 month, the symptom scores were clinically and statistically better in the patients who underwent TURP.

Perhaps equally important was the lack of bleeding associated with the laser technique, reflected in the fact that no patient needed a transfusion. The duration of catheterization and hospital stay were not as low as might be expected, but in the study the catheter was removed with no knowledge of the treatment received and the duration could probably be reduced with a more aggressive approach.

However, significant learning and training are required to use contact laser ablation and experience has shown that initially, only small glands should be treated. The current laser-delivery system is extremely crude and further refinements are expected which may ease the problem of treating a prostate with large lateral lobes. Although these results are generally applicable to those patients with a successful operation, information obtained after a year or more should be evaluated before advocating the widespread uptake of this technique.

References
1 Denis LJ. Introduction. Prostate (Suppl) 1989; 2: 1-4
4 Smith JA, Stein BS, Benson RC. Lasers in Urological Surgery. St Louis; Mosby Year Book, 1994
9 Buckley JF, Ligam V, Paterson P. Endoscopic laser ablation of the prostate gland (ELAP), AUA Abstracts 1994
10 Working group of the Department of Health and the Scottish Office Home and Health Department. Minimal access surgery: implications for the NHS. Edinburgh; HMSO, 1994

Authors
S. R. Keoghane, FRCS, Research Fellow in Urology.
D. W. Cranston, FRCS, Consultant Urologist.
K. C. Lawrence, MFPHM, Honorary Senior Registrar in Public Health Medicine.
H. A. Doll, MSC, Medical Statistician.
G. J. Fellows, FRCS, Consultant Urologist.
J. C. Smith, FRCS, Consultant Urologist.
Correspondence: Mr S. R. Keoghane, Department of Urology, The Churchill Hospital, Headington, Oxford OX3 7LJ, UK.

© 1996 British Journal of Urology 77, 382-385
A new approach to Nd:YAG sidefire laser in the uterus: 
in vitro studies

S.R. KEOGHANE FRCS*, F. RASLAN MRCOG, W. GRAY MBBS FRCPATH† & F.M. CHARNOCK FRCS FRCOG
Departments of Gynaecology, *Urology and †Pathology, The Churchill and John Radcliffe Hospitals, Oxford, UK

Summary. The effect on fresh hysterectomy specimens of a new type of water-cooled, side-fire Neodymium YAG laser probe that has potential in the treatment of menorrhagia has been examined. After varying power settings and exposure times were utilized, 50W for 60s appeared to give the optimum amount of tissue destruction in vitro.

Keywords: ND: YAG, laser ablation, endometrium

Introduction
Minimally invasive therapy is now an accepted part of the surgeon's armamentarium for the treatment of menorrhagia. Laser ablation of the endometrium is not a new concept [1], being performed in the main by a contact 'dragging' technique utilizing bare fibres [2], a technique that has been tried by urologists to vaporize the prostate [3]. The main advantage of the contact technique is an immediate tissue effect, similar to an endometrial resection, but this must be balanced against technical difficulties and the small area of tissue treated by 'the dragging' technique.

In treating benign prostatic enlargement, the sidefire technique, utilizing an Nd:YAG laser in its free mode, has the advantage of depth of penetration [4], producing tissue destruction by coagulation deep in the gland. This technique has theoretical advantages within the uterus, due to the speed of the procedure [5].

Methods
Fresh hysterectomy specimens taken from two women aged 50 and 53 years, with a clinical diagnosis of dysfunctional uterine bleeding, were treated with an SLT (Surgical Laser Technologies, Oaks, PA, USA) Nd: YAG laser, utilizing a side-firing free beam probe (SFB 1.0). This probe is relatively new, the characteristics of its beam profile being a diameter of 7012 μm with a centroid of 8442 μm at a power density of 1.34 MW/cm² (personal communication SLT). The maximum power output obtainable is 50W, the beam angle of emission being 90°, with approximately 30° of beam divergence.

