Magnetic resonance diffusion tensor imaging-guided focused ultrasound ablation of the porcine ventral intermediate nucleus

Karolina Piorkowska[1], Matthew Jenkins[1], Vivian Sin[1] , Nicole Silva[2] , Jessica Barrios-Martinez[3], Craig Macsemchuk[1] , Mojgan Hodaie[4], Frank Yeh[3], George M. Ibrahim[1], Adam C Waspe[1] Vibhor Krishna[2]

[1]Hospital for Sick Children, Toronto, ON, Canada [2]University of North Carolina, - Chapel Hill NC, USA [3]University of Pittsburgh, PA, USA [4]University Health Network, Toronto, ON, Canada

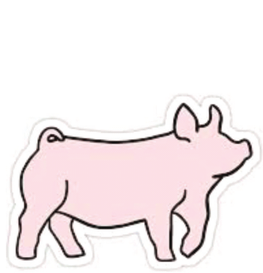
Karolina.Piorkowska@sickkids.ca

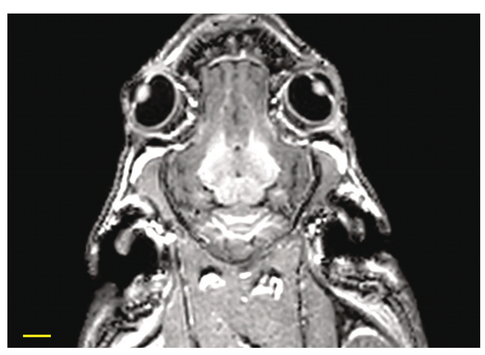
At-a-glance: Improving targeting accuracy by comparing two methods for focused ultrasound (FUS) ablation of the ventral intermediate nucleus in a porcine model: conventional formulaic versus diffusion tensor imaging (DTI)-guided

Introduction

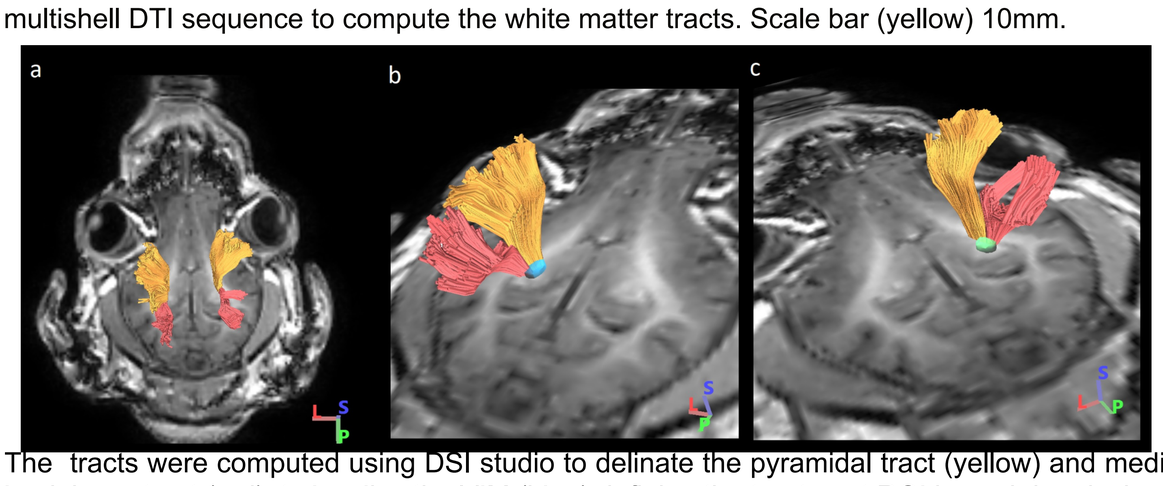
- Essential tremor (ET) is a common neurological disorder characterized by rhythmic, involuntary shaking leading to functional and psychological disabilities.
- Focused ultrasound (FUS) ablation is a Health Canada and FDA-approved treatment that is public and private insurance-reimbursed for ET patients who failed medications.
- FUS ablation targets the ventral intermediate nucleus (VIM), successfully alleviating tremor symptoms in most patients immediately and in long-term follow up studies.
- However sub-optimal results can be see in some patients: loss of efficacy (tremor recurrence in 25%) and adverse effects from off-target ablation (sensory and motor side effects in 20%).
- The success of VIM-FUS depends on the ability to accurately ablate 70% of the VIM volume while minimizing heat spread to the adjacent tissue.
- Stereotactic VIM targeting conventionally relies on localizing the VIM relative to the anterior and posterior commissures.
- Diffusion tensor imaging (DTI) reconstructs white-matter pathways, allowing high-resolution, three-dimensional visualization of the VIM.
- We developed a tractography-guided focused ultrasound (FUS) workflow that precisely outlines the full 3-D extent of the VIM for personalized targeting (3-d tractography).
- Single-center, single-arm trials of 3-D tractography–guided VIM-FUS show less off-target ablation, but the biophysical mechanisms are still unclear.
- We compared conventional formula-based targeting with our 3-D tractography guided workflow in a swine model, hypothesizing that 3-D tractography maximizes on-target VIM ablation while minimizing the risk of off-target injury.

