LASER PROSTATECTOMY AND ITS PLACE IN THE THIRD WORLD

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Introduction

A quarter of the male population above 40 and 43% of men between 60-69 years, have lower urinary tract symptoms (LUTS) in the presence of a reduced urinary flow rate due to benign prostatic enlargement (BPE). Approximately 10-15% of the male population will be considered for prostatic surgery at some point in their lives. Men of 40 years of age in the West appeared to have a 30-40% chance of undergoing prostatectomy if they survived up to 80. Transurethral resection of the prostate (TURP) has survived as the gold standard of prostate ablation. Rates of TURP reached a peak in 1987 and have dropped substantially as a result of better understanding of the relatively benign nature of the natural history of BPH and introduction of effective medical therapy (1-4).

Present day indications for surgery include (a) complicated BPE (upper tract dilatation, renal impairment, recurrent significant haematuria, infection, bladder stones and recurrent acute retention), (b) severe LUTS not responding to pharmacotherapy, (c) chronic retention with detrusor failure or chronic high pressure retention.

Over last 5-6 decades transurethral resection of prostate (TURP) using electro cautery is regarded as the gold standard in the surgical treatment of bladder outlet obstruction (BOO) secondary to BPE resulting in an immediate relief of symptoms with acceptable morbidity and mortality. However, TURP could occasionally be associated with immediate and long term cardiovascular side effects due to irrigant fluid absorption collectively known as TURP syndrome and also complications such as incontinence, impotence (5,6,7,8) and retrograde ejaculation. Complication rate have been shown to be associated with the size of the resected adenoma, type and hydrostatic pressure of irrigant used and the duration of resection.

Thermal ablation by other means of heating (Microwave hyperthermia, transurethral needle radiofrequency ablation (TUNA), high frequency focused ultrasound (HIFU) and laser or cooling (cryotherapy) have been tried with varying degrees of success depending on patient selection, definition of successful outcome, case load and the extent on specialisation. Despite claims made by proponents of these newer methods, none of these methods have so far managed to gain universal acceptance compared to the 'gold standard' – TURP and yet to stand the test of time (9,10, 11,12).

Out of these, laser prostatectomy has managed to gain a clear lead over the other methods and seem to be slowly but steadily closing the gap to become the new gold standard in affluent countries such as United States. However, in the third world the huge obstacle for laser seems to be the cost. Both initial investment recurrent expenditure and maintenance seem to be over powering its advantages over the conventional TURF making laser minimally cost effective in many aspects. Hence at this point in time it is essential for all referring clinicians to have a basic knowledge of the range of endoscopic

techniques available for the treatment of prostatic disease and to decide who will clearly benefit from the new expensive treatment modalities such as laser.

Effect of heat on tissues

When tissue is heated between 40 and 44°C (defined as "hyperthermia") minor tissue effects take place at tissue temperatures particularly within malignant tissues. As tissue is heated more by any method irreversible cellular damage occurs (defined as "thermotherapy"). If the temperature of target tissue is raised by a few degrees above 45°C then a cytotoxic effect will be achieved with a much shorter exposure time. Coagulation necrosis occurs with small and then larger vessel thrombosis leading to later sloughing and/or reabsorbtion of necrotic tissue. At temperature 60°C or higher, vaporisation with acute disruption of tissue due to steam formation occurs and at 100°C or higher temperature causes tissue burning, carbonisation and some immediate tissue removal and tissue disruption occurs due to volatile gas formation. In electro resection, temperatures in the range of 600-800°C could be created with immediate tissue destruction at the vicinity of the diathermy loop compared to newer modalities which use much lower temperatures (13,14,15).

Laser tissue effects

Laser tissue ablation is not new to the surgical field. However, application to urology especially to transurethral prostatectomy was introduced in the early 1990s.

When laser light strikes tissue energy is deposited and tissue is heated. The amount and rate of energy delivery and the degree to which a particular laser wavelength is reflected, absorbed, scattered or transmitted through the target tissue will determine the nature of the thermal process. The power density determines the rate of energy and therefore heat deposition onto the target tissue surface.

Earlier Neodymium – Yttrium Aluminum Garnet (Nd:YAG) laser or small, compact diode lasers with wavelengths causing similar tissue effects (805-980 nanometers) were used for coagulating BPE. Necrotic tissue was discharged for few weeks and prostatic oedema took several days to settle. Both of these effects cause long term catheterisation and much discomfort to the patient.

