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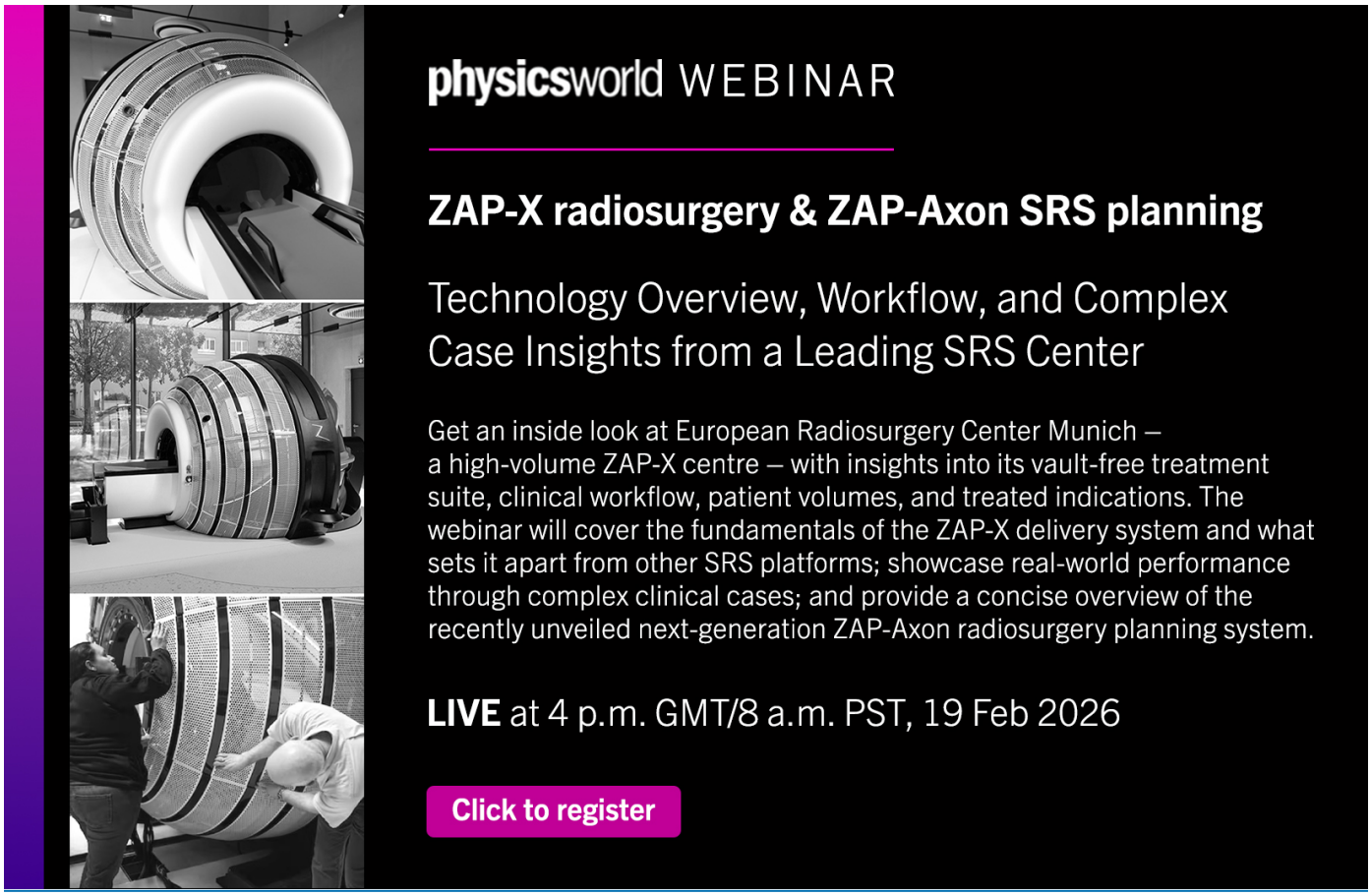

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PAPER

Creation and clinical utility of a 3D atlas-based model for visualising brain nuclei targeted by MR-guided focused ultrasound thalamotomy for tremor

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Abstract

Magnetic resonance guided focused ultrasound (MRgFUS) thalamotomy is an established treatment for tremor. MRgFUS utilises ultrasound to non-invasively thermally ablate or 'lesion' tremorgenic tissue. The success of treatment is contingent on accurate lesioning as assessed by tremor improvement and minimisation of adverse effects. However, coordinate planning and post-procedure lesion visualisation are difficult as the key targets, cannot be seen on standard clinical imaging. Thus, a computational tool is needed to aid target visualisation. A 3D atlas-based model was created using the Schaltenbrand-Wahren atlas. Key nuclei were manually delineated, interpolated and smoothed in 3D Slicer to create the model. Evaluation of targeting approaches across a seven-year period and patient-specific analyses of tremor treatments were performed. The anatomical position of MRgFUS lesions in the model were compared against varying clinical outcomes. The model provides an anatomical visualisation of how the change in targeting approach led to improved tremor suppression and a reduction in adverse effects for patients. This study demonstrates the successful development of a 3D atlas-based computational model of the brain target nuclei in MRgFUS thalamotomy and its clinical utility for tremor treatment analysis.

