

INTERSTITIAL TEMPERATURE MAPPING DURING PROLIEVE TRANSURETHRAL MICROWAVE TREATMENT: IMAGING REVEALS THERMOTHERAPY TEMPERATURES RESULTING IN TISSUE NECROSIS AND PATENT PROSTATIC URETHRA

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ABSTRACT

Objectives. Temperature mapping of the prostate during transurethral microwave thermotherapy and imaging of the resultant zones of tissue necrosis have been previously performed using several commercial systems. This study was performed using the Prolieve Thermodilatation System, which simultaneously compresses the prostate with a 46F balloon circulating heated fluid and delivering microwave energy into the prostate.

Methods. Interstitial temperature mapping during Prolieve treatment was performed on 10 patients with benign prostatic hyperplasia using 24 temperature sensors arrayed throughout the prostate. Voiding cystourethrograms were performed on 3 additional patients treated without temperature mapping to document the patency of the prostatic urethra 1 hour after treatment. Gadolinium-enhanced magnetic resonance imaging studies were performed on all patients 1 week after treatment to determine the extent and pattern of tissue necrosis resulting from transurethral microwave thermotherapy.

Results. Interstitial temperature mapping found that the heating pattern generated by the Prolieve system created average peak temperatures of 51.8°C an average of 7 mm away from the prostatic urethra. These temperatures were greater near the bladder neck and mid-gland than toward the prostatic apex. Subtherapeutic temperatures were seen adjacent to the urethra, consistent with the viable tissue seen on gadolinium-enhanced magnetic resonance imaging sequences. Magnetic resonance imaging also revealed necrotic zones that were consistent with sustained temperatures greater than 45°C. Voiding cystourethrograms showed widely patent prostatic urethras 1 hour after treatment.

Conclusions. Transurethral microwave thermotherapy with the Prolieve Thermodilatation System produced sustained therapeutic temperatures that resulted in tissue necrosis while maintaining viable tissue surrounding a temporarily dilated prostatic urethra.

The treatment of benign prostatic hyperplasia (BPH) has evolved to include three categories of treatment: medications, office procedures, and surgery. Medications have proven effective in some cases, and surgical resection of the prostate has long been the standard of care for BPH; however, limitations exist with each. Office-based proce-

dures using minimally invasive techniques have been increasingly used to provide relief of lower urinary tract symptoms because of the limited morbidity and no requirement for hospitalization.

Transurethral microwave thermotherapy (TUMT), which creates high temperatures within the prostate using a catheter that contains a microwave antenna,

This study was funded by an unrestricted educational grant from Boston Scientific Corporation, Marlborough, Massachusetts.

T. R. Larson is a paid consultant to the sponsor.

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has emerged as an attractive treatment option with good subjective and objective relief of lower urinary tract symptoms.¹⁻³ Although office-based microwave treatment has been performed with local anesthesia and sedation, many patients experience discomfort during treatment, and many require posttreatment catheterization because of the edema of the thermal injury.⁴ The recently Food and Drug Administration-approved Prolieve Thermodilatation System (Boston Scientific, Marlborough, Mass, and Celsion, Columbia, Md) was conceived with the objective of further reducing the side effects of microwave thermotherapy. The design hypothesis was that the use of a 46F transurethral balloon catheter circulating heated fluid would compress the prostate with the intent of reducing blood flow and thereby reducing the amount of microwave power needed to cause tissue necrosis. The balloon was also expected to provide temporary urethral dilation during resolution of the treatment-induced edema.

Interstitial temperature mapping of the prostate during TUMT and imaging of the resultant zones of necrosis has been previously performed on other clinically effective microwave thermotherapy systems.⁵⁻⁸ The purpose of this study was to document that the interstitial heating pattern generated by the Prolieve system is sufficient to create interstitial necrosis, while preserving the urethra and maintaining a dilated urethral lumen.

MATERIAL AND METHODS

Under an institutional review board-approved protocol and patient-informed consent, the interstitial prostatic temperatures were recorded in 10 patients diagnosed with BPH during treatment with the Prolieve Thermodilatation System.

