

# Investigations on ultrasound focal therapy for MRI-Guided transurethral treatment of the prostate: dual-frequency ultrasound heating in gel phantom

William Apoutou N'DJIN<sup>1,2</sup>, Charles MOUGENOT<sup>3</sup>, Ilya KOBELVSKIY<sup>1</sup>, Elizabeth RAMSAY<sup>1</sup>, Michael BRONSKILL<sup>1,2</sup>, and Rajiv CHOPRA<sup>1,2</sup>

<sup>1</sup>Imaging Research, Sunnybrook Research Institute, Toronto, ON, Canada, <sup>2</sup>Department of Medical Biophysics, University of Toronto, Toronto, ON, Canada, <sup>3</sup>Philips Healthcare, Toronto, ON, Canada

## Introduction

Standard treatments for localized prostate cancer such as radical prostatectomy and radiotherapy treat disease effectively but are associated with significant long-term complications with respect to urinary, sexual and bowel function. For low-risk patients (85% of the diagnosed patients), the after cancer life quality and maintenance of autonomy is essential to assess real treatment benefits. Ultrasound thermal therapy of localized prostate cancer offers a minimally-invasive non-ionizing alternative [1-3] that could be better suited for patients with low-risk localized disease. MRI-controlled transurethral ultrasound prostate therapy [4-6] has recently been investigated in a pilot human feasibility study [7]; however, only a small sub-volume of prostate tissue was treated to ensure safety to study participants. In this study, the feasibility of transurethral dual-frequency ultrasound focal therapy has been investigated experimentally in gel phantom.

## Material and Method

A database of pelvic anatomical models of human prostate cancer patients have been created using MR images obtained from our previous pilot human study of MRI-controlled transurethral ultrasound therapy. The largest human prostate boundary of this database (47 cm<sup>3</sup>) was used to fabricate an anatomical gel phantom made of a tissue-mimicking material (Zerdine<sup>®</sup>, CIRS Inc, USA) which included various MR characteristics to mimic prostate tissues, localized tumors and surrounding prostate tissues. A 9-element linear ultrasound transducer working in dual-frequency mode ( $f = 4.6/14.5$  MHz, surface: 9 x 5 x 3.5 mm<sup>2</sup>) was mounted at the tip of a 25-cm linear probe (6 mm in diameter). The transurethral ultrasound device was inserted at room temperature into a cylindrical container containing the phantom material whose attenuation coefficient at 1 MHz and speed of sound were 0.5 dB/cm and 1540 m/s respectively. The number of elements to use was determined during the treatment planning based on the size of the prostate (base to apex distance). The target boundaries were traced every 5 mm on T2w MR images to cover in 3D: (i) the entire prostate gland (Full prostate treatment strategy) (Figure 1a), (ii) a prostate region restricted to tumors (Focal therapy) (Figure 2a). Nine thermometry images were positioned relative to device features evident on image planning, and were centered on each transducer in multiple planes orthogonal to the applicator (Philips Achieva 3.0T scanner; torso XL coil; sequence: EPI; EPI factor: 13; thermometry: PRF shift; image size: 224 x 224 pixels; FOV: 26 cm; slice thickness: 5 mm; TE/TR: 15/133 ms; temperature uncertainty: ~0.5°C). These imaging parameters validated on healthy volunteers enabled full human prostate volume coverage from base to apex with temperature data updated every 6.2 seconds. Acoustic power of each element and rotation rate of the device were adjusted in real-time based on MR-thermometry feedback control to optimize heat deposition at the target boundary [4-7]. Experiments have been performed using a maximal surface acoustic power of 20W.cm<sup>2</sup> and dual-frequency ultrasound exposures: each element was driven at its fundamental frequency for target radii greater than 18 mm and at its 3<sup>rd</sup> harmonic for lower radii [6-7].