1. Introduction

Tremor is one of the most common movement disorders worldwide most often seen in essential tremor (ET), but can also be part of the disease profile in Parkinsons' disease and other less common conditions such as dystonic tremor. Various treatment options exist for tremor, including pharmacological and surgical approaches when medication becomes no longer effective [1]. Traditional neurosurgical options include deep brain stimulation (DBS), which electrically stimulates the tremorgenic brain tissue, often in or around the thalamus and radiofrequency ablation (RFA), which uses heat to create a permanent lesion at the target tissue [2]. Although these treatments achieve good suppression of tremor, they are invasive surgical approaches, and therefore, there are risks associated with anaesthesia and penetration of the brain, including haemorrhage and infection [2]. More recently, MR-guided focused ultrasound, (MRgFUS) which utilises the properties of sonic energy, converted into thermal energy at the target site, is being used to create thalamic lesions [3]. This technique is incisionless and, therefore, has a favourable safety profile in comparison to DBS and RFA [2]. One of the advantages of MRgFUS, is its ability for

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sonication targets to be set in sub-millimetre intervals and trial sonications to be performed at sub-ablative temperatures; this allows clinical response to be tested and, if necessary, the target moved before a permanent lesion is created. Indeed, the success of treatments at both alleviating tremor and minimisation of adverse effects is contingent on the accurate targeting of the tremorgenic brain nuclei and avoidance of crucial adjacent brain structures [4, 5].

The Ventral Intermediate (VIM) nucleus of the thalamus is the most commonly targeted tremorgenic tissue in MRgFUS thalamotomy [4], although some centres also target the posterior subthalamic area (PSA) [6, 7]. Due to limited contrast resolution, it can be challenging to directly visualise intrathalamic nuclei on standard clinical magnetic resonance imaging (MRI) at 1.5 and 3 Tesla (T). Advanced imaging techniques are being developed to address this issue [8–10] but these sequences are not yet universally available in the clinical sphere as they are heavily reliant on access to the latest scanners and a well-resourced medical physics support team. On ultra-high field MRI, at 7T, the VIM can be delineated with dedicated sequences [11]. Unfortunately, these scanners remain in the research space and are therefore not routinely utilised for clinical treatments. Accurate and reliable targeting of the VIM is, therefore, challenging. There are two main techniques used to locate the VIM in MRgFUS thalamotomy [4]. The most common method utilises local anatomical landmarks readily visualised on clinical MRI, including the anterior and posterior commissures, the third ventricle and internal capsule with predefined stereotactic coordinates to infer VIM position [4]. The second uses diffusion tensor imaging (DTI) to map the white matter tracts that run adjacent to the VIM, and thus approximate VIM position [5, 12]. As both these techniques infer VIM position, rather than directly visualise the nucleus, there is always a level of uncertainty as to whether the VIM itself is centred in the MRgFUS ablation site. Post procedure, standard clinical MRI sequences do allow an approximation of the ablation site, but as contrast resolution is limited, these techniques are unable to delineate the VIM itself. Thus, the accuracy of targeting is primarily assessed clinically by any improvement in tremor and the avoidance of adverse effects.

Given this difficulty in visualising tremor targets pre-procedure and the lack of a reliable tool to assess the accuracy of ablation sites post procedure, there remains ongoing debate on the best targeting approach in MRgFUS thalamotomy [4]. Indeed, optimising targeting would not only improve tremor suppression and reduce adverse effects but also reduce the number of sonications needed to achieve successful outcomes, thus reducing treatment times and improving patient experience. To achieve this, due consideration to individual variation in neuroanatomy must be given and therefore, a 'one size fits all' methodology is often not an appropriate approach in functional treatments for tremor. Current understanding of thalamic nucleic anatomy is based on a combination of historical neurosurgical atlases and modern imaging and computational techniques. The Schaltenbrand Wahren (Hassler Classification 1977) [13], Morel's Classification 1997 [14, 15] and Hirai and Jones [16] used histological techniques to delineate thalamic nuclei. Najdenovska *et al* utilised 7T MRI [11] and Mai *et al* have used computational modelling to further the field [17].