Methods

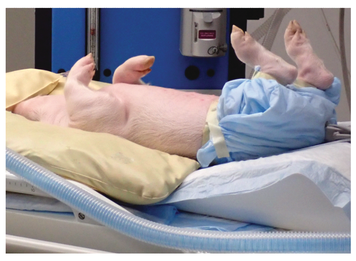


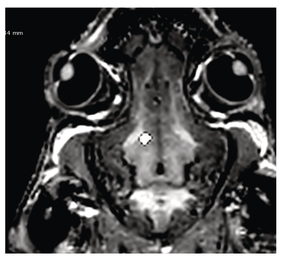


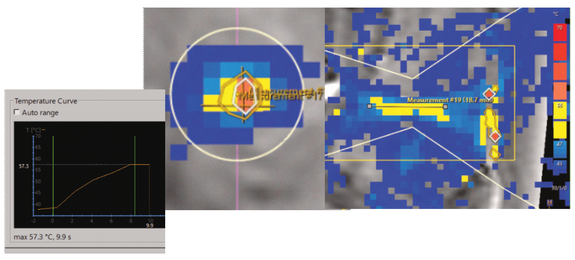
- Yorkshire piglets (n=9) 4.7 +/-1 kg were put under anaesthesia and placed prone within a Phillips 3T MRI and 32 channel head coil to acquire a pre-operative 3D T1-w FFE and a 115 direction multishell DTI sequence to compute the white matter tracts. Scale bar (yellow) 10mm.



- The tracts were computed using DSI studio to delinate the pyramidal tract (yellow) and medial leminiscus tract (red) to localize the VIM (blue) defining the treatment ROI in each hemisphere.
- DSI studio was used to perform a non-linear registration to overlay the DTI ROI onto the pre-operative T1-w image.
- Alternatively, the VIM was located 6mm lateral to midline, 3mm anterior to posterior commissure and 3mm superior to the intercommissural plane.