This system delivers 915 MHz of microwave energy at a maximum of 50 W through an 18F transurethral catheter. A unique component of this microwave catheter is a 46F × 3.6-cm balloon positioned in the prostatic urethra. The balloon is inflated with circulating heated water during the microwave treatment. The microwave energy output from the antenna positioned within the balloon is modulated under computer control by feedback from a rectal temperature measuring probe to prevent rectal temperatures greater than 42°C. The total treatment time is 45 minutes, with a 5-minute cooling period, during which the prostatic balloon remains inflated after the energy delivery has stopped.

Six closed-end 17-gauge plastic needle cannulas (Best Corporation, Richmond, Va) were placed through the perineum into the prostate under biplane transrectal ultrasound guidance into positions parallel to the transurethral treatment catheter. The needles were arrayed laterally and/or posteriorly to the urethra at distances of 2.2 mm to 2.5 cm, with the tip of the needle at the prostatic base. The transrectal ultrasound-measured distance from the urethral wall to each needle was recorded before balloon dilation. Fiberoptic temperature-measuring probes with four sensors spaced 1-cm apart were placed into each needle. This arrangement allowed for simultaneous interstitial temperature recording of up to 24 locations every 10 seconds in a three-dimensional grid pattern

surrounding the treatment catheter throughout the procedure, resulting in more than 6000 data points for each patient.

To document the acute posttreatment prostatic urethral caliber, standing voiding cystourethrography was performed on an additional cohort of 3 patients who had undergone standard Prolieve treatment with only intraurethral lidocaine topical anesthesia. These patients did not have transperineal temperature mapping needles placed into the prostate to exclude the confounding effects of edema caused by interstitial needle placement. Before treatment, the patient's bladder was filled retrograde through a 7F open-ended catheter with 300 mL of a mixture of saline and contrast. The patient was asked to void in a standing position during video fluoroscopic recording of the entire voiding sequence. The same process was repeated 1 hour after treatment with the Prolieve system.

One week after treatment, all patients underwent gadolinium-enhanced magnetic resonance imaging (MRI). Gadolinium defects appear darker than healthy tissue on MRI because of reduced or absent blood flow. Previous publications have correlated these defects with necrotic zones consistent with sustained temperatures greater than 45°C.⁹⁻¹¹ Multiple, dynamic T₁-weighted, fat-suppressed sequences were done with gadolinium enhancement. A series of dynamic sequences were obtained every 20 seconds from the gadolinium injections to 6 minutes after. Gadolinium defects were characterized and measured using the Analyze imaging software (Mayo Clinic, Rochester, Minn). This program calculates the volume of necrosis and the prostate volume.

The correlation between the maximal average temperature for each subject and the volume of necrosis was evaluated by the Pearson product moment method. A third-order polynomial trend line was fitted to the maximal average temperatures recorded at each distance from the urethra by the least squares method.

RESULTS

On inflation of the 15-mm diameter intraprostatic balloon, the transrectal ultrasound-measured maximal prostate diameter increased an average of 1.3 mm in width and 3.7 mm in height, reflecting prostatic glandular compression with little capsular expansion.

The intraprostatic temperatures typically reached sustained treatment temperature plateaus after a single slope ramp up of 3 to 9 minutes. A typical plot of all recorded interstitial temperatures during a single treatment is shown in Figure 1.

The transverse heating pattern was generally circumferential around the urethra, as illustrated by the trend line fitted to the maximal average temperatures for all patients at all measured distances laterally and posteriorly to the urethra (Fig. 2). The temperatures remained below therapeutic levels (less than 45°C) in the periurethral tissues immediately adjacent to the dilated balloon, rising to greater than therapeutic levels at distances of 2 to 14 mm, peaking at near 7 mm, with an exponential decay beyond. The sagittal heating pattern generated was a skewed ellipse, with greater temperatures observed near the bladder neck and mid-gland than at the prostatic apex. A three-dimensional depiction of mean treatment temperatures, observed in a single representative patient, lateral from the urethra and

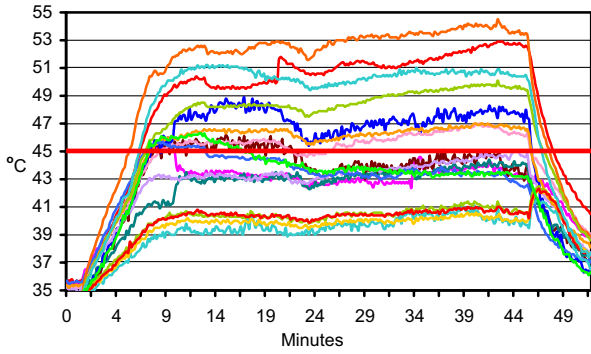


FIGURE 1. Intraprostatic temperature plot of representative subject. Note, sustained temperatures greater than 45°C during treatment. All recorded temperatures measured are displayed, including those outside treatment zone (each line represents temperature of individual sensor).

extending from the base of the prostate toward the apex is shown in Figure 3.

