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The Fast Gray Matter Acquisition T1 Inversion Recovery Sequence in Deep Brain Stimulation: Introducing the Rubral Wing for Dentato-Rubro-Thalamic Tract Depiction and Tremor Control

Maarten Bot, MD, PhD[1]; Rik Pauwels, MD[2]; Pepijn van den Munckhof, MD, PhD[1]; Maartje de Win, MD, PhD[3]; Vincent J.J. Odekerken, MD, PhD[4]; Martijn Beudel, MD, PhD[4]; Joke Dijk, MD, PhD[4]; Rob M.A. de Bie, MD, PhD[4]; P. Richard Schuurman, MD, PhD[1]

ABSTRACT

Background: The dentato-rubro-thalamic tract (DRT) is currently considered as a potential target in deep brain stimulation (DBS) for various types of tremor. However, tractography depiction can vary depending on the included brain regions. The fast gray matter acquisition T1 inversion recovery (FGATIR) sequence, with excellent delineation of gray and white matter, possibly provides anatomical identification of rubro-thalamic DRT fibers.

Objective: This study aimed to evaluate the FGATIR sequence by comparison with DRT depiction, electrode localization, and effectiveness of DBS therapy.

Materials and Methods: In patients with DBS therapy because of medication-refractory tremor, the FGATIR sequence was evaluated for depiction of the thalamus, red nucleus (RN), and rubro-thalamic connections. Deterministic tractography of the DRT, electrode localization, and tremor control were compared. The essential tremor rating scale was used to assess (hand) tremor. Tremor control was considered successful when complete tremor suppression (grade 0) or almost complete suppression (grade 1) was observed.

Results: In the postoperative phase, we evaluated 14 patients who underwent DRT-guided DBS: 12 patients with essential tremor, one with tremor-dominant Parkinson disease, and one with multiple sclerosis, representing 24 trajectories. Mean follow-up was 11.3 months (range 6–19 months). The FGATIR sequence provided a clear delineation of a hypointense white matter tract within the hyperintense thalamus. In coronal plane, this tract was most readily recognizable as a "rubral wing," with the round RN as base and lateral triangular convergence. The deterministic DRT depiction was consistently situated within the rubral wing. The number of active contacts located within the DRT (and rubral wing) was 22 (92%), of which 16 (73%) showed successful tremor control.

Conclusions: The FGATIR sequence offers visualization of the rubro-thalamic connections that form the DRT, most readily recognizable as a "rubral wing" in coronal plane. This sequence contributes to tractographic depiction of DRT and provides a direct anatomical DBS target area for tremor control.

Keywords: Deep brain stimulation, dentato-rubro-thalamic tract, deterministic tractography, essential tremor, FGATIR MRI

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Address correspondence to: Maarten Bot, MD, PhD, Department of Neurosurgery, Amsterdam University Medical Centers, Locatie AMC, Meibergdreef 9, Amsterdam 1105 AZ, The Netherlands. Email: m.bot@amsterdamumc.nl

[1] Department of Neurosurgery, Amsterdam University Medical Center, Amsterdam, The Netherlands;
[2] Department of Neurosurgery, University Medical Center Groningen, Groningen, The Netherlands;
[3] Department of Radiology, Amsterdam University Medical Center, Amsterdam, The Netherlands; and
[4] Department of Neurology and Clinical Neurophysiology, Amsterdam University Medical Center, Amsterdam, The Netherlands

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INTRODUCTION

In recent years, the dentato-rubro-thalamic tract (DRT) is considered to be an effective deep brain stimulation (DBS) target for essential tremor (ET).[1–3] The DRT section of interest for DBS is located between the red nucleus (RN) and ventral intermediate (VIM) nucleus of the thalamus.[4] These rubro-thalamic connections are not visible on the magnetic resonance imaging (MRI) sequences used for DBS planning nowadays.

Tractography with diffusion-weighted (DWI) MRI is therefore implemented for depiction of these fibers.[5] Commercially available stereotactic software only supports deterministic tractography. This technique can be deceptive because the possible course of the DRT is estimated in a way that can result in significant variability in depiction and correspondence with tremor control.[6–8]

Preferably, an MRI sequence is implemented that identifies the thalamus, the RN, and the rubro-thalamic fibers, providing direct visualization of the DBS target regions and facilitating the control of correct DRT depiction in this area by deterministic tractography.[9]

The fast gray matter acquisition T1 inversion recovery (FGATIR) sequence allows for excellent delineation of gray matter structures that are surrounded by highly myelinated areas, such as the thalamus (Fig. 1).[10] White matter projections within the thalamus may be discernable as well.[11]

In this exploratory pilot study, we evaluated whether the FGATIR MRI sequence could be used for direct visualization of rubro-thalamic connections and their correspondence with DRT depiction by tractography. This sequence could contribute to tractographic depiction of DRT, providing a direct anatomical DBS target area for tremor control.