Newer lasers such as holmium (2140 nm) potassium titanyl phosphate (KTP – "green light") and thulium lasers produce more avidly absorbed laser wavelengths and have more obvious superficial tissue vaporisation and disruptive effects. These devices (or wavelengths) can be used either closer to the tissue to create a high energy density for tissue disrupting and "vaporising" effect or held further away to achieve a primarily coagulating effect as desired.

In all these methods effective prostatic tissue destruction is demonstrated in the largely glandular canine model. However, the human gland is far more resistant to heating by any method. Differing epithelial: stromal ratios could explain this differences in response. prostatic needle biopsies and transrectal ultrasound (TRUS) images from human "laser failures" showed higher amount of stromal elements than glandular component compared to "successes". Also more homogeneous transition zone indicating more glandular element was demonstrated in successes on TRUS raising the possibility of selecting patients for any heat based treatment by TRUS or biopsy.

Methods of laser vaporisation

1) Transurethral endoscopic beam from a simple "bare" fibre

This is the most basic and common method of laser surgery to the prostate. The Nd:YAG laser was first widely used in this way during open surgery and then applied to endoscopic surgery. Initially the intention was to achieve coagulation of the target tissue, usually the prostatic lateral lobes. When more powerful Nd:YAG laser generators or more obviously vaporising wavelengths became available using argon, KTP and most recently holmium:YAG

and thulium, the techniques of localised vaporisation or cutting of the prostate or bladder neck tissue were put into wider usage. The simple transurethral endoscopic "bare" fibre is by far the cheapest laser option since no specialised equipment is used but may result in more urethral injury due to the extra manipulation needed to reach all the adenoma.

The holmium:YAG laser fired through a fine fibre close to the tissue surface can cut tissue by vaporisation and can achieve coagulation when held at a distance (or by using a beam deflecting device) thus reducing the power density at the point of beam impact. Development has been rapid: initially the holmium was used simply as a vaporising addition to Nd:YAG laser coagulation but this method was rapidly replaced by purely holmium vaporisation of the prostate or cutting of the bladder neck. It would be interesting to know the endoscopic and certainly the ultrasonic appearances of these glands after holmium and KTP resection as it is still not clear where all the adenomatous tissue is ablated, since only a relatively small proportion is resected and it is assumed that a similar amount is "vapourised".

Recently a technique of endoscopic incision and mobilisation of the prostatic lobes in a manner similar to open prostatectomy (laser enucleation) which is familiar to most urologists is becoming popular. Using holmium or thulium laser prostatic lobes are dislocated from the capsule. Removing the relatively large avascular pieces and lobes is done by a tissue "morcellator" or standard resection which extend the operating time. The early results are very comparable to TURP and open prostatectomy. especially when compared to the more complete removal of adenoma, early catheter removal and minimal post-operative dysuria (16,17).

2) Contact laser method: transurethral endoscopic fibre with a specialised "contact tip" (CT)

The less common direct application of laser heated probes (usually synthetic sapphire contact tips (CTs) is intended to remove enough tissue immediately to allow unobstructed post-operative voiding. The quality of data on CT methods has been strengthened by the Oxford laser prostate trial, a double blind RCT of contact tip methods versus TURP which is a good example of a study designed with appropriate statistical powers. There were no statistically significant differences between the 2 arms in terms of American Urological Association symptom score (AUA-7SS) response or flow rates at 3 or at 12 months follow up.

3) The interstitial application of laser energy using a "bare" or modified fibre

In this newer application method, inserting a small, relatively atraumatic fibre into the prostatic tissue either transurethrally, transrectally or percutaneously under ultra sound guidance and heating it up directly (interstitial laser coagulation or ILC) causes high temperatures and localised coagulative necrosis whilst preserving the prostatic urethral lumen. It is hoped, but not yet proven, to reduce post-operative dysuria following treatment. Since there is no generally agreed system for quantifying post-laser symptoms it is difficult to compare one method with another in any meaningful way.

Non thermal laser methods

Photodynamic therapy (PDT)

PDT involves the use of pure light wavelengths to activate previously administered photosensitising agents to cause cell injury by a non-thermal mechanism. Currently PDT has been more explored as a therapy for prostate cancer rather than for BPE. Experiments have been stimulated by the "transparency" of the prostate to certain wave lengths (20). Red light (630 nm) penetrates prostate deeply. PDT has several potential advantages over endoscopic or interstitial laser thermal coagulation. Tissues necrosed by PDT heal with more regeneration and less scarring than after thermal damage canine prostate experiments have suggested a role for newer photosensitisers such as the chlorins (22) and disulfonated aluminum phthalocyanine (A1S2Pc) and 5-aminolevulinic acid (ALA)-induced protoporphyrin.