Previous work has shown that the use of 3D computational models can be beneficial to improve visualisation and aid clinical practice in other forms of stereotactic neurosurgery for tremor [18, 19]. In DBS, where the target for treating ET is also the VIM nucleus, our prior work used a combination of a finite element model to predict the electric field induced by DBS and conductance-based axon models to predict the volume of tissue-activated [20, 21]. These were coupled with an anatomical model of the thalamus and the internal capsule to explain a clinically observed occurrence of adverse effects [18]. Similarly, such 3D modelling has proven to be useful for surgical planning tools, either available commercially or within the research sphere [22]. Indeed, any similar tool would be a welcome addition to the clinical practice of MRgFUS thalamotomy for tremor and would significantly aid pre-treatment planning. Furthermore, modelling also allows retrospective mapping of the anatomical location of lesions, which can be correlated with clinical outcomes to help predict the optimal position for tremor targeting. MRgFUS thalamotomy is typically performed unilaterally despite ET being a bilateral condition thus, outcomes from 3D modelling would particularly benefit those undergoing a second-side treatment at a later date [23].

Therefore, this study aims to create a 3D model of key brain nuclei for clinical assessment of MRgFUS thalamotomy to improve the visualisation of tremor targets, thus aiding both pre-operative planning and post-operative analysis of clinical outcomes in tremor treatments.

2. Method

2.1. Atlas-based 3D model construction

A select microscopic series from the right hemisphere axial slices of Brain LXXVIII in the Schaltenbrand-Wahren (S-W) atlas was chosen to allow visualisation of the key MRgFUS target nuclei. In our centre the S-W atlas is used in clinical practice, and the VIM is clearly delineated in multiple slices in this atlas. The model was centred on the VIM, with two of its neighbouring thalamic nuclei also included - the Ventralis Oralis Posterior (VOP), a motor nucleus which may have a secondary role in tremor-genesis

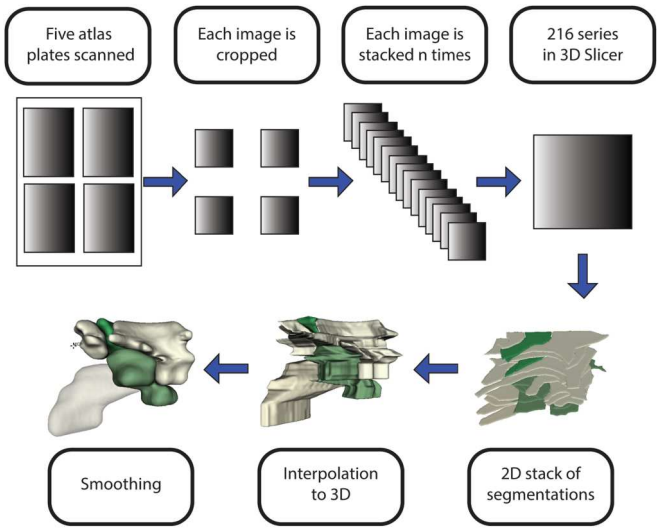

Figure 1. Summary of 3D atlas-based model construction workflow. Figure 1 is a schematic diagram showing the workflow for the construction of the 3D atlas-based model, from scanning of the atlas plates through to the final stage of smoothing in 3D-slicer.

and the Ventral Caudalis (VC), a known sensory nucleus which if sonicated can cause paraesthesia. At our centre, we routinely perform a double lesion MRgFUS thalamotomy [6, 24] of the VIM and PSA (which includes the Zona Incerta and the prelemniscal radiation). The model was extended to the subthalamic nucleus (STN), a key structure that lies anterior-inferior to the PSA and, if erroneously sonicated, can cause chorea. The overall modelling workflow is depicted in figure 1. First, plates 51–55 were scanned and cropped before being stacked in MATLAB (R2021a, MathWorks Inc.), and then individual brain nuclei were manually delineated in 3D Slicer (www.slicer.org) using the overlays in the atlas as a guide by a neuroradiologist and a computational neuroscientist together. The segmentations were then interpolated and smoothed to build the final model. 3D Slicer uses the ND morphological contour interpolation algorithm to complete this step as described previously [25]. Detailed methodology is provided in the supplementary data.

2.2. Utilising the atlas-based 3D model for clinical analysis

2.2.1. Targeting approach

Our centre's MRgFUS double lesion targeting approach (TA) of the VIM and PSA over a seven-year period was plotted onto the 3D atlas-based model. To account for the relatively small AC-PC length of the atlas brain, compared to modern brains, the model was linearly scaled to 26.79 mm, which is the average AC-PC length of the first 20 patients treated at our centre in 2023. This method assumed isotropic anatomical variation between patients, thus a simplification of nucleic relationships, but provided a single model allowing clear comparison of the targets across individual patients and patient populations. The VIM-TA and PSA-TA for 2016, 2019, 2021 and 2023 are provided in figure 4, coordinates are described in relation to the MCP. It was theorised that our centre's targeting approach has evolved with subsequent improvement in clinical outcomes post-thalamotomy. The model aims to provide a compelling visual representation of the change in practice across the study period, thus facilitating further analysis.

