

## Methods for 3D treatment envelope evaluation in transcranial MRgFUS

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### Introduction

Transcranial magnetic resonance guided focused ultrasound (tcMRgFUS) is a totally non-invasive treatment modality with great promise for many neurological disorders. In recent clinical trials, targets were near the geometric center of the skull convexity [1], minimizing the challenges of focusing the US through the skull bone. With non-central targets, focusing becomes more challenging since beam aberration and the risk of unintended heating of near-field tissue-bone interfaces increases. To determine the intracranial treatment envelope where therapeutic levels of FUS can be achieved, Eames *et al.* monitored FUS power deposition at the focal point with 2D MR temperature imaging (MRTI) [2]. Skull surface heating was not monitored. Here we present methods to determine the intracranial treatment envelope including relative skull heating for safety monitoring using 3D MRTI to monitor the fully insonified 3D field-of-view (FOV). Beam aberration due to focusing through the skull is evaluated with hydrophone scans. For this proof-of-concept work, a lamb model was used.

### Methods

**MRTI** A gradient echo 3D segmented echo planar imaging pulse sequence was used for MRTI utilizing the proton resonance frequency (PRF) shift method for temperature calculations. k-space was subsampled (reduction factor,  $R=4$ ) in the  $k_y$  (phase encode) direction, and fully sampled in the  $k_x$  and  $k_z$  (read out/slice encode) directions. Imaging parameters were: voxel size =  $1.0 \times 1.0 \times 2.0$  mm, FOV =  $192 \times 144 \times 60$  mm, TR/TE = 36/11 ms, bandwidth = 752 Hz/px, echo train length = 9, acquisition time = 4.32 s. All data was acquired on a 3T MRI scanner (Siemens Medical Solutions, Erlangen, Germany) using two in-house built 2-channel receive-only RF coils, zero-filled interpolated to  $0.5 \times 0.5 \times 1.0$ -mm spacing, and reconstructed with a temporally constrained reconstruction algorithm [3,4].

**FUS heating** A total of 32 sonications were performed in two axial planes (figures 1a-c) through the intact skull of a recently euthanized full-term lamb using a phased-array transducer (256 elements, 1 MHz, 13-cm radius of curvature,  $2 \times 2 \times 8$ -mm FWHM, Imasonic, Besançon, France) with hardware and software for mechanical positioning, and electronic beam steering (Image Guided Therapy, Pessac, France). The distal and proximal (relative to the transducer) planes (figure 1b and c) contained 20 and 12 sonications, respectively. The transducer was mechanically moved to five (four) different positions in the distal (proximal) plane, and from each mechanical position the beam was electronically steered  $\pm 5$  mm in both x and y, for 10 mm in-plane spacing. Each sonication was performed at 32 acoustic watts for 17.3 s.

**Hydrophone scan** Post-heating hydrophone (Model HNR-0500, ONDA, Sunnyvale, CA) scans were performed through the skullcap while electronically steering  $\pm 5$  mm in x and y from one mechanically fixed US transducer position. FOV was  $20 \times 20$  mm and resolution  $0.25 \times 0.25$  mm.

### Results

Figures 2a-c and d-f show coronal, transverse, and sagittal views of combined temperature maps from the 20(12) sonications in the distal(proximal) plane superimposed on magnitude images for anatomical reference. Figure 3 shows 2D thin-slab maximum intensity projections (MIPs) of heating occurring in the near-field inside the skull (excluding the focal spot) for one sonication in each plane. The ratio between the hottest voxel in the focal spot and the mean of the ten hottest near field voxels was calculated for all 32 sonications. These ratios are interpolated and extrapolated to the full intracranial volume in figure 4. Figures 5a-d and e-h show results from the hydrophone scan when focusing in water only and through the skullcap, respectively.

### Discussion

Figures 2b-c, e-f, and 3 show that substantial near-field heating occurred in all sonications. This results from the non-optimal transducer design for the current application. Due to the transducer's large natural focus depth (13 cm) and the small volume of the lamb brain, the energy entering the skull is spread over a relatively small area, which in combination with a high US frequency of operation (1 MHz) results in high energy deposition at the skull surface. For these reasons, and because only 32 relatively widely spaced (10-mm separation) sonications were performed, the derived treatment envelope (figure 4) should be seen as a proof-of-concept. The problems stemming from the non-optimal transducer design are alleviated in brain-specific clinical FUS systems by operating at a lower frequency (220 or 610 kHz) and spreading the ultrasound elements over a larger hemispherical surface. The hydrophone scans show that with the current transducer and experiment setup, only a slight phase aberration but a rather substantial intensity drop is to be expected when focusing through the skull. These results agree well with the observed temperature distributions.

