A MATHEMATICAL MODEL TO PREDICT INTRA-PROSTATIC TEMPERATURES AND TISSUE NECROSIS DURING TRANSURETHRAL MICROWAVE THERMAL ABLATION OF THE PROSTATE

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1. INTRODUCTION

Trans-urethral ablation of prostatic tissue by microwave radiation is now an accepted modality for the treatment of benign prostatic hyperplasia (BPH) BPH . The procedure involves elevation of intra-prostatic tissue temperatures by means of a microwave-delivery catheter inserted into the prostate via the urethra. The catheter contains a microwave antenna surrounded by coolant channels, the latter serving to reduce the temperature elevation of the urethral surface. Thermal energy generation occurs volumetrically within the prostate, resulting in temperature elevation to between 50 ℃ and 85 ℃ within the gland, while urethral surface temperatures typically remain under 42 ℃ due to the circulating cooling water. The high intra-prostatic temperatures achieved during therapy result in necrosis of a sizable volume of prostatic tissue. The concomitant reduction in prostate volume leads to alleviation of the mechanical obstruction of the urethra and, thus, a resolution of the symptoms associated with BPH. This paper presents a mathematical model for predicting intra-prostatic temperatures and necrosis zones during microwave treatment for BPH. The details of the model are presented and comparisons between model predictions and measurements in human patients are provided.

Spatial and temporal variations of perfusion have an important bearing on the temperature distribution in the prostate. Prior modeling attempts have hinted at the nature of these variations, but no comparisons have yet been made between model predictions and measured tissue temperatures during the entire course of a microwave treatment. Although good agreement has been obtained in prior studies by adjusting perfusion levels to match the steady state temperatures, there has been no attempt to incorporate the thermo-regulatory perfusion response into a predictive model of the tissue temperatures.

2. EXPERIMENTAL PROTOCOL

Interstitial temperature mapping studies were conducted on nine volunteer human subjects to obtain the necessary experimental database for model calibration. In all cases, the patients were administered a spinal anesthetic, and several fiber-optic temperature probes (Luxtron Corp., Mountain View, California.) were inserted into the prostate through nylon needle-tipped cannulae introduced percutaneously through the perineum. Patients were treated using the Urologix Targis microwave ablation catheter. Treatment duration was between 45 minutes and 60 minutes. A total of 16 interstitial temperatures were monitored for each patient. The temperature sensors were scanned once every 10 seconds, and the data were automatically logged into a laptop computer.

3. THE MATHEMATICAL MODEL

The computational domain is taken to be a long tissue cylinder encompassing the entire prostate as well as a layer of fatty tissue surrounding the capsule of the gland. The inner-most layer of tissue, 5 mm in radial extent, is taken to be the peri-urethral zone. The temperature field is assumed to be purely one-dimensional, i.e. only radial variations in temperature are considered, while axial and circumferential variations are ignored. The model is based on the Pennes bio-heat equation:

$$\rho_t c_t \frac{\partial T}{\partial t} = div(k\ grad T) - \omega \rho_b c_b (T - T_a) + Q + Q_m \quad (1)$$

The equation is solved numerically using appropriate boundary

conditions and input values for the thermophysical properties and the microwave heat generation rate, Q. The various empirical constants in the model were determined by bench-top experiments as well as by measurements of interstitial temperatures in human patients.

The model accounts for increases in blood perfusion with increases in tissue temperature. Tissue damage is evaluated by computing the value of the damage integral, and vascular shutdown is simulated by an abrupt reduction in the perfusion when a critical value of the damage integral is reached.

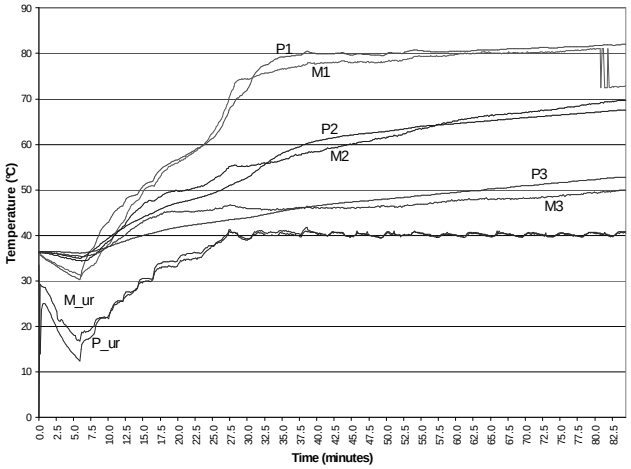

Fig. 1: Comparison of Measured and Predicted Interstitial Temperatures in One Patient (P = predicted, M = measured)

Figure 1 present direct comparisons of measured and predicted interstitial temperatures in one of the nine human subjects in the interstitial mapping study. The model was run retrospectively, using the actual coolant and power values used in the treatment. The agreement between the measured and predicted temperatures is seen to be very good. (Additional comparisons are presented in the full paper).

Figure 2 presents a comparison of the numerical model predictions with the data from analysis of MR images of treated prostates. The abscissa plots the necrosis area predicted by the one-dimensional model, while the ordinate plots the necrosis volume measured by MRI. The necrosis area is computed as $\pi\left(r_2^2 - r_1^2\right)$, where r_2 and r_1 are the radii of the outer and inner boundary of the necrotic zone. The best-fit line as well as the individual data points from 21 patients are shown. The plot shows that there is an approximately linear relationship between the calculated necrosis area and the measured necrosis volume. The standard deviation, σ, of the difference between the best-fit straight line and the measured necrosis volumes is 2.3 ml.

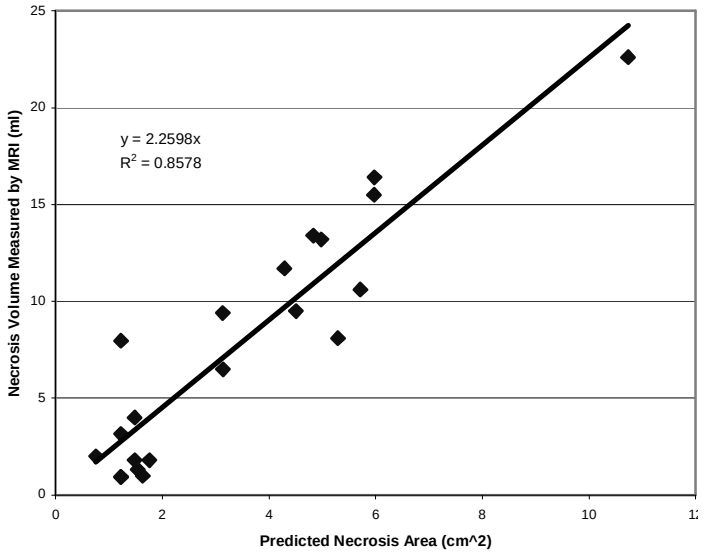

Fig. 2: Relationship between predicted necrosis area and measured necrosis volume

4. DISCUSSION AND CONCLUSIONS

The ability of the model to predict necrosis volumes within +/- 3.5 ml with 90% confidence (+/- 1.5σ) is clinically valuable. The model provides the clinician with the ability to adjust the treatment duration on a patient-specific basis to achieve a uniform volume of necrosis, optimally around 12 – 15 ml for the average 45 ml prostate. With the implementation of this model it is expected that outcomes from the Targis treatment will display greater uniformity from patient to patient.