2.2.2. Treatment analysis

Two different patient MRgFUS treatments were analysed using the atlas-based 3D model. The use of treatment data for research was reviewed and approved by the Research Ethics Committee (REC: 15/LO/1538 and 22/PR/0288). To account for individual variation in brain size and neuroanatomy, the model was first linearly scaled to the actual AC-PC length of the individual patient; then, the lesion sites were plotted into the scaled models using the MCP as the centre reference point. Although both patients selected for analysis achieved good tremor suppression, one patient had no adverse effects, and the other experienced choreic movements for approximately six months post-thalamotomy, after which the chorea resolved. Patient B was treated with two lesions at each target site due to insufficient tremor suppression after single lesioning. There were no intra-procedural adverse effects.

It was theorised that the 3D model could be used to ascertain the likelihood of the PSA sonication spot encroaching on the STN during treatment. The model aims to provide a compelling visual representation of the lesion locations, thus facilitating further analysis.

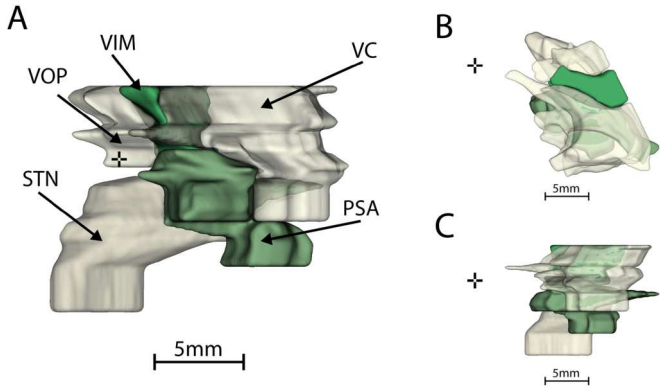

Figure 2. The final 3D Atlas-based model of the key brain for MRgFUS treatment analysis. The final 3D model in (A) sagittal, (B) axial and (C) coronal views. The VIM nucleus is dark green and flanked by the VOP and VC in light grey. The PSA is light green, and the anterior STN is grey. The MCP is shown as a crosshair marker.

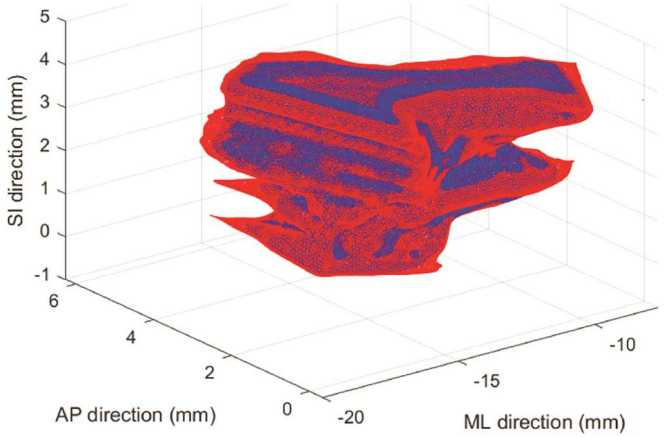

Figure 3. Analysis of the effect of smoothing on model construction. The unsmoothed 3D VIM segmentation is shown in red, and the final smoothed VIM is in blue (5-pixel kernel). The impact of smoothing on the interpolated jagged edges and the overall volume of the VIM is demonstrated.

3. Results

3.1. The 3D atlas-based model

The final 3D atlas-based model for clinical assessment of MRgFUS thalamotomy contains the two tremor targets (VIM, PSA) as used in double lesion treatments at our centre and the three key adjacent structures (VOP, VC, STN). The model is shown in figure 2 in three orthographic planes: sagittal, axial, and coronal, which allows correlation with modern imaging. This can be readily achieved using the mid-commissural point (MCP) as a spatial reference point. The model measures approximately 16.2 mm (AP) × 17.4 mm (ML) × 12.5 mm (SI). The relative size and position of the two tremor targets (in green) compared to the key adjacent nuclei (in grey) are neatly demonstrated. The effect of smoothing (table 1) on VIM volume is demonstrated in figure 3 and further described in the supplementary data. Furthermore, we computed the dice coefficient between the unsmoothed model and the model with the 5 pixel smoothing kernel and found that for all nuclei this exceeded 0.95, and 0.97 for the VIM. Comparing this to 10 pixel smoothing this coefficient dropped to 0.92 for the VIM. The model is successful as a visualisation tool for these brain structures that currently cannot be delineated on clinical MRI, and therefore, its clinical utility is considerable.

Table 1. Demonstrating the effect of smoothing with differing kernel sizes on the volume (mm^3) of the segmented brain nuclei.