In the first case, the 600 μm diameter semi-rigid fibre was passed down the working channel of a 23.5F cystoscope, necessitating dilation of the cervix to 24 F. Irrigating the specimen with warm normal saline, under video-endoscopic control, laser ablation was carried out in four planes, attempting to follow the established protocol in the prostate [6], 50W was used for 60s, anteriorly,

Figure 1. Beam position for specimen 2.
posteriorly and to the left lateral region. As a visible perforation occurred at this site, the duration of exposure was decreased in the right lateral wall to 30 s.

The technique was modified for the second case, to more accurately assess the tissue effect. After bisecting the specimen, it was placed in a water bath at 37°C and the fibre was used in a side-fire mode, under water, free of the cystoscope (Figure 1).

The right side of the specimen was treated by the ‘painting’ technique for a total of 40 W for 30 s, until visible blanching of the tissue occurred, while the left side was treated with varying power settings with the probe.
Nd: YAG sidefire laser in uterus

Table 1. Beam position and exposures

<table>
<thead>
<tr>
<th>Beam position</th>
<th>Exposure</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>40 W for 10 s</td>
</tr>
<tr>
<td>2</td>
<td>45 W for 20 s</td>
</tr>
<tr>
<td>3</td>
<td>40 W for 20 s</td>
</tr>
<tr>
<td>4</td>
<td>45 W for 45 s</td>
</tr>
<tr>
<td>5</td>
<td>40 W for 30 s</td>
</tr>
</tbody>
</table>

between 1 and 5 mm from the tissue surface. Exposure times are shown in Table 1.

Both specimens were placed in formalin and sent for histological examination.

Results

In the case of specimen 1, the endometrium where preserved, was measured to a depth of 18 mm, and showed low grade secretory and proliferative activity.

Macroscopically, specimen 1 revealed lesions between 3 mm and 6 mm in diameter, microscopically showing destruction of the endometrium involving the visible burn site and adjacent endometrium. The largest burn cavity was 9 x 6 mm, with a rim of surrounding coagulative necrosis of myometrium varying from 1 to 2 mm in thickness (Figure 2). At the margins of the cavity the endometrial lining was destroyed over an area of approximately 5 mm.

Microscopic assessment of the right side of specimen 2, that had received 40 W for 30 s, via a painting technique, revealed an endometrial depth of 22 mm, and within this, an occasional small focus of laser destruction which appeared to affect only the upper layers (Figure 3) and did not appear to extend into the myometrium at any site. The most prominent area of destruction was less than 1 mm in depth of penetration into the endometrium.

Histological examination of the left side of this specimen that received various regimens showed no evidence of tissue destruction.

Discussion

In the prostate, many different regimens have been tried [7, 8], and while the extent of tissue damage depends on power setting, beam spot size, lasing angle and lasing time, in these experiments, the power setting and the lasing time were the variables tested. In vivo, however, tissue vascularity may diminish the effect by conducting heat away.

The potential advantage of this type of laser probe, other than decreasing haemorrhage [5], lies with its re-usability and inherent water cooling. Contact between fibre and tissue has until recently been a problem due to heat build-up and consequent damage to the reflective surface. Water cooling makes fibre ‘burn out’ unlikely, thus hopefully decreasing operating time and reducing costs, a vital consideration in any form of laser surgery.

Acknowledgement

The authors would like to thank Mr David Wilde for his help with this study.

References

3 Shanberg AM, Tansey LA, Baghdassarian R. The use of the neodymium YAG laser in prostatectomy. J Urol 1983; 133: 351A
4 Shanberg AM, Lee IS, Tansey LA, Sawyer DE, Rodgers LW, Ahlering T. Depth of penetration of the Nd: YAG laser in the human prostate at various dosimetry. Urology 1994; 8: 809-12

© 1995 Blackwell Science Ltd, Minimally Invasive Therapy, 4, 227-229
containing extensive areas composed mainly of macrophages with lipid-rich cytoplasm (Fig. 2). No neoplastic tissue was observed, obviating total cystectomy.

This intense xanthogranulomatous reaction involved urachal remnants, omentum and umbilicus.

The post-operative course was uneventful and the patient remains asymptomatic one year after surgery, with a normal abdominal CT.

Comment
Pathological changes of xanthogranulomatous disease and its systemic manifestations are well known. Diagnosis of this rare case of urachal xanthogranulomatous disease was based on the histological findings of large clusters of macrophages with lipid-rich cytoplasm (foam cells) [1,2].