Temperatures greater than 45°C were recorded in all patients, and 8 of 10 patients had temperatures greater than 50°C. The mean maximal temperature recorded for all patients was 51.8°C, and the absolute maximum was 56.9°C. The average power delivered in the 10 temperature-mapped patients was 43.3 W and the average total energy was 113.7 kJ.

Gadolinium-enhanced MRI sequences revealed zones of necrosis that correlated with the temperature maps of the areas showing sustained temperatures greater than 45°C. The average volume of necrosis was 6.45 g or 9.0% of the total prostate volume. Prostates with greater recorded maximal average temperatures correlated with larger volumes of necrosis ($r = 0.73$ $P \leq 0.05$, $R^2 = 0.54$). A zone of viable tissue, evidenced by brighter gadolinium-enhanced tissue and averaging 5.0 mm radially, surrounded the urethras (Fig. 4).

The posttreatment standing voiding cystourethrograms of the 3 patients treated without temperature mapping showed patent prostatic ure-

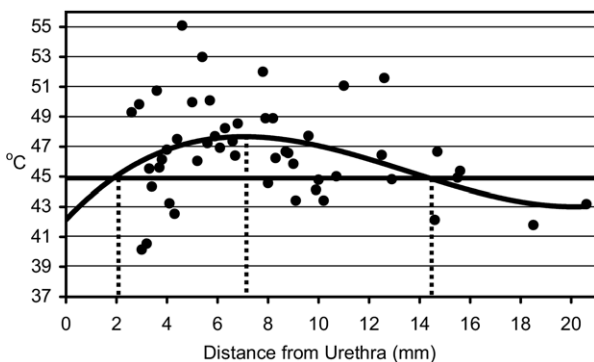


FIGURE 2. Trend line fitted to maximal average temperatures from all sensors of all subjects. Temperatures greater than 45°C are required for thermotherapy.

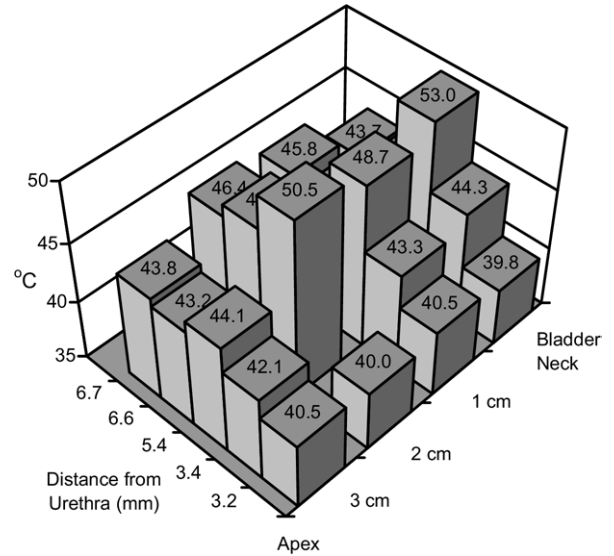


FIGURE 3. Average treatment temperatures lateral and parallel to urethra of representative subject.

thras in all patients with calibers of approximately 1.5 cm. This compares with the approximately 5-mm caliber before treatment (urethral caliber estimated by comparison with the 7F filling catheter; Fig. 5). A minimal postvoid residual urine volume was seen in these patients after treatment.