MATERIALS AND METHODS

Patients

We implemented 3T DRT deterministic tractography using the Brainlab Elements software (Brainlab AG, Munich, Germany) in DBS for ET since October 2017 and the FGATIR sequence since September 2019.[4,8] From October 2019 until October 2020, a total of 24 DBS electrodes were placed in 14 patients (bilateral in nine patients with ET and in one patient with multiple sclerosis [MS] tremor, unilateral in three patients with ET and in one patient with Parkinson disease [PD]).

The medical ethics committee of our institution reviewed the study protocol and confirmed that the Dutch Medical Research Involving Human Subjects Act (WMO) is not applicable. For this retrospective analysis, patient consent was not considered necessary.

Image Acquisition at 3T and 7T MRI

The following MRI sequences were acquired before surgery on a 3T Philips Ingenia scanner (Philips Healthcare, Best, The Netherlands): 1) three-dimensional (3D) axial T2-weighted, repetition time (TR) 2500 ms, echo time (TE) 230 ms, field of view (FOV) 250 mm, slice thickness 1.1 mm, scan duration four minutes; 2) DWI, TR 8234 ms, TE 96 ms, b value 1200 s/mm^2, 32 gradient directions, scan duration five minutes; 3) 3D sagittal FGATIR, TR 7.39 ms, TE 3.43 ms, FOV 240 mm, slice thickness 1.0 mm, scan duration seven minutes; and 4) 7T Philips Achieva scanner (Philips Healthcare), 3D sagittal with turbo spin echo imaging, TR 3000 ms, TE 324 ms, FOV 250 × 250 × 190, 100° flip angle, voxel size 0.7 mm, scan duration seven minutes.

Acquisition of 3T MRI sequences is part of standard care and performed several weeks before surgery during patient assessment. Since 2015, acquisition of 7T MRI sequences has been discussed with all patients and usually performed on the day of hospital admittance (the preoperative day). The medical ethics committee of our institution has reviewed the study protocol for 7T MRI and waived formal protocol approval under the Dutch Medical Research Involving Human Subjects Act.

Surgical Procedure

Our surgical procedure for DBS in tremor has been described in detail previously.[12–14] The trajectory was planned so that it made contact with the DRT (as depicted by tractography) at the level of VIM nucleus of the thalamus and/or toward the posterior subthalamic area (PSA). This approach resulted in targeting (and test stimulation) both above and below the level of posterior commissure (PC), depending on the course of the DRT. Stimulation

