Technical Feasibility of MRI-controlled Interstitial Ultrasound Brain Therapy

William Apoutou N'DJIN[1,2], Mathieu BURTNYK[1,3], Nir LIPSMAN[4], Michael BRONSKILL[1,2], Michael SCHWARTZ[4], Walter KUCHARCZYK[3], and Rajiv CHOPRA[1,2]

[1]Imaging Research, Sunnybrook Research Institute, Toronto, ON, Canada, [2]Department of Medical Biophysics, University of Toronto, Toronto, ON, Canada, [3]Department of Medical Imaging, University Health Network and the University of Toronto, Toronto, ON, Canada, [4]Division of Neurosurgery, University of Toronto, Toronto, ON, Canada

Introduction

High-Intensity focused ultrasound (HIFU) therapy is an emergent technique which presents several advantages: the technique is non/minimally invasive, non-ionizing for the patient and the treatment can be guided/monitored in real-time by medical imaging. Transcranial HIFU treatments in brain monitored with MR-thermometry aim to achieve a totally non-invasive treatment for the patient [1,2]. The recent emergence at the clinical level of minimally-invasive focal therapy such as laser-induced thermal therapy (LITT) has demonstrated promise in the management of brain metastasis [3], although control over the spatial pattern of heating is limited. Delivery of HIFU from minimally-invasive applicators enables high spatial control of the heat deposition in biological tissues, large treatment volumes and high treatment rate in well chosen conditions (no acoustic barrier) [4,5]. In this study, the feasibility of MRI-guided interstitial ultrasound therapy in brain was studied in-vivo in a porcine model.

Materiel and Method

A prototype system developed for MRI-controlled transurethral ultrasound therapy of localized prostate cancer treatment [6,7,8] was used in this study. An acute pig model was utilized in this study, which was approved by the local animal care committee. Five pigs (30-50 kg) were treated under general anesthesia (Ketamine: 20mg/kg; Atropine: 0.04 mg/kg; 1-3% isoflurane) and under mechanical ventilation (Oxygen: 2L/min). Two burr holes of 12 mm in diameter were created in the animal's skull (~2-3 cm anterior to the coronal suture, 0.6 cm lateral to sagittal suture), to allow the insertion of the therapeutic ultrasound applicator (probe) into the brain at two locations (right and left frontal lobe). A 4-element linear ultrasound transducer (f = 8 MHz, surface: $4 \times 5 \times 3.5$ mm^2) was mounted at the tip of a 25-cm linear probe (6 mm in diameter). The number of elements to use was determined during the treatment planning based on the space available to generate ultrasound exposures. The target boundary was traced to cover in 2D a surface compatible with the treatment of a 2 cm brain tumor (**Figure 1**). 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 [4,6,7]. The axial thermometry slice was centered on the activated elements (GE Signa 1.5T scanner; sequence: real-time FSPGR; thermometry: PRF shift; image size: 128 x 128 pixels; FOV: 16 cm; slice thickness: 5 mm; TE/TR: 9/39.1 ms; temperature uncertainty: ~1.5°C). Before the treatment, the body temperature of the animal was measured with a rectal thermometer to provide the base temperature. Two MRT-controlled ultrasound brain treatments per animal have been performed using a maximal surface acoustic power of 10W.cm^{-2}. After heating, post-treatment anatomical images (T2w FSE, TE/TR: 100/5650 ms) and pre-contrast injection images (T1w 3D-FSPGR, TE/TR: 5/10) were acquired. Then, a clinically-approved gadolinium-based contrast agent (Omniscan, 0.1mmol/kg) was administered intravenously to visualize the pattern of thermal damage produced in the brain. Immediately after imaging, animals were euthanized and the brain was removed for gross-sample analysis.