## Results

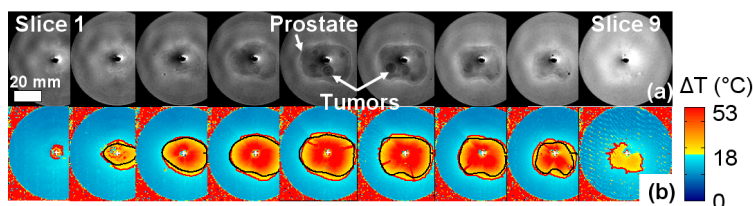
The gel phantom contained 4 tumor-mimics ranging 5 to 10 mm in diameters. The volume of the reconstructed prostate boundaries in the anatomical gel phantom was 52 cm<sup>3</sup> and prostate radii ranged from 8 to 31 mm. (i) For full prostate heating, 7 elements of the device were used to cover the entire prostate length. The heating process was completed within 35 min (treatment rate: 1.8 cm<sup>3</sup>/min). Ultrasound exposures at the fundamental frequency allowed full heating of the largest prostate radii (> 18 mm), while exposures at the third harmonic ensured homogeneous treatment of the smallest radii. Undertreated and overtreated regions represented respectively 2% and 17% of the prostate volume. The targeting error was 2 ± 3 mm (Figure 1b). (ii) For focal therapy, the target region was optimized to maintain safe regions in the prostate and to cover all tumor-mimics. Only 5 ultrasound elements were used to treat successfully all tumor-mimics (Figure 2b). The heating process was completed within 26 min (treatment rate: 1.1 cm<sup>3</sup>/min). Undertreated and overtreated regions represented respectively 7% and 7% of the prostate volume. The radial targeting error was 0 ± 2 mm.

## Discussion

The feasibility of MR-thermometry controlled heating in a human prostate geometry has been demonstrated using a transurethral dual-frequency ultrasound device and validated clinical imaging settings. Two different strategies have been tested successfully. Full prostate volume heating was fast and accurate compared to standard HIFU prostate treatments. Dual-frequency ultrasound exposures allowed optimal heat deposition in all prostate regions. The focal therapy strategy allowed successful heating of all targeted regions in shorter time. It maintained safe regions in the prostate and enhanced safety in prostate surrounding regions.

## Conclusion

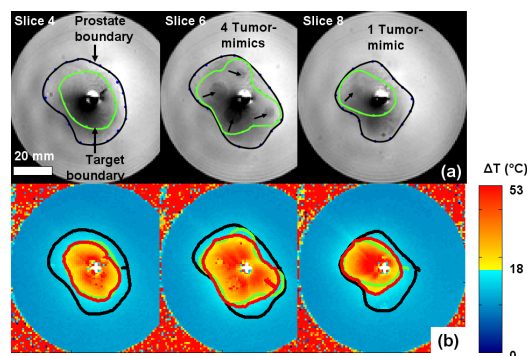
MRI-guided transurethral ultrasound procedure enables full treatment and focal therapy in human prostate geometry. The focal therapy strategy is promising as regard to safety and could contribute to enhance the post-treatment autonomy of the patient. This transurethral treatment approach showed enough flexibility to adapt to future orientations for the management of the localized prostate cancer.



**Figure 1:** Full prostate treatment strategy: MR Magnitude image + thermometry

## References

- [1] Chapelon JY et al. *Eur J Ultrasound* 1999; 9(1):31-3
- [2] Uchida T et al. *Int J Urol* 2006; 13(3):228-233
- [3] Diederich CJ et al. *Med. Phys.* 2004; 31(2):405-413
- [4] Chopra R et al. *Med. Phys.* 2008;35(4):1346-1357
- [5] Burtynk M et al. *Int J Hyperthermia* 2009;25(2):116-1
- [6] N'Djin WA et al. *Int J Hyperthermia* 2011; in press
- [7] Chopra R et al. *Int J Hyperthermia* 2010;26:804-821.



**Figure 2:** Focal prostate gland treatment strategy

## Acknowledgements

Financial support was received from the Terry Fox Foundation and from the NIH (1R21CA159550)