The initial clinical and radiological diagnosis was urachal carcinoma. In our case, there were difficulties in pre-operative differential diagnosis by radiological study alone. The usefulness of CA 125 antigen for diagnosing urachal carcinoma is doubtful, the pre-operative histological study being mandatory. Umbilicotomy with total cystectomy must be postponed until a histopathological diagnosis of carcinoma is established [3]. This case demonstrates that urachal xanthogranulomatous disease does exist. Differential diagnosis with urachal carcinoma is difficult and a radical approach, based only on clinical and radiological findings, may lead to overtreatment of a benign local evolutive urachal process.

References
1 Goodman M, Curry T, Russell T. Xanthogranulomatous pyelonephritis (XPG): a local disease with systemic manifestations. Medicine, 1979; 58: 171–81

Authors
W. Carrere, Urologist.
R. Gutiérrez, Urologist.
B. Umbert, Urologist.
M. Solé, Pathologist.
V. Menéndez, Urologist.
P. Carretero, Professor of Urology and Chief.
Correspondence: Dr W. Carrere, Department of Urology, Hospital Clinic I Provincial, C/Villarroel 170, 08036 Barcelona, Spain.

British Journal of Urology (1996), 77, 613–614

CASE REPORT

Contact laser prostatectomy in anti-coagulated patients: mixed results
S.R. KEOGHANE and D.W. CRANSTON
Department of Urology, The Churchill Hospital, Oxford, UK

Case report

Case 1
A 71-year-old man receiving anticoagulant drugs underwent contact vaporization of the prostate using the SLT (Surgical Laser Technologies, Oaks, PA, USA) Nd:YAG laser with an MTRL 10 6 mm sapphire-tipped probe.

His prostate volume was 50 mL and INR at the time of surgery was 2.2. The intra-operative blood loss was 20 mL, the operating time 25 min, and the patient made an uneventful recovery, being discharged on the third-day after treatment. However, the patient was readmitted 2 weeks later with a minor secondary haemorrhage, which stabilized with conservative management.

Case 2
A 68-year-old man with an INR of 2.2 and prostate volume of 93 mL underwent contact vaporization, the intraoperative blood loss was 35 mL with an operating time of 40 min. The patient was discharged after 4 days with a urethral catheter in place, having failed to void. At 2 weeks, after a trial without catheter, the patient was voiding with a good flow rate.
Case 3

A 76-year-old man, with a prostate volume of 112 mL and an INR of 3.0, was in urinary retention with a urethral catheter in situ for 10 weeks before surgery. There was minimal bleeding peri-operatively (125 mL), with an operating time of 60 min.

However, on returning to the ward, reactionary haemorrhage continued for 12 days. The patient's haemoglobin level fell from its pre-operative value of 14.4 to 8.5 mg/L, resulting in an angina attack, and 5 units of blood were transfused. Treatment with warfarin was stopped during this time. The bleeding stabilized within 7 days after operation and the patient was discharged home with a catheter in situ, having failed to void.

Comment

Using the contact laser to perform prostatectomy in anticoagulated patients was considered following a randomized controlled trial which demonstrated minimal blood loss when using this technique to treat patients with bladder outflow obstruction [1].

Laser prostatectomy has been used previously in a series of patients receiving anti-coagulants, with a mean INR of 2.4, using the non-contact side-fire technique [2]. Although no measurements of peri-operative blood loss were described, no patients in that series required a blood transfusion and only one required a bladder washout for clot retention. Others have stated categorically that anti-coagulation is a contra-indication to contact vaporization [3], because there is no deep coagulation within the gland. A combination of side-fire coagulation and contact vaporization may be the correct procedure to combat reactionary haemorrhage in anticoagulated patients.