COMMENT

The Prolieve Thermodilatation System is the newest Food and Drug Administration-approved TUMT office-based thermotherapy device. Comprising a unique treatment catheter containing a

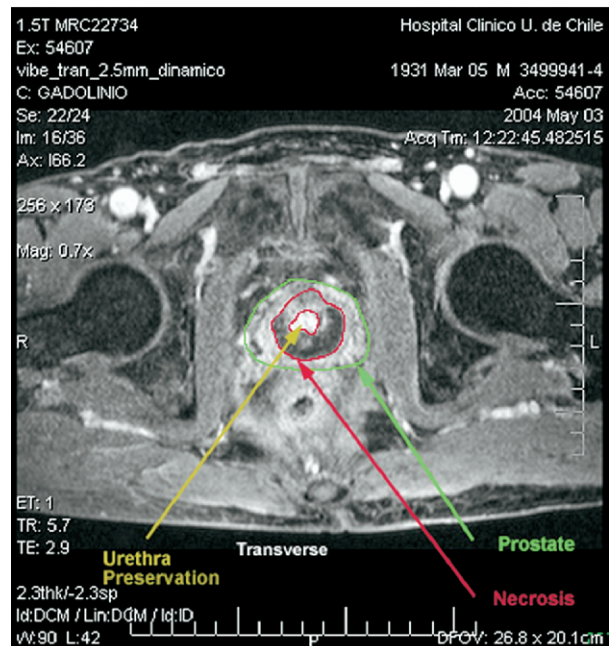


FIGURE 4. Gadolinium-enhanced MRI scan showing areas of necrosis and viable prostatic tissue.



FIGURE 5. Standing voiding cystourethrograms before (top) and (bottom) 1 hour after treatment.

balloon that dilates the prostatic urethra to 46F during treatment, the Prolieve system creates a heating pattern of sustained temperatures greater than 45°C that result in tissue necrosis deep in the prostate without causing high temperatures or necrosis at the urethra, as shown by the gadolinium-enhanced MRI findings after treatment.

This thermodilation system and treatment technique differs from the technique of balloon dilation or “balloon divulsion” of the prostate as a primary treatment for BPH, as described by Cataneda and Reddy¹² in initial human trials in 1987. This technique was intended to disrupt the prostatic capsule and/or the anterior commissure with balloons of 75F to 120F.¹³ Randomized trials of balloon divulsion have reported initial improvements in symptom scores and peak urinary flow rates and have generally concluded that these improvements were temporary, with symptoms returning toward baseline within 1 to 12 months.¹⁴

Several effects may be attributed to the Prolieve 46F prostatic compression balloon that differenti-

ates Prolieve system treatment from other TUMT or balloon devices. First, this diameter balloon allows for complete circumferential contact with the urethral wall when it is inflated with circulating fluid heated to subtherapeutic temperatures, thereby maintaining the entire urethral wall at relatively constant subtherapeutic temperatures. Additionally, although we did not have access to Doppler ultrasonography to measure blood flow in these patients, the observed tissue compression within the unyielding prostatic capsule may act to tamponade prostatic blood flow, reducing the heat removal effect of blood flow.¹⁵ This tissue compression also reduces the depth through the tissue that the microwave energy needs to penetrate during heating. These conditions reduce the amount of microwave power required to heat the mid-gland prostatic tissues to therapeutic temperatures. The “mid-energy” Prolieve system produces a maximum of 50 W compared with 60 to 80 W for the “high-energy” systems and 23 W for the lowest energy system. This lower power requirement may have led to the minimal medication requirement and mild treatment discomfort reported in the initial clinical use of the Prolieve system.¹⁶ Finally, balloon dilation of the prostatic urethra has been shown in this study to be sustained, at least in the immediate postprocedure period. Dilation maintained during resolution of postthermal therapy prostatic edema without urethral sloughing could explain the limited catheterization requirement reported after Prolieve treatment.¹⁶

The amount of necrosis generated by the Prolieve treatment is somewhat less than that reported for some TUMT devices and more so than for others.^{8,17,18} This mid-energy treatment, combined with the compression balloon, could provide an optimal balance of reduced power requirements, leading to increased patient comfort, and resulting in the type of tissue necrosis documented in other clinically effective microwave thermotherapy devices. These attributes, combined with preservation of a dilated urethra allowing reduced numbers of patients requiring postprocedural catheterization, should provide a more tolerable office-based treatment for lower urinary tract symptoms. The clinical outcome after Prolieve treatment was outside the scope of the present study; however, preliminary reports have shown promising results.¹³

CONCLUSIONS

TUMT with the Prolieve Thermodilatation System produced sustained therapeutic temperatures that resulted in tissue necrosis while maintaining viable tissue surrounding a temporarily dilated prostatic urethra. Additional research is required

to correlate the observations of the present study with clinical improvement in patients' symptoms.

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