Segment	Unsmoothed	5 pixel	10 pixel	15 pixel
VIM	64	61	55	50
VC	324	320	306	295
VOP	55	52	46	41
STN	195	193	186	179
PSA	162	160	150	141

3.2. Utilising the model for clinical assessment of MRgFUS thalamotomy

The MRgFUS targeting approaches (TA) used at our centre in 2016, 2019, 2021 and 2023 for the VIM and

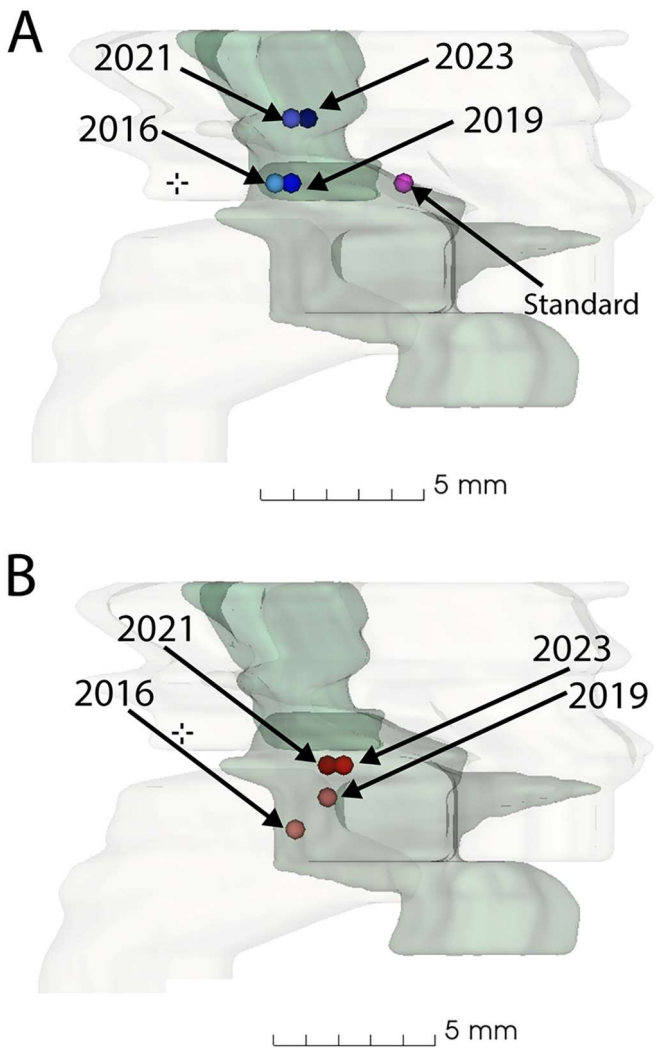

Figure 4. 3D model analysis of single centre MRgFUS targeting over a seven year period. (A) The VIM targeting approach (VIM-TA) at our centre from 2016–2023 in various shades of blue and the traditional VIM-TA in pink, (AP) 25% of intercommissural line (ICL) length, anterior to PC; (ML) 14 mm lateral; and (SI) on the ICL plane. The model clearly demonstrates the evolving targets' relationship with thalamic nucleic anatomy. (B) The PSA targeting approach (PSA-TA) at our centre from 2016-2023 in various shades of red. The model clearly demonstrates the evolving targets' relationship with the nucleic anatomy, in particular, the PSA itself and the STN.

Table 2. Listing the targeting approach coordinates for VIM and PSA for our centre from 2016–2023. Coordinates are given in relation to the mid-commissural point; where a range is provided, the mid-point is plotted in the 3D model.

	AP (mm)	ML (mm)	SI (mm)
2016 VIM-TA	3.00	13.00–15.00	0.00
2019 VIM-TA	3.50	13.00–15.00	0.00
2021 VIM-TA	3.50	13.00–15.00	2.00
2023 VIM- TA	3.00–5.00	13.00–15.00	2.00
2016 PSA-TA	3.50	13.00–15.00	−3.00
2019 PSA-TA	4.50	12.50–14.50	−2.00
2021 PSA-TA	5.00	12.50–14.50	−1.00
2023 PSA- TA	5.00	12.50–14.50	−1.00

PSA (table 2) were mapped onto the 3D atlas-based model scaled to modern AC-PC length (figure 4). The model neatly demonstrates the superior and posterior shift over the last seven years as our clinical practice has evolved (figure 4(A)). The VIM-TAs are plotted in various shades of blue and are compared to the traditional approach in pink. In 2016, our centre's VIM-TA was in the anterior VIM near the VIM/VOP border and at the inferior border of the nucleus at the level of the AC-PC plane. However, by 2023 there is a distinct superior and posterior shift towards the middle of the VIM. This change in our clinical practice aligns with previous studies reporting changing targeting approaches globally [4]. Furthermore, our centre's VIM-TA is consistently anterior to the traditional approach. The model successfully demonstrates the advantages of the 2023 VIM-TA over the 2016 and traditional approaches; by placing the sonication target in the middle of the VIM, the subsequent MRgFUS lesion will be centred in the nucleus, thus improving tremor suppression for patients.