### Conclusions

This work describes methods for 3D treatment envelope evaluation that simultaneously monitor the focal spot and all near- and far-field tissue-bone interfaces. Results from FUS heating studies are complemented with hydrophone scans to characterize beam aberration and intensity losses. The described methods can be useful from a safety perspective to evaluate existing transducer designs, and validate new designs aimed at expanding the treatable volume in tcMRgFUS.

**References** [1] Elias *et al.* N Engl J Med. 2013 369(7):640-8. [2] Eames *et al.* 3<sup>rd</sup> International Symposium on Focused Ultrasound 2012, p. 124. [3] Todd *et al.* MRM 2009 62(2):406-19. [4] Todd *et al.* MRM 2012 67(3):724-30. **Acknowledgements** This work was supported by The Focused Ultrasound Surgery Foundation, Siemens Healthcare, The Ben B. and Iris M. Margolis Foundation, and NIH grants F32 EB012917-02, and R01s EB013433, and CA134599.

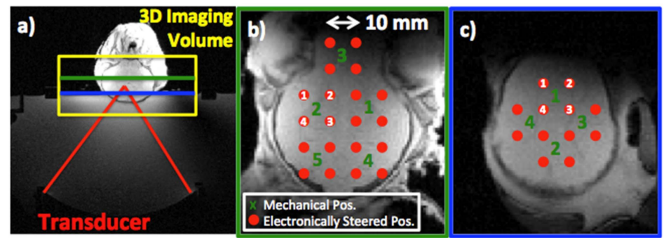


Fig 1. a) Transverse view of experimental setup, with lamb in supine position. The yellow box indicates the 3D imaging FOV, and green and blue lines indicate locations of coronal slices, spaced 8mm apart, in figures 1b) and 1c), respectively. 1b) and 1c), red dots indicate sonication locations in the two coronal planes. Note that mechanical position 3 and 4 for the proximal plane only consists of 2 electronic positions each.

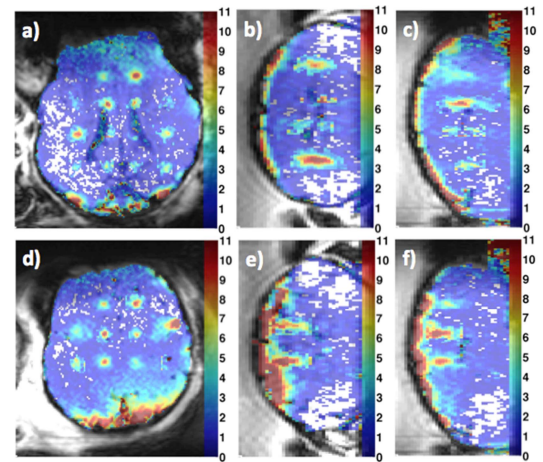


Fig 2. Coronal, transverse, and sagittal views of temperature increase MIP for the 20 sonications in the distal (a-c) and 12 sonications in the proximal (e-f) planes overlaid on magnitude images, respectively.

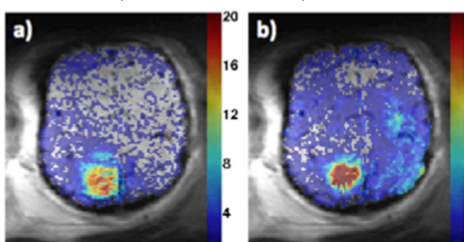


Fig. 3. a) and b) 2D temperature MIPs of near-field heating inside the skull for one sonication in the distal and proximal plane, respectively. More near-field heating is observed when focusing closer to the skull.

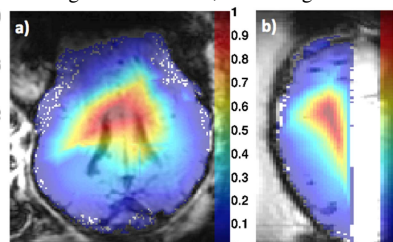


Fig. 4. Evaluation of the treatment envelope. a) and b) coronal and sagittal views of the ratio between the hottest voxel in the focal spot and the mean of the ten hottest voxels in the near field, extrapolated to the full intracranial volume.

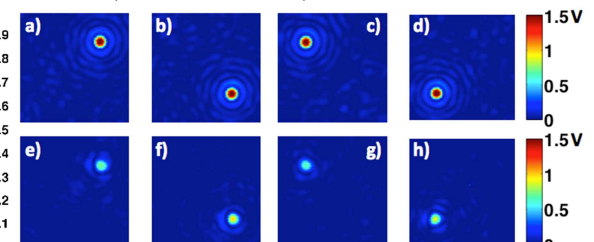


Fig. 5. Hydrophone scan with steering  $\pm 5$  mm in x and y in a) - d) water only, and e) - h) through skullcap, respectively. Intensity drop between 42 and 62% and slight beam aberration can be observed when focusing through the lamb skull.