References

1 Keoghane SR, Cranston DW, Lawrence KC, Doll HA, Fellows GJ, Smith JC. The Oxford laser prostate trial: a randomised controlled trial of contact vaporisation of the prostate versus TURP. AUA abstract 1995

Authors

S.R. Keoghane, FRCS, Research Fellow in Urology.
D.W. Cranston, DPhil, FRCS, Consultant Urologist.
Correspondence: Mr S.R. Keoghane, Department of Urology, The Churchill Hospital, Headington, Oxford, UK.
REVIEW

New technology in urology: why assessment needs to be more scientific

S.R. KEOGHANE*, K.C. LAWRENCE*, A.M. GRAY† and D.W. CRANSTON*

*The Department of Urology, The Churchill Hospital, Oxford, †The Health Services Research Unit, University of Oxford and ‡Wolfson College, Oxford, UK

Keywords Minimally invasive therapy, urology, new technology, prostatectomy, randomized controlled trial, laser

Introduction

In recent years, an enormous amount of interest and energy has been directed towards the development of 'minimally invasive therapy' (MIT). These alternative methods of performing operations or procedures that have been in routine use for a long time [1] have not always been subjected to rigorous scientific evaluation. Benign prostatic enlargement (BPE), with its significant impact on both numbers of patients and consequent use of health resources [2,3] has had more than its share of 'innovations' [4], but what is of concern about this new influx of technology is the delayed appearance or absence of methodologically sound, prospective, randomized controlled trials.

While phase-I studies are obviously vital to the development of a new therapy, the question remains as to why, when this work has already been circulated to the urological community, do urological surgeons continue to experiment in an uncontrolled manner with the health of their patients when the new treatment modality has no proven advantages and may even cause harm to patients? Using experience gained primarily from the Oxford Laser Prostate Trial [5] and based on separate contributions, the authors have attempted to give a balanced view on the advantages of co-operation between departments in the design and analysis of a randomized controlled clinical trial (RCT).

The surgeon

The ease of access to the prostate through endoscopy has resulted in an influx of advanced technologies to the surgical procedure of prostatectomy, not all of which are truly 'minimally invasive'. The aim of most of these techniques is to produce a similar effect to a TURP.

Examples of therapies that initially appeared attractive are prostatic thermotherapy, balloon dilatation and prostatic stenting, all of which were advocated and practised for some time before data were produced refuting any claims of benefit. The two definitive trials of thermotherapy were reported in 1994. Nawrocki et al. [6] described an elegant double-blind RCT of 120 patients who were allocated to one of three groups, i.e. a placebo treatment with no heat emission to the prostate, a placebo procedure with heat and finally, the transurethral therapy. The groups receiving standard and simulated microwave treatment showed little difference in clinical improvement; the AUA symptom scores changing from a median of 19 to 9.5 and 17.5 to 9.5, respectively. Similar corresponding changes occurred in the peak urinary flow rate, whilst the untreated group showed no clinically relevant deterioration or improvement.

Similar results have been reported by Venn et al. [7] in a randomized trial of 122 patients. Others have reported better results with this technology [8] but too few patients were involved in these studies for them to be scientifically rigorous and the statistical power of these trials was too low to detect clinically important differences. Balloon dilatation of the prostate became popular in the late 1980s, apparently solely based on 'case series' studies. Although these studies appeared to contain many patients [9], they had no control treatment and therefore contained a major source of bias.

Donatucci et al. [10] conducted a randomized trial comprising 51 patients, comparing balloon dilatation with TURP. Their conclusions were that balloon dilatation did not appear to be as effective as TURP and probably offered only temporary relief of symptoms. A second much-cited study by Lepor et al. [11] reported on a small randomized 'blinded' trial comparing balloon dilatation to cystoscopy in 33 patients. Both groups of patients had a significant improvement in their symptom scores at 1 and 3 months after treatment and neither
group showed any significant change in their peak flow rates. The authors concluded that the efficacy of balloon dilatation previously described by some authors was really a placebo effect, findings now accepted by most urological surgeons, although it is interesting that a long-term RCT with adequate statistical power never appeared for this particular form of technology.

We have seen the gradual demise of the prostatic stent and now transurethral needle ablation, diode and interstitial lasers and electrocautery vaporization comprise the latest trends in prostate destruction; again, these technological achievements are being hailed as great breakthroughs and indeed, are being promoted in clinical practice by surgeons and commercial companies alike. When will any evidence of their efficacy and of comparability to existing methods appear?

