Transurethral Microwave Thermotherapy in the Treatment of Benign Prostatic Hyperplasia

ERNEST W. RAMSEY, M.B., B.CH., F.R.C.S.
PROFESSOR OF UROLOGY
UNIVERSITY OF MANITOBA
WINNIPEG, MANITOBA, CANADA

Benign prostatic hyperplasia (BPH) is a nonmalignant enlargement of the prostate uncommon before the age of 40 but occurring in most men as they age. The symptoms of BPH are generally attributed to bladder outlet obstruction from the enlarging prostate gland. However, not all men with enlarged prostates are symptomatic, and similar voiding symptoms can occur from other causes in the absence of BPH. Symptomatic BPH is a major health problem and a major expense to the healthcare system. Transurethral resection of the prostate (TURP) has been the treatment of choice for over 50 years, and until recently, approximately 400,000 TURPs have been performed annually in the United States at an estimated cost of $4 billion to $5 billion per year.[1] TURP is an effective treatment for relief of prostatic obstruction and has generally been referred to as the "gold standard."

Apart from its high cost, TURP is also associated with some problems. Approximately 20% to 25% of patients do not have a satisfactory long-term outcome. TURP has become a safe procedure with a mortality rate of less than 0.5%; however, complications include loss of ejaculation, urethral strictures, bladder neck contracture, and occasionally, impotence, urinary incontinence, and the need for blood transfusion. Repeat surgery may be required in as many as 15% to 20% of men followed for over 10 years. It is likely that many men have tolerated the symptoms instead of undergoing surgery.

Because of these complications, there has been great interest in alternative treatments for BPH. These have included drug therapy using either alpha adrenergic blockers, currently used in the treatment of hypertension to relax the smooth muscle of the prostate, or five-alpha reductase inhibitors which reduce the size of the prostate by decreasing the amount of dihydrotestosterone available. Major technological advances have also produced myriad treatment options which are currently undergoing evaluation.

These new treatments involve the delivery of heat to the prostate in an effort to cause tissue destruction, thereby relieving the obstruction (Table 1). Lasers have been widely used and are claimed to offer major advantages compared to TURP in decreased morbidity and shorter hospital stay.[2,3] However, the optimal technique for laser use remains unclear, and further investigation is required. A recent innovation is the use of a modified rollerball electrode. This simple device is used with a standard resectoscope and uses standard radio frequency electrical current. By utilizing a high setting on the cutting modality, it is capable of causing tissue vaporization similar to that of a laser.[4] The obvious advantage is the reduced cost of equipment. This technique is currently undergoing investigation. Transurethral needle ablation (TUNA) involves the endoscopic insertion of needle electrodes into the prostate to cause coagulation necrosis within the prostatic tissue while preserving the urethra.[5] Initial results with this technique are encouraging. High intensity focused ultrasound (HIFU) involves the use of a transrectal ultrasound probe which is capable of causing necrosis at precise points within the prostate.[6] These procedures, with the possible exception of the TUNA, have required general or spinal anesthesia, and all are operator-dependent. The ideal treatment for symptomatic BPH should provide good subjective and objective improvement and minimal morbidity; it should also be carried out as a single outpatient session under local anesthesia at reasonable cost. Transurethral microwave thermotherapy (TUMT) has the potential to meet these goals.

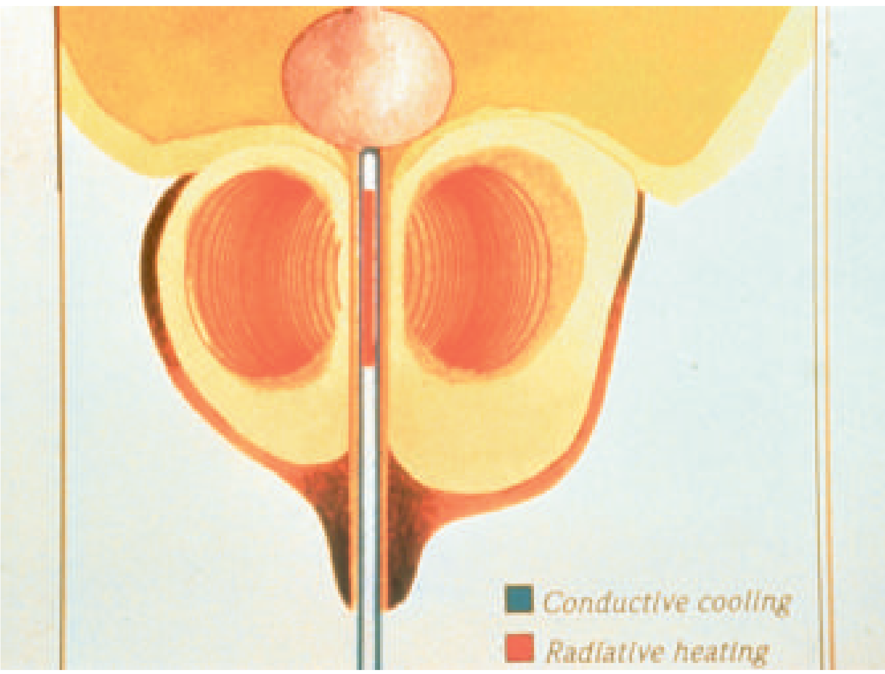

Figure 1. Microwave antenna in prostatic urethra causes heating within prostate.