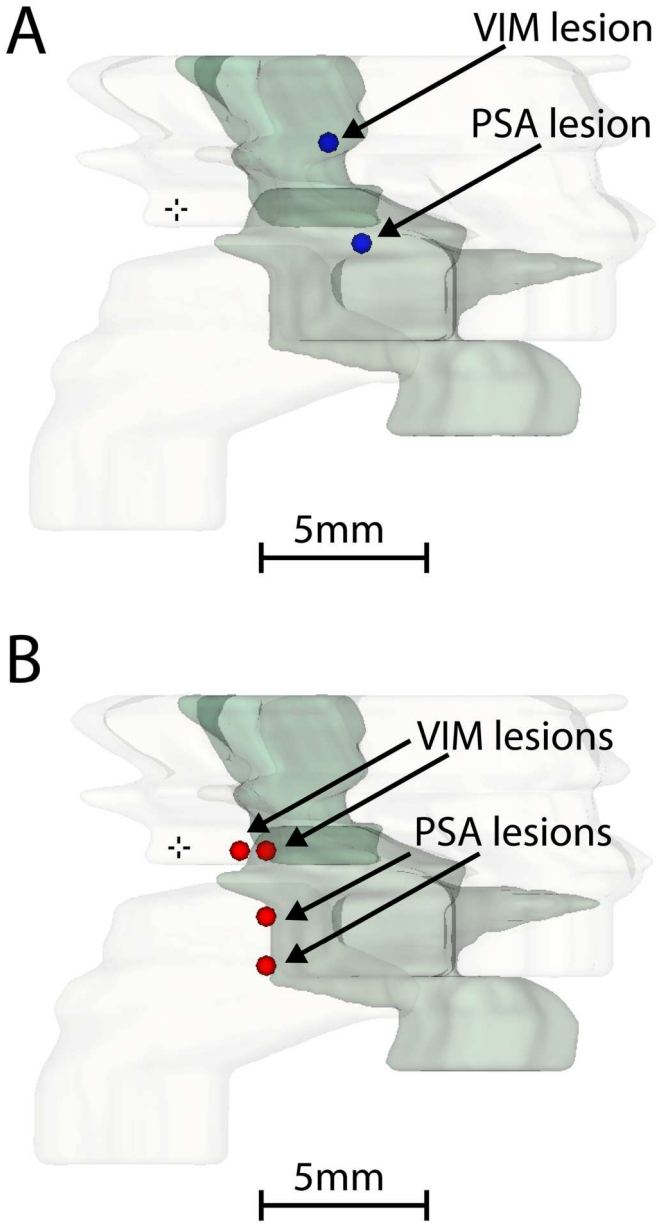

Figure 5. 3D model analysis of individual patient MRgFUS treatments. (A) MRgFUS lesion sites (in blue) for patient A, who achieved good tremor suppression without adverse effects. Both ablation sites lie within the body of the target nuclei (VIM and PSA). (B) MRgFUS lesion sites (in red) for patient B, who experienced chorea for six months despite good tremor suppression. Both ablation sites lie at the anterior border of the target nuclei (VIM-VOP and PSA-STN).

Interestingly, a similar superior and posterior migration was noted in the targeting approach for the PSA (figure 4(B)). The PSA-TAs are plotted in various shades of red. Given that double lesion thalamotomy is not routinely performed globally, there is no traditional PSA-TA for comparison. In 2016, the PSA-TA was placed at the anterior border of the PSA. From 2016 to 2023, the PSA-TA moved towards the AC-PC line and away from the anterior-inferior STN, which can cause chorea if erroneously sonicated. Again, the model successfully demonstrates the advantages of the 2023 VIM-TA over 2016, placing the sonication target in the superior aspect of the PSA and providing increased distance from the STN, thus decreasing the risk of the lesion encroaching on the STN and causing unwanted adverse effects.

Finally, the model was scaled to individual AC-PC lengths and used to visualise the actual MRgFUS lesion locations for two patients treated at our centre with different clinical outcomes (figure 5). Patient A achieved good tremor suppression without adverse effects and was treated in 2023. The scaled model neatly demonstrates that VIM and PSA ablation sites are centred within the target nuclei (figure 5(A)); both the VIM and PSA lesions are consistent with the targeting approaches at the time. Unfortunately, patient B, who was treated in 2016, experienced choreic movements for approximately six months post-

Table 3. Listing the lesion coordinates (in relation to the midcommissural point (MCP)) for patients A and B, alongside their AC-PC lengths. The models above were scaled to these AC-PC lengths.