Clinical research is not difficult, but producing results that answer an important question reliably is! In future, urological surgeons wishing to fully evaluate a new therapy should take note of the guidelines for evaluating new technology issued by the WHO International Consensus Committee [12] which should hopefully put an end to the vast amount of largely meaningless data that appear in the literature.

The Economist

The introduction of new surgical technologies will almost invariably have significant economic consequences. Capital equipment costs may be substantial, as may the costs of disposable equipment. Human capital will also have to be acquired, in the form of new skills for surgical, anaesthetic and nursing staff, and this may require not simply the training of existing staff, but a reconfiguration of the existing mix of staff. Within the hospital, MFTs have often reduced lengths of stay but have involved longer surgical procedures, thus shifting costs from the wards into the operating theatres. The earlier discharge of in-patients may also mean a transfer of costs from the hospital to primary care and community services. Finally, the patients, their families and, indirectly, society as a whole, may face other economic consequences, e.g. a new surgical procedure performed on a day-case basis may impose costs on informal carers that previously would have been borne by the NHS, but may also result in an earlier return to work by the patient, with consequent benefits to the individual and to society.

Economists are interested in identifying and quantifying these economic consequences, but are also concerned to relate the net change in costs to the net change in outcomes, i.e. in the cost-effectiveness of new technologies. The logic of the analysis of cost-effectiveness is that scarce resources should be concentrated in areas where maximum health gain can be obtained from the available resources. But decisions to restrain new treatments or to reduce or eliminate those already in use, to expand those that are more cost-effective, are painful, controversial and unlikely to command assent without the support of scientific evidence. In recent years, there have been substantially more published economic evaluations in health care [13,14]. Most commonly, these have been independent exercises based on outcome and cost data collected retrospectively from literature surveys, advice from epidemiologists and clinicians, and previous costing studies or published mean unit-costs. There is a place for such studies, but too often the evidence selected has been partial, collected and selected unsystematically, and open to challenge.

An alternative approach is to integrate an economic evaluation within a randomized controlled trial, thus collecting resource and outcome data prospectively from the same population and subjecting all economic data to the normal rigours of statistical analysis. Such studies have been very rare in the past; Adams et al. [15] found that just 121, or 0.2% of over 50 000 RCTs published between 1966 and 1988, included economic analyses, several of which were of poor quality. However, the advantages of this approach have increasingly been argued [16,17] and the inclusion of an economic component is becoming a routine part of trials funded by the Medical Research Council and the NHS National Research and Development Programme [18]. Such prospective economic evaluations raise some interesting issues, particularly when applied to new surgical procedures.

First, to demonstrate a significant difference in costs, a study must have adequate statistical power. At present, power calculations are performed invariably on the clinical endpoints and the economic evaluation has to work within the resulting size of the trial. However, it is possible that the economic data will have a high variability between patients, so that only large differences in economic outcomes between the trial arms will be detectable. As economic information is accumulated from surgical trials [19], the importance of this issue can be better assessed; meanwhile, it is interesting to speculate whether funding agencies would underwrite larger surgical trials if calculations of statistical power based on economic endpoints showed them to be necessary.

Second, new surgical techniques raise important questions about the timing of an economic evaluation. The experience of the operator may initially be low, resulting in slower operating times, poorer outcomes and hence lower cost-effectiveness. Similarly, the cost of capital equipment or consumables may be higher in the initial phase of a new technology than when it has diffused more widely [20]. Consequently, it may be misleading to make judgements about a new technology using the cost-effectiveness derived soon after its introduction [21].
Third, the perspective adopted by the economic evaluation may be important. As noted above, newer surgical methods may result in costs being redistributed within the health services and between the health service and patients. Most economists would argue that it is important to collect information in a trial on costs incurred by patients if there is reason to believe that the technology being evaluated could have a differential effect on patient costs. Such costs could also be important in influencing the patients’ acceptance of the new technology. However, it is also true that the fundamental reason for the growth of economic evaluation in health care is the pressure on health-care resources and the need to make informed choices about allocating these resources. There may also be practical difficulties in collecting information on the costs incurred by patients, possibly involving questionnaires, interviews, extra data sheets and more costs to the trial. Thus, in most cases, cost-effectiveness from the perspective of the health service is likely to take precedence, unless the inclusion of patient costs seriously alters the results.