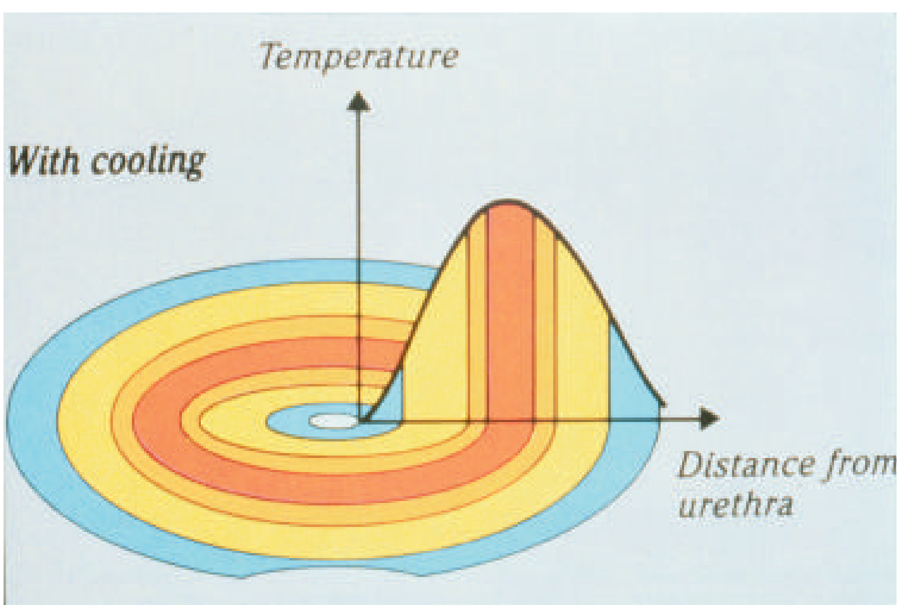

Figure 2. Microwave heating of prostate with urethral cooling.

PRINCIPLES OF TREATMENT

Microwaves cause heating due to molecular excitation. The devices used for BPH utilize frequencies in the range of 900 to 1300 MHz; the higher the frequency, the less tissue penetration occurs. At tissue temperatures up to 45°C, there is no destruction (hyperthermia), while at temperatures above 45°C, coagulative necrosis occurs (thermotherapy). The degree of tissue destruction obtained will depend upon the temperature and the length of time for which this temperature is maintained. Hyperthermia either by the transrectal or transurethral route has been investigated extensively in the treatment of BPH and has been clearly demonstrated not to be of benefit in relieving obstruction.[7]

To achieve higher temperatures within the transitional zone where BPH occurs, the microwave antenna needs to be placed in the prostatic urethra (Fig. 1). The procedure involves the insertion of a specially designed Foley-type catheter. The microwave antenna is placed a short distance below the retention balloon to sit within the prostatic urethra. The urethra is sensitive to temperatures in excess of 45°C while prostatic tissues are relatively insensitive. The use of urethral cooling through the catheter permits temperatures up to 70°C to be obtained within the prostate while maintaining urethral temperatures

Table 1. Heat delivery to the prostate

Laser	→	sidefiring	→	coagulation
		sidefiring	→	vaporization
		contact	→	vaporization
		interstitial	→	coagulation
Rollerball				
Transurethral needle ablation (TUNA)				
High-intensity focused ultrasound (HIFU)				
Transurethral microwave thermotherapy (TUMT)				

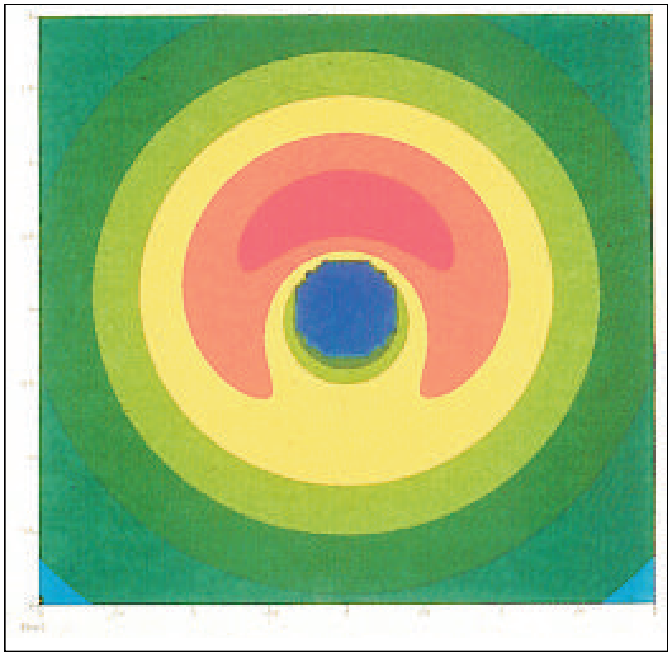

Figure 3. Microwave energy and heating directed laterally and anteriorly with T3 device (Courtesy of Urologix).