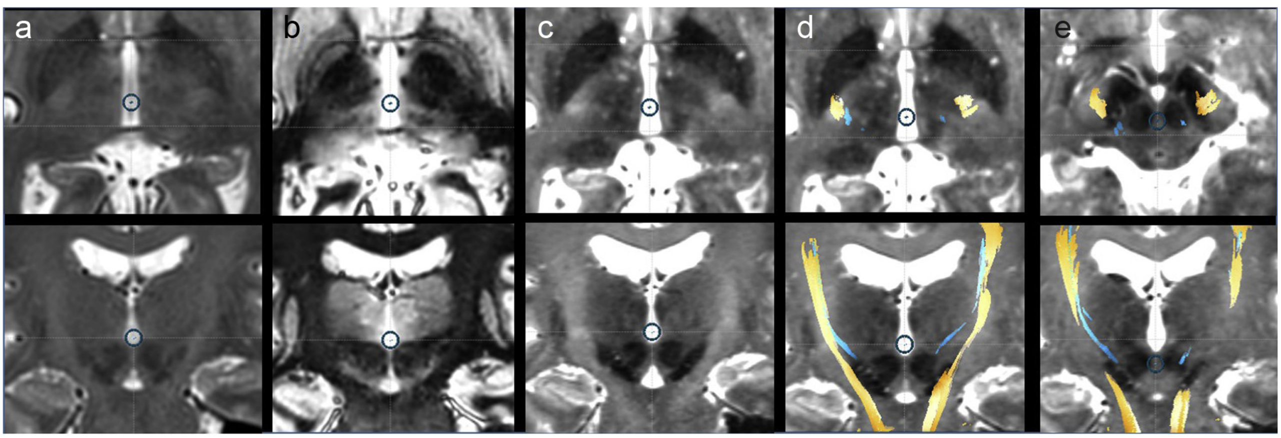

Figure 1. Overview of thalamic and subthalamic region on T2 and FGATIR MRI and identification of rubro-thalamic fibers on FGATIR. Imaging is aligned to the commissural line, the left side of the panel represents the right side of the hemisphere, and axial represented depth is at the posterior commissural line. The panels show an axial and corresponding coronal view, at the level of the commissural line. a. 3T T2 MRI. b. 3T FGATIR MRI. c. 7T T2 MRI. d. 7T T2 MRI with deterministic depiction of bilateral corticospinal (yellow) and rubro-dentato-thalamic (blue) tracts. e. 7T T2 MRI with deterministic depiction with both tracts at the level of the RN. [Color figure can be viewed at www.neuromodulationjournal.org]

was performed using 2-mm intervals (every 2 mm along the trajectory). Trajectory alignment with the DRT depended on other trajectory requirements such as prefrontal entry point on the top of a gyrus, avoiding ventricles, caudate nucleus, and blood vessels.

In 12 patients, awake intraoperative test stimulation in one track was used to confirm tremor suppression and to evaluate the thresholds for side effects of stimulation, after which the final implantation depth along the trajectory was determined. In two patients (PD, unilateral, and ET, bilateral), the electrode was placed under general anesthesia. The position of the implanted electrodes was verified using intraoperative cone beam computed tomography.

DRT Deterministic Tractography

Tractography of the ipsilateral DRT was done using the following regions of interest (ROIs) in the Brainlab Elements software (Brainlab AG): ipsilateral cortical primary motor area, ipsilateral PSA (between the posterior part of the subthalamic nucleus and the RN), ipsilateral cerebellar peduncle, and dentate nucleus.[14] For DBS surgery, only a noncrossing DRT depiction was constructed. Findings by our group and others suggest that there is both a crossing and noncrossing branch of the DRT on DWI that can be used for DBS target planning.[6,14] This study only evaluates correlation with tremor control (correlation with anatomy would require combining imaging with postmortem histologic analysis). The corticospinal tract was depicted using the following ROIs: ipsilateral cortical primary motor area, cerebral peduncle, and anterior medulla oblongata. The fractional anisotropy (FA) was set at 0.2 (standard software setting) when starting tractography. This was adjusted for obtaining a (visual) smoothly depicted track including the known anatomical landmarks. The range of FA for all DRTs was between 0.14 and 0.37. For every track, the maximum angulation was set and kept at 20° (standard software setting). Also, for every track, a minimum length of 80 mm was set and kept (standard software setting).

During DRT tractography, no particular emphasis was placed yet on the FGATIR sequence. In the postoperative phase, the sequence was compared with DRT depiction, electrode localization, and effectiveness of DBS therapy.

Patient Assessment and DBS Programming

The essential tremor rating assessment scale was used to assess (hand) tremor.[15] Tremor control was considered successful when complete tremor suppression (grade 0) or almost complete suppression (grade 1) was observed. Stimulation-induced side effects, including dysarthria and gait ataxia, were categorized as moderate or severe. Moderate side effects did not lead to disabilities in daily living, whereas severe side effects implied noticeable impairment in daily life. Patients were followed at regular intervals in outpatient follow-up care by nurses specialized in DBS programming.

Analysis of Active Contacts Relative to Deterministic DRT and Rubral Wing

The distance from the center of the active electrode contact used for DBS to the DRT was measured in millimeters by inflating a sphere around the active electrode contact until it touched the DRT in the planning software. To calculate the distance in millimeters between active electrode contact and the rubral wing, a center of gravity of the rubral wing (CoGRW) was determined lateral in the rubral wing using the Brainlab Elements (Brainlab AG) software (Fig. 2). For evaluating consistency, the first and second authors independently evaluated the location of the active electrode contacts, DRTs and CoGRW.

