

# MR Thermometry for Predicting Thermal Damage: Interstitial Laser Coagulation in an *In Vivo* Canine Prostate

R.D. PETERS<sup>1,4</sup>, J. TRACHTENBERG<sup>3,5</sup>, W. KUCHARCZYK<sup>2,5</sup>, AND R.M. HENKELMAN<sup>1,2,4</sup>

*Dept. of <sup>1</sup>Medical Biophysics, <sup>2</sup>Medical Imaging, and <sup>3</sup>Surgery, University of Toronto*

*<sup>4</sup>Sunnybrook & Women's College Health Sciences Centre and <sup>5</sup>The Toronto Hospital, Toronto, Canada*

**Introduction:** MR image-guidance for interstitial thermal-coagulation therapy has proven to be a valuable tool for three primary roles (i) device localization, (ii) thermal monitoring, and (iii) post-treatment lesion assessment. However, a quantitative understanding of how temperature-time exposure relates to thermal damage is crucial if the predictive value of real-time MR thermal-mapping is to be fully realized [1]. In this study, results are presented on interstitial laser coagulation (ILC) of an *in vivo* canine prostate model which are used to evaluate three models of thermal damage. The models were analyzed for their ability to classify an isoeffect along the lesion margin as derived from post-treatment MR images as well as direct histological evaluation of the excised canine prostate. Histological evaluation shows that the thermal-injury boundary can be predicted from a threshold-critical temperature of approximately 51°C or an equivalent  $t_{43}$  period of 200 minutes. The methods described in this study are expected to have direct implications for the treatment of benign prostatic hyperplasia and prostate cancer with ILC, which will be the focus of future human studies.

### Methods and Materials:

In this study a diode laser was used (Indigo 830e, Indigo Medical Inc., Cincinnati OH) for applying ILC in the prostate glands of two male Labrador dogs [2]. At surgical laparotomy, two laser fibres and four Luxtron fibre-optic thermal probes (Luxtron Corp., Santa Clara CA) were inserted into the right and left sides of the prostate gland.

The PRF-shift method of MR thermometry was used where temperature-induced phase shifts were obtained from a gradient-echo acquisition [3]. All imaging was performed on a 1.5 T MRI system (GE SIGNA) using a 5-inch surface coil placed on the dog's abdomen. An SPGR sequence was used to acquire three axial 5mm-thick slices (TE=30ms, TR=50ms, FOV=160mm, 256 x 128 matrix). The laser fibres were oriented parallel with the main-magnetic field to eliminate magnetic susceptibility-related errors in PRF-shift thermometry.

Upon localization of the laser fibres with a 3D-SPGR sequence, two ILC applications were made in each prostate with simultaneous MR thermal mapping. A typical ILC application consisted of maintaining a target temperature of 85°C (as measured by a thermal sensor in the laser fibre) for 3 minutes. MR thermal mapping was terminated once the entire prostate returned to uniform body temperature.

Post-treatment images were used to assess the thermal-coagulation volume and consisted of T1-weighted (TE=20ms, TR=500ms) and T2-weighted (TE=85ms, w/resp. trig.) images before and after a single-dose injection of gadodiamide (0.2 ml/kg, Omniscan, Nycomed Inc., Princeton NJ). Histological examination of the excised prostates was also performed with H&E staining to provide a true measure of the extent of coagulative necrosis.

The thermal lesion margins were manually traced on the post-treatment T1- and T2-weighted images and digitized histological sections and used to assess the thermal-damage model's ability to classify an isoeffect. Three models of thermal damage were assessed using the MR-thermal maps from the four ILC applications. The first was based on a critical-threshold or maximum temperature model. A second model included the effect of treatment time and was based on the Arrhenius-damage integral [4], expressed as the equivalent

heating time at 43°C ( $t_{43}$ ):

$$t_{43} = \sum_i K^{T_i - 43^\circ\text{C}} \Delta t \quad (1)$$

where  $K$  is equal to 2 when  $T > 43^\circ\text{C}$  and equal to 4 when  $T < 43^\circ\text{C}$ . The third model treated both time and temperature in a linear manner and consisted of a simple temperature-time product ( $TTP$ ):

$$TTP = \sum_i \Delta T_i \cdot \Delta t \quad (2)$$

where  $\Delta T_i$  is the temperature elevation from baseline body temperature for image  $i$ . A discriminant analysis was used to determine the optimal threshold model that described the onset of thermal coagulation, which was assessed from the margin boundaries from the post-treatment MR images and histological evaluation.

**Results:** The MR-thermal maps showed the evolution of non-radial temperature distributions within the prostate tissue that eventually dispersed once laser power was terminated. The standard deviation of temperature in the unheated region of the prostate was less than 1.5°C. Some spurious signals were seen outside of the prostate and likely corresponded to phase artifacts from small motions in the abdomen.

The post-treatment T1- and T2-weighted images showed a hypointense lesion encircling the laser fibres with Gd-contrast enhancement. The histological H&E stained sections revealed a region of necrosis that was sharply defined with an abrupt transition zone between normal prostatic and necrotic tissue, on both a 4-hour and 24-hour survival period.

The threshold model values determined from the histology sections (see table) provided the only consistent findings among all four ILC applications. In particular, the average critical temperature was  $51 \pm 2^\circ\text{C}$  and  $t_{43}$  was  $200 \pm 3$ -fold min., ie. 67 – 600 min. The  $TTP$  model values were not found to provide results as consistent as the first two models did.

Lesion	max. $T$ (°C)	$t_{43}$ (min.)	$TTP$ (min.°C)
1	$50 \pm 2$	$1.8 \times 10^2 \pm 10$ -fold	$62 \pm 8$
2	$49 \pm 3$	$1.0 \times 10^2 \pm 10$ -fold	$80 \pm 12$
3	$56 \pm 6$	$1.0 \times 10^4 \pm 100$ -fold	$74 \pm 20$
4	$49 \pm 2$	$1.8 \times 10^2 \pm 5$ -fold	$118 \pm 62$

**Conclusion:** Thermal-mapping modalities, such as MRI, must supply more than simple temperature measurements within tissue to ultimately realize their clinical importance or necessity. A better understanding of how temperature exposure relates to actual thermal damage is necessary in order to properly establish the predictive value of real-time MR-thermal mapping. Post-treatment MR images may provide conspicuous margins that don't necessarily reflect the true extent of thermal coagulation, and often require a delay period for a host response which places a severe limitation on their prognostic value during thermal treatment.

[1] S.J. GRAHAM, *et al. MRM* 41:321-328 (1999).

[2] U.G. MUELLER-LISSE, *et al. JMRI* 8:31-39 (1998).

[3] Y. ISHIHARA, *et al. SMRM Proc.* 4803 (1992).

[4] S. SAPARETO. *Int. J. Rad. Oncol. Biol. Phys.* 10:787-800(1984).