below the 45°C threshold. This permits the patient to tolerate treatment under topical anesthesia with the added advantage of preserving the urethra so that tissue sloughing does not occur.

The intraurethral temperature is monitored by means of a thermal sensor. Thermal sensors are also placed in the rectum to monitor rectal temperatures. The procedure is performed as a single outpatient treatment under topical anesthesia. In most reports, TUMT has not led to transurethral resection (TUR)-like defect, although several recent reports using higher temperatures indicate that a TUR-like defect can occur.[8,9] It is thought that the tissue necrosis leads to a decrease in urethral resistance. Other suggested benefits include destruction of alpha-adrenergic nerve fibers and changes in the sensory part of the voiding reflex.

RESULTS OF TUMT

Until recently, the Prostatron™ device (Technomed Medical Systems, Lyon, France) has been the most widely used system, with over 25,000 patients having been treated worldwide in over 70 centers. The morbidity from TUMT has been minimal. When a catheter has not been left in place following treatment, temporary urinary retention has been reported in 10% to 25% of patients. Loss of ejaculation appears to be uncommon. Even with higher temperatures, there has been no evidence of damage to structures such as the rectum, external sphincter, or ureteral orifices.

A number of studies have compared TUMT to no treatment (SHAM). Devonec et al. reported results from a multicenter trial with a 12-month follow-up which was in favor of TUMT.[10] There was a decrease in the Madsen symptom score (MSS) of 52% versus 2% and a peak flow increase of 29%, compared with a decrease of 6% for TUMT and SHAM respectively. Blute et al. reported results from a similar U.S. study with a three-month follow-up.[11] The MSS decreased by 55% versus 28% while peak flow increased by 57% versus 27% for TUMT and SHAM respectively. A Swedish study compared TUMT with TURP.[12] A two-year follow-up showed that the mean MSS had decreased from 12.1 to 2.6 mL/sec in the TUMT group and from 13.6 to 1.1 mL/sec in the TURP group. The mean peak flow rate increased from 8.4 to 12.8 mL/sec in the TUMT group and from 8.3 to 19.7 mL/sec in the TURP group. While improvement in the peak flow was greater than the TURP group, little difference was seen in improvement in symptom score. A recent follow-up in this study has indicated that results have been maintained for up to three years.[13]

The clinical outcome of TUMT has been shown to be related to the degree of prostatic heating. Carter and Ogden recorded intraprostatic temperatures during treatment and demonstrated that results clearly improved with high-

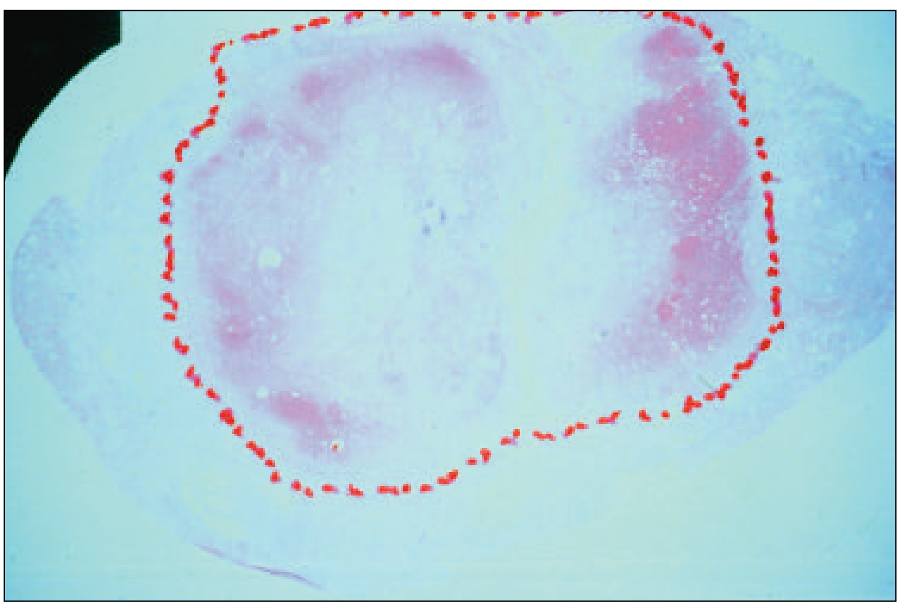

Figure 4. Enucleated BPH specimen following TUMT with T3 Urologix device. Coagulative necrosis is seen in the transitional zone (Courtesy of Dr. D. Bostwick, Mayo Clinic, Rochester; Dr. T. Larson, Mayo Clinic, Scottsdale; and Dr. A. Corica, University of Nacional de Cuyo, Mendoza, Argentina).