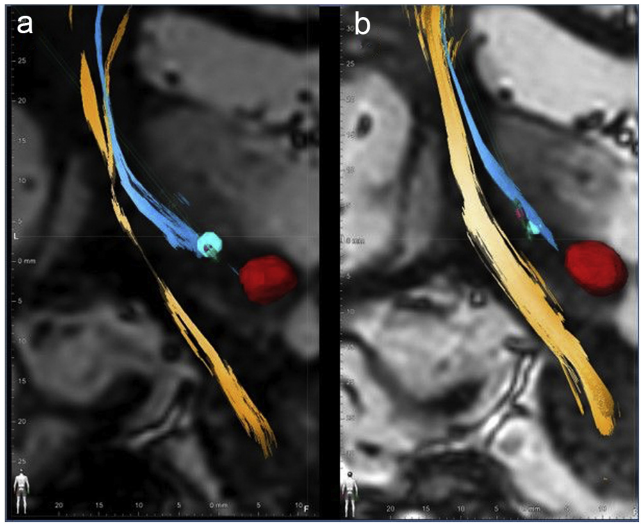

Figure 2. Comparison of active electrode contacts within the DRT and CoGRW. a and b. A coronal oriented 3T FGATIR MRI of two different active electrode contact locations. The CoGRW was determined in the most lateral point of the rubral wing (green). a. The active electrode contact (purple) to coincide with the DRT (blue) and CoGRW. b. The active electrode contacts to be situated inside the DRT, just above the CoGRW. The CST (orange) and RN (red) are also depicted. CST, corticospinal tract. [Color figure can be viewed at www.neuromodulationjournal.org]

Data Analysis

Because of the exploratory nature of the study, data were analyzed descriptively.

RESULTS

Tremor Alleviation and Side Effect Profiles

In all 21 awake electrode placements, a single track along the planned trajectory was sufficient for complete intraoperative tremor control. In the two asleep cases, a single trajectory was used for placement within the tractography-based DRT depiction. During the most recent follow-up (range 6–19 months), adequate tremor control (grade 0 or 1) was noted for 18 (75%) implanted electrodes. Two patients (14%) experienced stimulation-induced dysarthria and three (21%) gait ataxia. One patient was changed to a Percept PC pulse generator (Medtronic Inc, Minneapolis, MN) six months after DBS implantation to lower the pulse width for treatment of stimulation-induced dysarthria and gait ataxia. After lowering the pulse width to 40 µs, the side effects improved.

Surgical Complications

Three patients had surgery-related adverse events. One experienced slight dysarthria caused by a subcortical hemorrhage in the left supplementary motor area, showing full recovery after four weeks. One experienced headache possibly caused by a minor hemorrhage along the tract of the right electrode, showing full recovery after four weeks. One shortly experienced an allergic reaction (self-limiting) with angioedema and exanthema two days after surgery, for which no underlying cause could be identified.

A complete overview of trajectory findings is stated in Table 1.

The FGATIR Sequence: Visualization of Rubro-Thalamic Area, DRT Depiction and Tremor Control

The FGATIR sequence provided a clear delineation of the hyperintense thalamus in the hypointense surrounding internal capsule for all patients (Fig. 1). A hypointense white matter tract within the thalamus, generally visible from the level of the PC, was distinguishable in both axial and coronal projections. In coronal plane, this tract was most readily recognizable as a "rubral wing," with the round RN as base and lateral triangular convergence (Fig. 3). In axial plane, this resulted in an oval, oblique orientation, and decreasing lateral section toward the more medial situated RN (Fig. 3).

For all 14 bilateral thalamic areas (cerebral hemispheres not subjected to DBS also were included), deterministic DRT depiction was situated within the rubro-thalamic white matter as visualized by the FGATIR sequence (Fig. 4b). In coronal plane, this was readily identified by the DRT following the rubral wing. In axial plane, the DRT was situated at the posterior and lateral section (Fig. 3). Being deliberately depicted as ipsilateral, the DRT continued closely lateral of the RN toward the superior peduncle and dentate nucleus.

All DBS electrodes were situated within the deterministic tractography-based DRT depiction and in rubro-thalamic white matter as visualized by the FGATIR sequence (Fig. 4c). During this visual evaluation, the full rubral wing was considered, not the CoGRW (Fig. 4d).

Of the 18 active electrode contacts resulting in successful tremor control (grade 0–1), 16 (88%) were situated within the DRT, compared with 12 (66%) within the CoGRW. Mean distance between outside CoGRW active contact points and CoGRW was 1.7 (SD 0.92) mm.

The six active electrode contacts resulting in suboptimal tremor response were situated within the DRT and represent four patients (one with MS and three with ET). The mean center coordinates of the DRT at 2 mm superior to PC were located at 14.9 lateral (range 11.7–19.0), 7.2 anterior (range 3.8–9.0).