		AP (mm)	ML (mm)	SI (mm)	AC-PC (mm)
Patient A (no AE)	VIM	4.25	13.00	2.00	25.50
	PSA	4.75	12.50	−1.00	
Patient B (chorea)	1st VIM	2.65	11.25	−0.10	26.20
	2nd VIM	1.85	11.25	−0.10	
	1st PSA	2.65	11.25	−2.10	
	2nd PSA	2.65	11.25	−3.60	

treatment despite good tremor suppression. The scaled model clearly demonstrates that multiple VIM and PSA lesions were performed, suggesting a difficult treatment (figure 5(B)). Unfortunately, the two PSA lesions lie at the VIM/STN border. Thus, it was likely that the lesion encroached onto the STN, causing chorea. Interestingly, both VIM lesions were demonstrated at the inferior VIM/VOP border, consistent with the VIM-TA at the time. Both patients' lesion coordinates are listed in table 3.

4. Discussion

The 3D atlas-based model has been successful at providing a visualisation tool for these important brain nuclei that cannot be delineated on standard clinical MRI. The model clearly demonstrates the MRgFUS thalamotomy tremor targets and their key adjacent structures (figure 2). The nuclei are well defined, with distinct boundaries, and thus, the model displays the important inter-nucleic relationships of the tremor targets. This study demonstrates the utility of the model for MRgFUS thalamotomy in both pre-operative planning and post-operative analysis of clinical outcomes. The ability of the model to be scaled to individual brain size (using the AC-PC length), provides a further benefit towards achieving individualised and precise tremor treatment analyses.

The model demonstrated the differing MRgFUS lesion locations of two patients, which, when correlated to clinical outcomes, provided a clear rationale for the adverse effects experienced by patient B (figure 4). Indeed, the model in these case examples supports our previous work that inferior lesioning of the PSA increases the risk of chorea [6]. Additionally, for both patients, if they choose to return for treatment of tremor in the contralateral arm, the model can be used to plan the target coordinates for the second site MRgFUS procedure. The utility of the model is further demonstrated in our previously published work assessing intraprocedural sensory disturbances [26]. These analyses could not have been performed to the same level of detail on the patients' pre or post-operative MRI brain scans, due to the restrictive contrast resolution. Thus further ratifying the value of the model for MRgFUS clinical teams and their patients.

A further benefit of the model is its potential as a standardising tool for MRgFUS treatment analysis, as it is based on the widely used S-W atlas, the gold standard in neurosurgical stereotactic planning. The model is reproducible, adaptable, and can be adopted at MRgFUS centres internationally, allowing for its use in the assessment of individual patient treatments, cohort analyses and multi-centre studies. This is demonstrated in our recent work [4] where the model was used to compare the VIM targeting approach of 30 MRgFUS international centres. In this study the model allowed visualisation of a global shift in VIM targeting from the inferior border of the VIM at the AC-PC line to the centre of the VIM, 2 mm superior. This analysis could not have been performed on standard clinical imaging, due to limited contrast resolution that does not allow delineation of individual thalamic nuclei. The detail that the model provides allows for comparison of target position within the volume of a single nucleus.

There are several limitations to using the S-W atlas for the construction of a 3D model for MRgFUS treatments. Firstly, the model is created from a single brain, which cannot be representative of all age groups and other demographic characteristics. Brain LXXVIII is a 40-year-old female who passed away from pulmonary tuberculosis and is assumed to have normal brain anatomy, with no known underlying brain pathology reported in the S-W atlas. However, a typical MRgFUS thalamotomy patient is over 60 years old and, by definition, has a neurological disorder—tremor. The underlying pathophysiology for tremor is most often ET, but MRgFUS thalamotomy is also performed to treat tremor in Parkinsons' disease and other less common conditions such as dystonic tremor. The impact of these neurological conditions on the size, shape and position of the thalamic nuclei is not yet known. To widen the demographic representation, future 3D models could be based on a combination of atlases or even multiple brain imaging involving real tremor patients that could utilise automatic segmentation software to ensure accuracy and efficiency in model construction [27–30].

A further consideration in selecting the S-W atlas, is that its macroscopic dissection was performed along Reid's plane. This extends from the inferior orbital margin to the external auditory meatus and,

therefore, is not identical to the AC-PC plane, which was used for the microscopic dissection and is also used for standard MR imaging. However, given that the thalamic nuclei modelled are relatively small structures that sit centrally in the brain, the difference between Reid's plane and the AC-PC plane is likely to be minimal. Furthermore, all sonication locations or targets were plotted with respect to the MCP and, therefore, in the AC-PC plane. Future 3D models for MRgFUS may consider the use of other brain atlases that include thalamic nuclei for base data, such as Morel's, although each altas has its own strengths and drawbacks [14, 17, 30, 31]. The S-W atlas was chosen for this model as it is the most widely used neuroanatomical atlas and is the gold standard in stereotactic neurosurgery.