Fourth, the economic evaluation may sometimes require follow-up data beyond the clinical requirements of a trial. For example, a valid endpoint from a clinical perspective may be a treatment failure, as measured by re-admission or re-operation. However, from an economic perspective, re-admission or re-operation are not endpoints as such, but are events with consequences on resources which are attributable to the original intervention. Consequently, the economist may require more detailed information than does the clinical investigator about these events and their aftermath, so that the resources used can be measured, costed and included in the evaluation.

Each of these issues needs to be recognized explicitly and can best be addressed within the context of a multidisciplinary collaboration. Considering economic endpoints when performing the initial power calculations will ensure that the team knows in advance the likely size of any detectable cost difference and can discuss whether this is feasible or meaningful. Plausible future changes in the skills of the operator and the costs of equipment can be agreed within the team and analysed within the framework of the economic evaluation, using sensitivity analysis. If the economist is involved in the trial from the design stage, the collection of data can be designed with the requirements of the economic evaluation in mind, thus minimizing the impact on the costs of the trial.

The Researcher

When a new surgical technology has been assessed, the methodology has often been insufficiently rigorous to withstand scientific scrutiny and the findings too easily dismissed. As a result, technologies have been introduced in a haphazard manner, often driven more by political and market forces and professional peer-pressure than by the strength of the scientific evidence available to support them.

Resources for health care and for clinical research are increasingly constrained; investigators managing clinical research projects have a responsibility to ensure that their research is conducted in a manner that will maximize the utility of the research when making both clinical and policy decisions. A badly designed or conducted study is an unethical study.

Above all, the lack of data gathered in the context of an RCT has often led to prolonged controversies about the relative risks and benefits of a particular technology. For example, the long-standing debate about the excess long-term mortality observed after TURP when compared to the open alternative is one which is likely to remain unanswered [22]. The evidence suggesting such an excess has been assimilated from uncontrolled studies with no randomized data. As a result, few clinicians would be prepared to change their practice on the basis of these results. This is because the potential for selection bias is great; was mortality after TURP higher because patients undergoing TURP were initially sicker? In the absence of an RCT, in which such confounding factors are distributed evenly between the arms of a trial by randomization, this question will probably be impossible to answer.

Difficulties with RCTs in the evaluation of surgical interventions have been described. Problems with variables related to the surgeon and technique, ensuring that the patients and observers are unaware of the treatment, the training and experience of the surgeon and changes in technology have all been cited as potential problems [23]. However, these difficulties are usually surmountable when discussed with a strong multidisciplinary team [24] and the RCT remains the ‘gold standard’ for the assessment of treatment efficacy and effectiveness. Such trials must be of sufficient size to avoid both type-1 errors, referred to as statistical significance (i.e. reporting a treatment difference when there is none), and type-2 error, referred to as statistical power (reporting no treatment difference when there is). The study design must also eliminate bias at each stage; ‘blind’ randomization, ‘blinding’ of patients and observers, a complete follow-up and high rates of response to questionnaires, and careful handling of treatment crossovers and post-randomization losses when the data are analysed all play a part.

In recent years, it has also been increasingly recognized that methodological rigour must be matched by the provision of data on which practical decisions can be based. A trial of a treatment conducted in a ‘plastic bubble’ will be of little practical use for making decisions.
on a routine operating list. A strong move is developing towards a more pragmatic attitude in surgical trials, with a view to increasing the general applicability of trial results [25], away from efficacy and towards effectiveness, with broader criteria for inclusion, a flexible definition of interventions, the surgeon's standard practice as the control procedure and an analysis based on intention-to-treat. How will the technology perform on a routine operating list, with routine anaesthesia, in a district general hospital? The methodology of surgical intervention studies is urgently in need of further research on the design of pragmatic trials. In particular, the issue of operator experience and its effect on outcome remains little explored, despite its implications for the training of physicians, specialization and the use of resources. The changing relative risk which may arise as a physician gains experience and training in a particular technique is often neglected and may lead to the results of a trial being misapplied. The use of covariance adjustment and regression models to assess the contribution of such factors to outcome is likely to develop rapidly in the future, given the particular relevance of the issue to the expanding field of minimal access therapy.