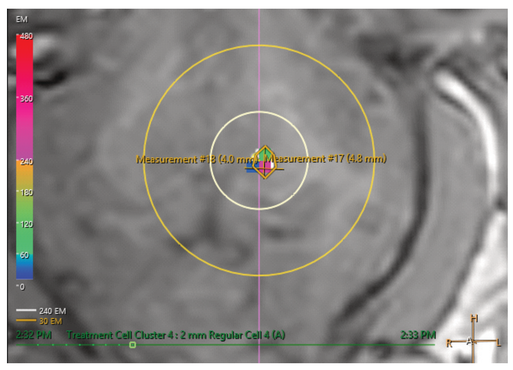


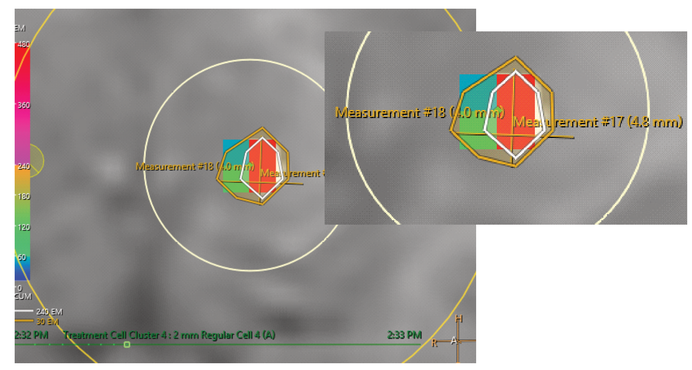
- After a craniectomy and pre-treatment MRI, the piglets were placed supine on the Sonnalleve V2 HIFU table and coupling was achieved with a 4cm gel pad and degassed ultrasound gel.
- A new T1-w planning image was acquired and DSI studio was used to manually transform and co-register the pre-operative T1-w image containing the VIM ROI to the treatment planning images acquired during FUS for real-time guidance (3D tractography group).
- The contralateral VIM was planned using conventional measurements.
- Two FUS sonications were performed (60W, 1.44MHz, F#1.03) to achieve 240CEM at the sonication target as monitored by MR thermometry (blue >43˚C, yellow <56˚C< red)
- Following post-treatment MRI, piglet brains were perfusion fixed and paraffin embedded then 4µm sections stained with hematoxylin and eosin (H&E), cresyl violet or luxol fast blue (LFB) for histologic analysis.

Results

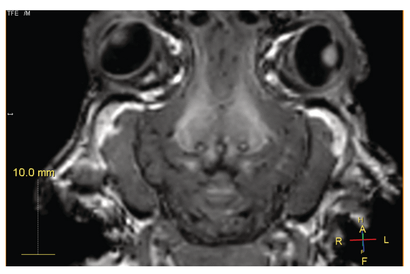
	Conventional (n=6)	DTI (n=4)
Piglet weight	6.1 +/- 0.9 kg	7.4 +/- 0.3 kg
Test shot heating (20W 15.94s)	47.1 +/- 3.6˚C	46 +/- 2.1˚C
FUS sonication time	8.8 +/- 1.8 seconds	7.7 +/- 0.9 seconds
FUS cooling time	5.9 +/- 0.8 minutes	6 +/- 0.9 minutes
FUS max temp	58.9 +/- 2.6˚C	59.8 +/- 3.6˚C
Thermal spread axial	5.1 +/- 1.2mm	5.3 +/- 0.7mm
Thermal spread sagittal	4.5 +/- 1.0mm	3.6 +/- 0.9mm
Thermal spread coronal	11.5 +/- 3.0mm	10.4 +/- 2.6mm

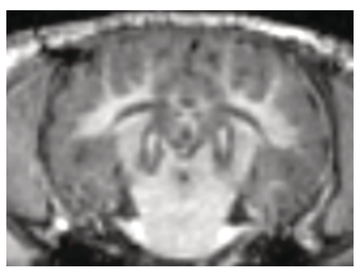
- The FUS treatment parameters did not differ between the groups: similar piglet weight, marginal warming with test shots, sufficient cooling time and FUSA sonication times that reached maximum temperatures during MR thermometry that equal 240CEM at the centre, and the thermal spread of >30CEM also was similar in all planes.

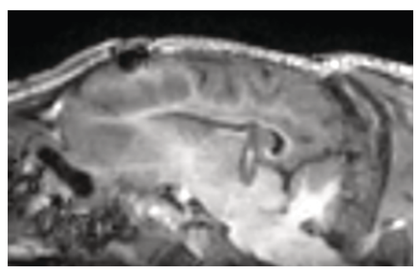




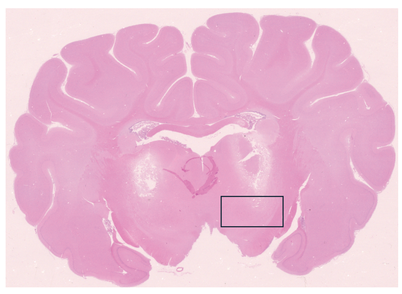
- Thermal dose measurements (>30 CEM yellow outline and 240 CEM white outline) generated by the Sonnalleve software in the 3-D tractography group showed precise ablation of the VIM (white).