Consistency for electrode localization relative to the rubral wing (and center of gravity) was high. All electrode contacts were evaluated by the first author, and the determined location relative to the rubral wing was in accordance with the findings by the second author, without exception.

Deterministic tractography representation of the corticospinal tracts was also conducted, and all tracts coursed lateral of the thalamus in the adjacent hypointense area, indicating the internal capsule on the FGATIR sequence (Fig. 4b).

DISCUSSION

The FGATIR sequence offers visualization of rubro-thalamic connections that form the DRT, most readily recognizable as a "rubral wing" in coronal plane. All deterministic DRTs were situated within the rubral wing, and the majority of the active contacts inside the DRT and rubral wing induced successful tremor control.[2,3] This sequence contributes to tractographic depiction of DRT and provides a direct anatomical DBS target area for tremor control. To our knowledge, this comparison of FGATIR, deterministic DRT depiction, and concurrent evaluation with tremor control for DBS in ET has not been described previously and provides a shortcut for stereotactic planning that can be implemented directly.

The anatomical visualization of the (hyperintense) thalamus and (hypointense) rubro-thalamic fibers by the FGATIR sequence can be considered superior to previously applied sequences for DBS planning when targeting the thalamic part of the DRT. The rubral wing as seen in coronal images can be used for guidance of DRT tractography, preventing an erroneous course. This is of importance because deterministic tractography can be deceptive. The technique estimates the possible course of the white matter bundle of interest, but results can vary widely, depending on the included ROIs used for tractography.[3,7,8] The VIM itself is part of the DRT, and the DRT must therefore run through the actual VIM. The tractography and FGATIR here possibly provide a better estimation of the optimal location for treatment than either standard stereotactic atlas-coordinates or the software-based VIM ROI. Combining the two MRI techniques could possibly optimize tremor control and reduce the risk of side effects for DRT DBS. Because the internal capsule is readily visible, this could prevent trajectories in too close proximity to corticospinal fibers.

Other groups evaluating the FGATIR sequence in DBS also recognized its usefulness in thalamus depiction. Sudhyadhom et al[10] concluded the sequence-enabled localization of the thalamus and displayed sharper delineation of this structure compared with T2 weighted sequences. They described a hypointensity just inferior to the thalamus, which they concluded could fit into the description of the zona incerta. Morishita et al[9] evaluated the FGATIR sequence in seven patients with DBS. They used the sequence to identify the VIM nucleus by using manual-based segmentation. The VIM was used as ROI for DRT depiction; however, the possible visualization of rubro-thalamic fibers on the FGATIR sequence was not discussed. Nowacki et al[16] noted that the visualization of the internal capsule and the bordering thalamus on the FGATIR sequence can be used for determining the lateral VIM coordinate. In axial plane, we found the rubro-thalamic fibers to form an oval, oblique orientation, hypointense area (indicated in red in axial sections of panels a2 and b2 of Fig. 3). The most posterior-lateral ending can be used for targeting (range 13.0–16.0 mm lateral relative to the PC). This also was the area where the DRT was consistently situated.

In patients with successful tremor control, active electrode contacts were more often situated within DRT depiction compared with the CoGRW. The CoGRW was chosen in the lateral part of the rubral wing, situating it closer to DRT depiction and away from the RN. Active contact points located outside the CoGRW were located just above or below, inside, or close to DRT depiction. When using the CoGRW for targeting, it seems sensible to place an electrode contact within, as well as one above and below, so that these areas also can be explored for stimulation (Fig. 2).

Not all electrode implantations resulted in successful tremor control (grade 0 or 1). One patient with tremor owing to MS did not experience a beneficial effect on tremor after implantation of two bilateral DBS electrodes. A recent meta-analysis provided level III evidence that DBS is effective in the treatment of MS tremor.[17] However, the authors discussed a publication bias, and because of small studies, the effect reported may be overestimated. This may suggest that not every individual MS patient benefits from DBS. One patient with ET experienced bilateral intention tremor six months after surgery (grade 2 right, grade 3 left). Because of a small therapeutic window, DBS programming took more time to control tremor without worsening of side effects (intention tremor improved to a grade 1 right and grade 2 left after the evaluation period of this study). In two patients with ET, intention tremor improved from a

Table 1. Overview of Electrode Placement, Tremor, and Stimulation Characteristics.