er temperatures.[14] Similar results have been reported by Trachtenberg et al.[8] Devonec and colleagues have also demonstrated improved results with increasing energy levels culminating in temperatures which produced a cavity within the prostate.[9] Unfortunately these higher temperatures have been associated with increased morbidity.

Reports using TUMT have varied widely in their results. This probably relates to the inability to attain and maintain high temperatures or to maintain a temperature over 45°C for a sufficient time. It may be that slightly lower temperatures (but >45°C) for a longer duration may be as effective as higher temperatures for a shorter period of time. The former would be better tolerated by the patient and may be associated with fewer complications. With the initial input of microwave energy into the prostate, intraprostatic temperature tends to remain fairly stable despite the increasing amount of heat being delivered. This is likely due to the marked vasodilation occurring within the gland with shunting away of heat. After this, there is a rapid rise in temperature which can be maintained with decreased energy input and is probably related to coagulation of blood vessels with resulting decreased blood flow. There is considerable variation from patient to patient due to differences in prostate size, ratio of glandular to stromal tissue, and blood supply. Ideally, one would monitor the intraprostatic temperatures, but this currently involves the insertion of thermal sensors directly into the prostate and thus would be too invasive for general use.

INNOVATIONS

There has been some skepticism regarding the value of TUMT which likely relates to the initial poor results from hyperthermia and the variable results reported with thermotherapy. As discussed above, the variable results with TUMT are likely related to the inability to maintain adequately high temperatures for a sustained period of time. With the TUMT devices currently in use, heating is circumferential (Fig. 2). As a result, rectal temperatures tend to rise, causing the power to shut off. This results in an immediate fall in intraprostatic temperature. As a result, heating is intermittent, making it difficult to maintain an adequate intraprostatic temperature to cause necrosis. A new device, the Urologix T3, using a different microwave antenna and a preferential nonsymmetrical heating pattern, permits the microwave heating to be directed laterally and anteriorly (Fig. 3). This prevents a rise in rectal temperature and permits sustained high temperatures within the prostate. This does not imply that heating does not occur posteriorly but that it is better controlled. Microwave energy produces heat not only by induction, which involves limited tissue penetration, but also by conduction. As a result, large areas of necrosis can result. Figure 4 shows an enucleated BPH specimen following T3 treatment with the Urologix device. Extensive coagulative necrosis is seen in the transitional zone.

Initial results with this device have yielded excellent subjective and objective responses.[15] Over 100 patients have been treated at the initial three investigative sites, and six-month follow-up data are available for 71 patients. The AUA symptom score decreased from a mean of 20.4 to 7.9 (61%). A greater than 50% improvement was seen in 74% of patients. Mean peak urine flow rate increased from a mean of 8.7 to 13.2 mL/sec (52%). A greater than 30% increase in peak flow was seen in 74% and a greater than 50% increase in 59% of patients. The bothersome index decreased by 68%. In patients followed for one year, these results have been maintained. Complications have been insignificant. A Foley catheter has generally been left in place for two to five days, although some patients are now managed without a catheter. Short-term urinary retention after catheter removal has occurred in 9% of patients, and all resolved in 3 to 30 days.

The subjective benefit obtained by this treatment is similar to that with TURP. The improvement in urine flow rates is less than with TURP; this difference may be due to the destruction of the bladder neck which occurs with TURP while being preserved with T3. While it may be possible to treat the bladder neck with T3, this may result in increased complications such as bladder neck contracture and loss of ejaculation, which occurs in over 70% of men after TURP but is seen rarely with TUMT.

T3, therefore, appears to be effective in reducing symptoms of BPH, and it is indeed symptom relief which patients seek. Is it necessary to achieve the high flow rates seen with TURP? Such flow rates exceed that found in age-matched men who have no symptoms. Comparison of mean flow rates obtained with the Urologix T3 device were 90% of those of age-matched asymptomatic men in the Olmsted County study.[16]

CONCLUSION

T3 fulfills the criteria of an outpatient procedure which can be performed under topical anesthesia and with minimal morbidity. Although there has been some skepticism with regard to its efficacy, it has become clear that achieving good results depends on the ability to sustain high intraprostatic temperatures. Innovations in design have made this possible. While more long-term data are required, results to date suggest that T3 will be a valuable treatment option for men with symptomatic BPH. STI

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