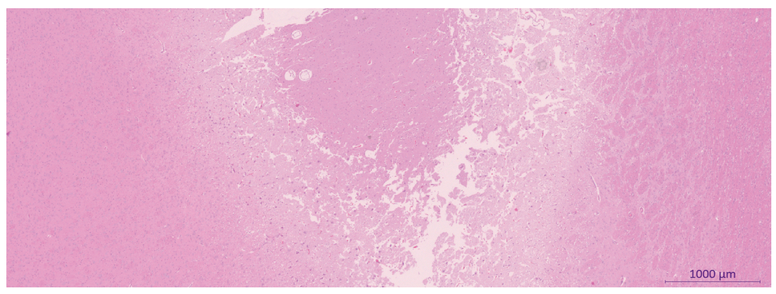


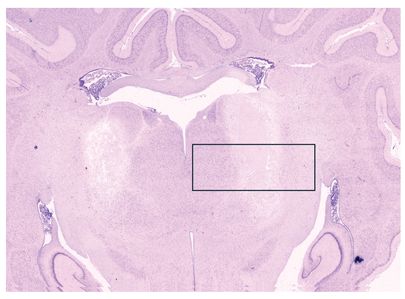


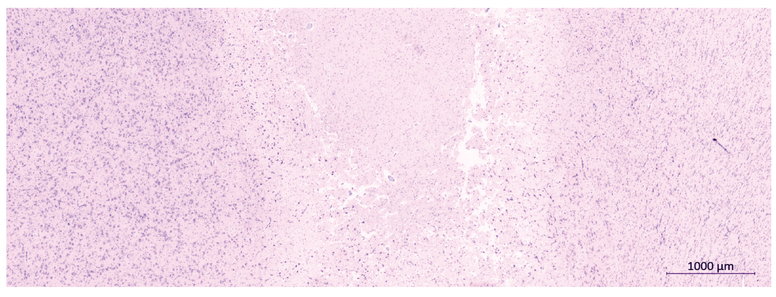


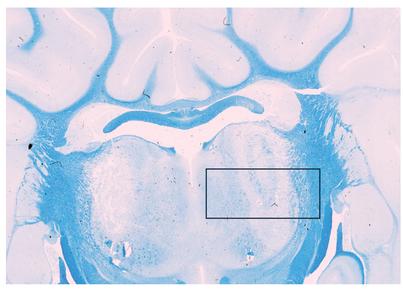
- The post-treatment T1w images in axial, coronal and sagittal view show the bilateral sonication locations with a hyperintense core and hypointense ring of cytotoxic edema.

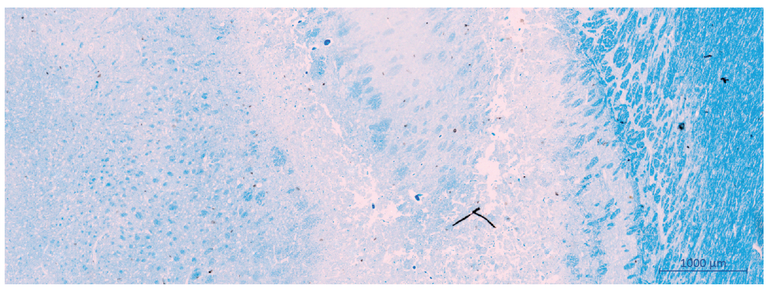












- H&E coronal view and microscopic zoom shows a central area of necrosis with a general homogenization of cellular material with a peripheral area with pyknotic cells and vacuous space transitioning to healthy thalamic tissue.
- Cresyl violet coronal overview shows neuronal shape and patterns within the thalamus and brain; the central necrotic area is void of neurons indicating connections were severed, peripheral area has disorganized and pyknotic neurons indicating affected and potentially changed areas.
- LFB overview shows myelinated tracts through the coronal cross section; the peripheral area shows a marked reduction in myelination

Acknowledgments and Affiliations

Funding from

NIH

UNC HEALTH

UHN Krembil Brain Institute

Hodaie Lab

Surgical Imaging Laboratory
Multimodality Imaging in Stereotactic and Functional Neurosurgery

University of Pittsburgh

Fiber Tractography Lab

DSI Studio

SickKids

PCIGITI
Wilfred and Joyce Posluns Centre for Image-Guided Innovation and Therapeutic Intervention

GMI

Conclusions

- Interim data show that sonication parameters are consistent between conventional and 3-D tractography-guided VIM FUS ablation when using clinically relevant settings.
- Initial results indicate high concordance between the planned VIM region-of-interest and ablative thermal dose in the few samples analyzed; quantitative comparison of targeting accuracy between groups is ongoing.
- Post-treatment T1-w and T2-w MRI clearly delineate the ablation core, which aligns with histological evidence of cellular necrosis and is distinguishable from the surrounding perilesional edema.
- The 3-D tractography-based FUS planning pipeline is reproducible, reducing FUS planning ambiguity, and is readily translatable to clinical practice.