Interestingly, there are two further microscopic series in the S-W atlas that contain the VIM. However, the coronal series did not fully delineate the VOP, and the sagittal series did not include the MCP. Both missing brain structures are crucial for the evaluation of MRgFUS treatments; thus, the axial series was chosen for the 3D model creation. Nowinski *et al* have previously investigated the differences in VIM size across the three microscopic series of the S-W atlas, demonstrating variation in its volume [26]. Some of this variation is perhaps expected across different brains of dissimilar demographics. However, it is important to note that two of these series come from the same brain, just different hemispheres. Further work is needed to establish whether laterality affects thalamic nuclei, specifically in the context of handedness, motor usage and/or tremor disorders.

Further comparison to Nowinski *et al*'s reconstructed VIM from the axial microscopic series of the S-W atlas, demonstrated that our 3D model of the VIM was smaller in volume at 60.5 mm^3 (compared to 69 mm^3). This decrease in volume can be explained by differences in the interpolation algorithms used in the two studies, compounded by the effect of smoothing on our atlas-based model (figure 3). Smoothing contributes to a visually pleasing model design that is more representative of the organic shape of brain nuclei. The atlas-based VIM model was smoothed by a 5-pixel kernel, which decreased its volume by 5% (figure 3). However, this level of smoothing was chosen to maintain VIM volume as the Dice coefficient was 0.97, future models may adapt smoothing parameters as necessary [4, 32]. There were several further subjective technical choices made during model creation, for example, the selection of resolution size required balancing anatomical detail against computing power; 10 pixels per mm was chosen. Early iterations of the model included the entire thalamic volume and several large adjacent brain structures. However, these were excluded from the final design as the model was intended for MRgFUS clinical evaluations, and these structures were not likely to be lesioned during tremor treatments. Future models could include the whole thalamus and internal capsule, for example, for assessment of large-volume ultrasound heating [33–35].

The 3D atlas-based model is successful as a visualisation tool for MRgFUS thalamotomy sonication sites allowing for clinical evaluation as described in this study. However, to optimise tremor treatments, further work is required to compare the modelled lesion locations against MRgFUS parameters, patient factors and clinical outcomes. Due consideration of patient factors (target nucleus size and position, severity of brain atrophy, and skull density ratio) as well as technical MRgFUS parameters (energy delivered and duration, and sonication spot size and shape) will be crucial to accurate analysis and help identify the optimum target location and sonication parameters for each patient treatment. Such analyses would be improved with patient-specific 3D modelling of the tremor targets. This may be achieved in the near future by utilising the superior contrast resolution of ultrahigh field 7T MRI [36], or by co-registering an expanded whole thalamic 3D model to individual routine MRI with a calculated whole thalamic volume. Future imaging-based models could also incorporate DTI, specifically to demonstrate the location of the medial lemniscus (ML) and pyramidal tracts (PT) that run in the internal capsule adjacent to the VIM and/or the dentatorubrothalamic tract (DRTT), which runs through the VIM itself [37–39]. Incorporating the ML, PT and DRTT into an MRI-based patient-specific 3D model would help confirm the VIM's position, providing increased confidence for pre-operative MRgFUS target planning [12, 40].

As previously described, there remains uncertainty about the average VIM size and position. Thus, the creation of imaging-based patient-specific 3D models could facilitate the building of an anatomical library or database that would allow for cohort analyses. Studies investigating the possible age, gender, laterality and disease state differences of the tremor targets are needed. Future developments in ultra-high field MRI that could allow image acquisition and delineation of the PSA would lead to similar studies investigating the second tremor target, thus improving target planning for double lesion MRgFUS thalamotomies.

5. Conclusion

This study demonstrates the successful creation of a 3D atlas-based model of the key brain nuclei in MRgFUS tremor treatments that currently cannot be visualised on clinical MR imaging. This model can be adapted to individual patient brain size and used for pre-operative target planning and post-operative treatment analysis. The clinical utility of the model is proven in these analyses, and as the S-W atlas is readily available, other MRgFUS centres can incorporate the model into their

own medical practice. Here we plot two patient treatments as a proof of principle of the utility of this model. The model has also been used to plot multiple patients in a recent study on FUS induced illusions of self motion [32] and to plot multi-centre targeting approaches [4]. Indeed, the advantages of an atlas-based 3D model include its reproducibility, adaptability, and potential to be adopted widely at MRgFUS centres internationally, allowing for its use in the assessment of individual patient treatments, cohort analyses and multi-centre studies.

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Data availability statement

All data that support the findings of this study are included within the article (and any supplementary files).

Ethical statement

The use of treatment data for research was reviewed and approved by the Research Ethics Committee (REC: 15/LO/1538 and 22/PR/0288).

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