A further methodological problem has been the lack of standardization of outcomes used in clinical assessment. This precludes the aggregation of the data at a later stage into a meta-analysis [26]. The selection of the most appropriate outcome measure for use in a clinical trial is often less clear than might be expected, but it is certainly difficult to justify a study which does not include a measure of outcome centred on the patient, given the range of measures now available [27]. Such measures should be reviewed carefully before use, to ensure they have the measurement properties necessary for the study in question. The development of the AUA symptom score has been a notable advance in this field. It has the properties required of an evaluative measure (longitudinal construct validity and responsiveness) and has undergone extensive validation [28]. However, what happens if an intervention has a better short-term outcome in terms of symptom score, but leads to a higher rate of re-operation? Similarly, what happens if radical surgery for prostate cancer increases survival, but has a negative effect on the quality of life? Alternative approaches to dealing with such 'trade-offs' in clinical trials are currently being explored [29]. In practical terms, a baseline survey which examines the level of evidence required for differences in outcome sufficient to make clinicians change their practice, or policy-makers to shift resources, is likely to aid in trial design and to ensure that the results are implemented. Methods for involving patients more closely in the initial stages of trial design are also being investigated.

For statistical reasons, a primary outcome should be selected when the trial is designed, but a trial should also provide a profile of risks and benefits for different outcomes that can be presented to patients to guide them in their choice of treatment. The decision about their treatment must be influenced by the value that they attach to different outcomes and by their attitude to risk. The model of shared decision-making in clinical care is gaining increasing popularity and an accumulating body of evidence suggests that patients involved in such decisions have a more positive view of their clinical outcomes and express greater satisfaction with their care [30]. Where such motivational factors are likely to have a strong influence on outcome, the use of a randomized preference trial should be considered when the trial is designed [31].

It is no longer acceptable to undertake research that does not meet high scientific standards. Neither is it acceptable simply to say that a new urological technology works. We must understand the scientific quality on which such conclusions are based, to which study population they apply, in what clinical setting and in whose hands, and at what cost. We must also understand the compromises which may exist between short- and long-term outcome and the values that patients attach to these. Finally, we must understand how the technology can be introduced in a way which will maximise cost-effectiveness if scarce resources are to be best used. This is most likely to occur if a multi-disciplinary team is involved when the trial is designed.

The current influx of new technologies in the treatment of BPE presents the urological community with a challenge and an opportunity within the context of the reformed NHS. A validated and simple evaluative measure of outcome exists for BPE (the AUA-7 symptom score). A national network would enable urologists to ensure that new technology is introduced in a manner consistent with scientific evidence, and purchasers to ensure that care is purchased in accordance with such standards and in a manner which will maximise cost-effectiveness. The Internet provides a method for the easy exchange of trial and outcome data among investigators, clinicians and purchasers. Such a collaborative network requires trust, but above all scrupulous honesty, about the conclusions which can be drawn from aggregated data. A combined effort between purchasers and providers could set an international standard for the evidence-based introduction of new technology and, if successful, could be extended into other areas. Such a 'golden bridge' of science is a vision of the future to which researchers in the field must aspire.

Acknowledgements

Dr Lawrence's fellowship was funded by the MRC
References


4 Watson G. Minimally invasive therapies of the prostate. Minim Inv Ther 1992; 1: 231–40


6 Nawrocki JD, Bell TJ, Lawrence WT, Ward JP. A randomised trial controlled study of therapy. RAUS abstract 1994.


27 Spiller B. Quality of Life Assessments in Clinical Trials. New York, Raven Press: 1990


Authors

S.R. Keoghane, FRCS, Research Fellow in Urology.
K.C. Lawrence, MSc, MFPHM, Honorary Senior Registrar in Public Health Medicine.
A.M. Gray, DPhil, Senior Research Associate, Wolfson College.
D.W. Cranston, DPhil, FRCS, Consultant Urologist.
Correspondence: Mr S.R. Keoghane, Department of Urology, Cheltenham General Hospital, Sandford Road, Cheltenham, UK.