Outcome of laser ablation of prostate

Endoscopic laser prostatectomy by these different methods appear safe. Although claimed to be safe in large prostates (>100gms), it is usually quicker if one avoids big prostates (>60gms). Rapid charring of the adenoma surface should be avoided as it leads to high surface temperatures and effects but less deep penetration of light. Amount of tissue evaporated in these large glands are not documented clearly in most studies and long term results are awaited (26,27).

Whether size of the prostate is an important consideration is unclear. It was reported that video laser assisted prostatectomy (VLAP) and TURP led to similar symptomatic responses but that VLAP only lowered the "obstructive grade" (measured by pressure flow studies) in those men with prostate size below 50 mls whereas TURP was effective for all prostate sizes. Some reported that size did not impact on the success of the vaporising method (TUVP) in their experience (28). Similarly, men presenting with acute urinary retention seem to do equally well as purely symptomatic men following VLAP or TURP (27,28).

A period of obstruction and "irritability" is common, especially after coagulating laser. Laser methods are reported to be almost equivalent to TURP in terms of symptom response. However, increase in flow rates (Urodynamic improvement) which should be at least 50% compared to nearly 100% following a TURP were not achieved in early studies. In most studies flow rate results were expressed as means and averages which could be misleading. It is suggested that studies should report the proportion of subjects achieving 50% or greater improvement in flow rates and /or symptoms. Improvement in post void residual urine also carries the same reporting problem in many studies (18,19, 20,21,25).

Early reports on laser resection tend to come from enthusiasts and are usually encouraging. Whether this remains true when performed in more routine and widespread urological practice is not yet known. These techniques are more popular in some countries than others and were minimally taken up in general urological practice in South Asia for instance (22,23,24).

Variability in methods and results is to be expected since we still do not know the answers to many basic questions such as how much tissue to be removed to guarantee a good, long term result. It is probably less than what is thought earlier but yet to be proven by long term – at least 10 year-follow up studies. Laser techniques have shown to overcome obstruction by pressure flow studies despite relatively modest tissue left compared to a TURP.

Health economics in laser

While as a procedure laser prostic surgery is nearly 4-5 times more expensive than a conventional TURP it becomes even more expensive for larger glands if and when more than one disposable fibre has to be used (eg. KTP "green light" laser). This is in addition to the high initial cost for non installation of consumables. A prospective, double blind, laser RCT comparing the safety, efficacy and cost, found VLAP is no more expensive than TURP, when the initial cost is ignored in their institution. The Oxford laser RCT found TURP to be more cost effective than contact tip laser methods, mainly due to the cost of consumables. But if fibres are carefully used more than once (18,19,29) and if competition among fibre producers intensified then this cost could fall substantially. Most of the holmium and thulium laser machines fibres are reusable. While some lasers (KTP laser) are exclusively used for prostate, others (holmium and thulium) could be used for stone disintegration making them more cost effective. Thus if the laser is specific for prostate (eg. KTP "green light") and could not be used for other urological procedures such as stone disintegration (eg. holmium and thulium), a further loss of cost effectiveness takes place (29,30-33).

Consequently there has been growing interest in modification of resection method and instruments to reduce these complications. Modified thermo-electric methods utilising much higher energy levels (electro, vaporization – Vapotrode^{TM}), trans urethral resection with bipolar diathermy in saline

(TURIS™) to avoid hypontraemia, and staged resection has the advantage of familiarity and availability of same instruments used for TURP with lower incident of complications. Most of these methods are more cost effective in the third world as there is cost saving at all stages of their application.

Conclusion

Laser procedures has a shorter learning curve, cause little bleeding, less taxing for the patient, and can be even day case procedures – which are considerable advantages. An instant channel is created, with less bleeding without absorption of fluid it can be used on ill patients, including those anticoagulated with heparin, warfarin, nonsteroidal anti-inflammatory drugs and aspirin and no post-operative irrigation is required. However, despite some excellent reports, laser prostatectomy methods in general use, do not yet seem as predictably effective in increasing flow rates as TURP though the symptomatic improvement is nearly as good. Amount of tissue ablation varies from study to study and the long term result of partial ablation of prostatic adenoma is not known. It is also important to pay attention to the new more cost effective modifications of standard TURP which are posing a challenge to laser techniques such as new vaporising roller (Vaportrode™) or thick, flat loop and bipolar resection in saline. The challenge of the laser methods has led to a reappraisal of endoscopic prostatic resection to find the most cost effective and "patient friendly" methods avoiding inherent TURP complications.