Results

The analysis was performed on 6 comparable treatments from three animals (full rotation of the device over 360° in the brain). Due to the small size of the pig brain, only 2 - 3 elements were used for ultrasound heating. In all, it was possible to increase accurately the temperature of the brain tissues in the targeted region over the 55°C threshold necessary for the creation of irreversible thermal lesion. Tissue changes were visible on T1w contrast-enhanced images immediately after treatment. These changes were also evident on T2w FSE images taken 2 hours after the 1st treatment and correlated well with the temperature images (**Figure 2**). On average, the targeted volume was 4.7 ± 2.3 cm^3 and the 55°C treated volume was 6.7 ± 4.4 cm^3. The volumetric undertreatment and overtreatment were respectively 0.1 ± 0.1 cm^3 and 0.7 ± 0.6 cm^3. The radial targeting accuracy was on average 1 ± 3 mm. Treatments were completed within 7 ± 3 min, that is an average treatment rate in brain of 0.9 ± 0.7 cm^3/min.
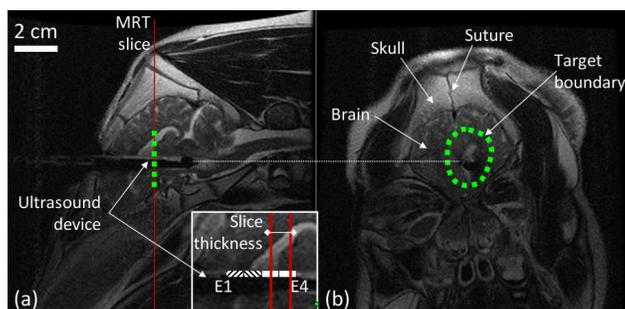

Figure 1: In-vivo treatment planning during interstitial pig brain treatment. T2w anatomical MR imaging of the animal head. **(a)** Sagittal view, **(b)** axial view
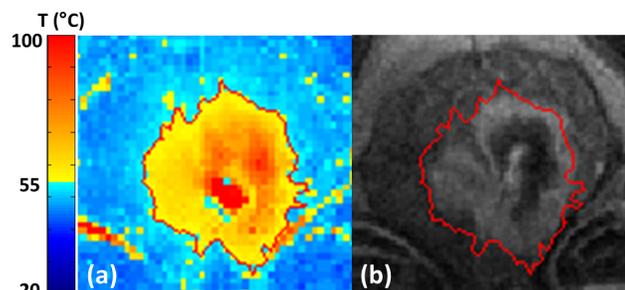

Figure 2: After the HIFU treatment: **(a)** MR thermometry, cumulative temperature; **(b)** T2w anatomical image.

Discussion

The feasibility of using interstitial ultrasound devices to produce controlled regions of heat (coagulation) using MRI-guidance and temperature feedback has been demonstrated. The treatment was fast, well tolerated and a good targeting accuracy was achieved, typically within 2 mm. The small size of pig brain posed challenges due to proximity of skull bone, ventricles, and medial longitudinal fissure. Future investigations will focus on device miniaturization, targeting of specific brain structures/tumors and on the control of heat deposition in 3D.

Conclusion

MRI-controlled interstitial ultrasound therapy of brain tissue is feasible. This minimally-invasive approach avoids the need to propagate ultrasound through the skull by inserting an ultrasound transducer directly within the brain. This approach to spatially controlled heating could be used for tissue ablation or drug delivery.

References

[1] Hynynen K and Jolesz FA. Ultrasound Med Biol 1998;24:275–283.
[2] Tanter M et al. J Acoust Soc Am 1998;103:2403–2410.
[3] Carpentier et al. Neursurgery 2008;63(1):ONS21-ONS29
[4] Chopra R et al. Med Phys 2008;35:1346–1357.
[5] Melodelima D et al. Med Phys. 2006 Aug;33(8):2926-34.
[6] Chopra R et al. Phys Med Biol 2005;50:4957–4975.
[7] Burtnyk M et al. Int J Hyperthermia 2009;25:116–131.
[8] Chopra R et al. Int J Hyperthermia 2010;26:804–821.

Acknowledgements