At present even in the developed West only holmium laser enucleation of prostate (HoLEP) trans urethral, microwave hyperthermia (TUMT) and radio-frequency needle ablation (TUNA) are unequivo-cally recommended for use. Other methods such as phtoselective vaporization (PVP – green light) bipolar resection in saline, high frequency ultrasound (HIFU),water induced thermotherapy (WIT), botulinum toxin and ethanol injection are considered as investigational techniques. It is advisable for developing countries to wait for the long term results before embracing this expensive newer methods as the equipment and technology for these are rapidly evolving (34).

Introduction of various laser methods has been rapid but it is important to remember that there are still few properly powered randomised controlled trials (RCTs) from which informed judgments can be made in this evolving subject. Early data on short-term mortality, morbidity, complication rates and outcome are available. However, further details of cost effectiveness, long term outcome and patient preference are awaited (34). The explosion of laser treatment options should not be regarded as a threat but as a development that reinforces the primary role of the urologist as the only healthcare professional equipped to guide the symptomatic or obstructed man to the best treatment option for him to undergo. In the third world the pros and cons should be studied well before subjecting a patient to a newer procedure or advising a healthcare institution to purchase these rather expensive equipment with a substantial recurrent expenditure.

Long term outcome for laser resections are awaited to be compared with, over 50 years experience of TURP. It must also prove to produce better results over the other emerging more economical, minimally invasive methods. Only when we have these data it deserves wider use especially in the third world, with a defined role as the universal gold standard in prostate surgery.

References

1. Garraway W, Collins G, Lee R. High prevalence of benign prostatic hypertrophy in the community. *Lancet* 1991; 338.

2. Neal D. Evaluation and results of treatments for prostatism. *Urol Res* 1994; **22**: 61.

3. Barry M. Epidemiology and natural history of benign prostatic hyperplasia. *Urological Clinics of North America* 1990; **17**: 495.

4. Lu-Yao G, Barry M, Chang C, Wasson J, Wennberg J. Transurethral resection of the prostate among Medicare beneficiaries in the United States: time trends and outcomes. Prostate Patient Outcomes Research Team (PORT). *Urology* 1994; **44**: 692.

5. Mebust W, Holtgrewe H, Lockett A, Peters P, and committee. Transurethral prostatectomy immediate and postoperative complications. A comparative study of 13 participating institutions evaluating 3,885 patients. *Journal of Urology* 1989; **141**: 243.

6. Roos N, Wennberg J, Malenka D, Fisher E, McPherson K, Andersen T, Cohen M, Ramsey E. Mortality and reoperation after open and transurethral resection of the prostate for benign prostatic hyperplasia. *New England Journal of Medicine* 1989; **320**: 1120.

7. Hargreave T, Stephenson T. Potency and prostatectomy. *British Journal of Urology* 1977; **49**: 683.

8. Perera ND, Hill JT. Erectile and ejaculatory failure after transurethral prostatectomy. *Ceylon Medical Journal* 1998; **43**(2):74-8.

9. Devonec M, Cathaud M, Carter S, Berger N, Perrin P. Transurethral microwave application: temperature sensation and thermokinetics of the human prostate. *Journal of Urology* 1990; **143**: 414A.

10. Green N. Cryosurgery of the prostate gland in the unfit subject. *British Journal of Urology* 1970; **42**: 10.

11. Foster RS, Bihrle R, Fry F, Donohoe J. Transrectal focussed ultrasound ablation of prostate: the first 15 patients. *Journal of Urology* 1992; **147**: 237A (Abstract 93).

12. McNicholas T, Steger A, Bown S. Interstitial laser coagulation of the prostate: an experimental study. *British Journal of Urology* 1993; **71**: 439.

13. Pantelides M, Whitehurst C, Moore J, King T, Blacklock N. Photodynamic therapy for localised prostate cancer: light penetration in the human prostate gland. *Journal of Urology* 1990; **143**: 398.

14. Gottfried HW, Vogel U, Hautmann R. Human and canine TULAP – what makes the difference? *Journal of Urology* 1994; **151**: 331A.

15. Hefty R, Mattfeld T, Gottfried H, Kleinschmidt K, Hautmann R. The critical role of the epithelium-stroma ratio in the laser treatment of BPH. *Journal of Urology* 1995;**153**: 231A.

16. Johnson D, Cromeens D, Price R. Use of the holmium:YAG laser in urology. *Lasers in Surgery and Medicine* 1992; **12**: 353.

17. Shah T, Alsudani M, Akbar M, Aslam M, Fowler L, McNicholas T. An inexpensive and effective method of laser ablation of the prostate. *Journal of Urology* 1995; **153**: 414A.

18. Mackey M, Chilton C, Gilling P, Fraundorfer M, Cresswell M. The results of holmium laser resection of the prostate. *British Journal of Urology* 1998; **81**: 518.

19. Keoghane S, Cranston D, Lawrence K, Doll H, Fellows G, Smith J. The Oxford laser prostate trial: a double blind, randomised, controlled trial of contact vaporisation against transurethral resection; preliminary results. *British Journal of Urology* 1996; **77**: 382.

20. The Oxford laser prostate trial: economic issues surrounding contact laser prostatectomy. *British Journal of Urology* 1996; **77**: 386.

21. Narayan P, Tewari A, Aboseif S, Evans C. A randomised study comparing visual laser ablation and transurethral evaporation of prostate in the management of benign prostatic hyperplasia. *Journal of Urology* 1995; **154**: 2083.

22. Costello A, Bowsher W, Bolton D, Braslis K, Burt J. Laser ablation of the prostate in patients with benign prostatic hypertrophy. *British Journal of Urology* 1992; **69**: 603.

23. Kabalin J, Gill H Bite G, Wolfe V. Comparative study of laser versus electrocautery prostatic resection: 18-month follow up, with complex urodynamic assessment. *Journal of Urology* 1995; **153**: 94.

24. Cowles R, Kabalin J, Childs S, Lepor H, Dixon C, Stein B, Zabbo A. A prospective randomised comparison of transurethral resection to visual

laser ablation of the prostate for the treatment of benign prostatic hyperplasia. *Urology* 1995; **46**: 155.

25. Anson K, Nawrocki J, Buckley J, Fowler C, Kirby R, Lawrence W, Paterson P, Watson G. A multicentre, randomised, prospective study of endoscopic laser ablation versus transurethral resection of the prostate. *Urology* 1995; **46**: 305.

26. De Wildt M, Testa E, Rosier P, Wijkstra H, Debruyne F, de la Rosette J. Urodynamic results of laser treatment in patients with benign prostatic hyperplasia. Can outlet obstruction be relieved? *Journal of Urology* 1995; **154**: 174.

27. Te Slaa E, De Wildt M, Rosier P, Wijkstra H, Debruyne F, de la Rosette J. Urodynamic assessment in the laser treatment of benign prostatic enlargement. *British Journal of Urology* 1995; **76**: 604.

28. Jung P, Mattelaer P, Wolff J, Mersdorf A, Jakse G. Visual laser ablation of the prostate: efficacy evaluated by urodynamics and compared to TURP. *European Journal of Urology* 1996; **30**: 418.

29. Narayan P, Tewari A, Fournier G, Toke A. Impact of prostate size on the outcome of transurethral laser evaporation of the prostate for benign prostatic hyperplasia. *Urology* 1995; **45**: 776.

30. Rajbabu K, Chandrasekara SK, Barber NJ, *et al*. Photo selective vapourisation (PVP) of the prostate with KTP laser in men with prostates >100ml. *British Journal of Urology International* 2007; **100**: 593-8.

31. Narayan P, Tewari A, Schalow E, Leidich R, Aboseif S, Cascione C. Transurethral evaporation of the prostate for treatment of benign prostatic hyperplasia: results in 168 patients with up to 12 months of follow up. *Journal of Urology* 1997; **157**: 1309.

32. Dixon C, Machi G, Theune C, Lepor H. A prospective, double blind, randomised study comparing the safety, efficacy and cost of laser ablation of the prostate and transurethral prostatectomy for the treatment of BPH. *Journal of Urology* 1994; **151**: 229A.

33. Gilbert H, O'Boyle P, Mcloughlin J, Speakman M. Multiple use of fibres in the visual laser ablation of the prostate. *British Journal of Urology* 1996; **77**: 839.

34. de La Rosette, Graves S, Fitzpatrick JM. Minimally invasive treatment of male lower urinary tract symptoms. *Urologic Clinics of North America* 2008; **35**: 505-18.