No.	Tremor etiology	Hemisphere	Target coordinates relative to PC	Coronal/sagittal angle	Test stimulation side effects	Postoperative tremor stunning (d)	Coordinates active contact relative to PC	DBS CP distance to DRT (mm) DBS mA	Postural tremor	Intention tremor	Follow-up (mo)	Side effects dysarthria/ gait ataxia
1	ET	Left	X 15.3 Y 3.8 Z 2.6	21.8°/29.3°	No	15	X 16.1 Y 3.8 Z 3.5	DM 0 1.7	4 → 0	4→ 0	19	M/-
		Right	X 15.2 Y 5.0 Z 1.7	20.7°/23.6°			X 16.6 Y 5.6 Z 3.9	DM 1.5 1.9	3 → 0	3→ 1		
2	ET	Left	X 15.0 Y 9.0 Z 2.0	38.8°/32.6°	Yes, dysarthria	30	X 12.7 Y 6.8 Z −1.2	VM 0 3.5	4 → 0	4→ 1	17	-/M
		Right	X 16.0 Y 9.0 Z 2.0	39.3°/23.5°			X 14.3 Y 6.8 Z −0.6	DM 0 3.1	3 → 0	3→ 1		
3	ET	Right	X 15.7 Y 8.9 Z 4.6	27.0°/35.6°	No	11	X 13.3 Y 4.6 Z −1.1	VM 0 2.0	1 → 0	2→ 1	16	-/-
4	ET	Left	X 14.3 Y 8.4 Z 0.2	21.1°/24.1°	No	40	X 14.0 Y 8.2 Z −2.2	DM 0 2.0	4 → 0	3→ 0	14	M/M
		Right	X 14.1 Y 6.1 Z 0.2	22.2°/27.3°			X 14.5 Y 5.4 Z −1.3	DM 0 2.0	4 → 1	4→ 1		
5	PD	Right	X 12.5 Y 5.4 Z 4.0	30.4°/29.7°	General anesthesia	14	X 14.0 Y 7.6 Z −1.0	DM 0 1.8	3 → 0	2→ 0	14	-/-
6	MS	Left	X 13.0 Y 5.8 Z 2.3	19.3°/32.7°	No	14	X 12.4 Y 5.2 Z 0.5	DM 0 3.5	2 → 0	2→ 3	11	-/-
		Right	X 13.0 Y 5.8 Z 2.3	19.3°/24.1°			X 11.7 Y 4.3 Z −2.5	VM 0 3.9	4 → 3	4→ 4		
7	ET	Left	X 15.5 Y 8.0 Z 2.0	20.7°/25.7°	No	14	X 12.4 Y 5.4 Z −2.0	DM 0 2.4	3 → 0	4→ 1	10	-/-
		Right	X 16.0 Y 6.5 Z 2.0	32.0°/28.7°			X 15.2 Y 5.7 Z 0.7	DM 0 1.9	4 → 0	4→ 2		
8	ET	Left	X 8.6 Y 5.2 Z −3.9	34.7°/24.9°	No	14	X 9.3 Y 4.9 Z −1.9	DM 0 1.5	0 → 0	4→ 0	10	-/M
		Right	X 8.8 Y 5.4 Z −3.9	29.0°/29.7°			X 10.5 Y 6.9 Z 0.3	DM 0 1.7	0 → 0	2→ 1		
9	ET	Left	X 15.2 Y 8.7 Z 1.8	22.5°/27.9°	Yes, dysarthria	13	X 13.1 Y 5.5 Z −5.0	VM 0 2.1	2 → 0	2→ 0	10	-/-

(Continued)

Table 1. *Continued*

No.	Tremor etiology	Hemisphere	Target coordinates relative to PC	Coronal/sagittal angle	Test stimulation side effects	Postoperative tremor stunning (d)	Coordinates active contact relative to PC	DBS CP distance to DRT (mm) DBS mA	Postural tremor	Intention tremor	Follow-up (mo)	Side effects dysarthria/ gait ataxia
		Right	X 14.4 Y 7.6 Z 1.4	25.9°/28.6°			X 13.4 Y 4.7 Z −5.8	VM 2 2.4	3 → 0	4→ 1		
10	ET	Left	X 15.5 Y 9.0 Z 2.0	25.0°/34.8°	Yes, dysarthria	21	X 14.7 Y 7.2 Z −0.3	DM 0 3.2	3 → 0	3→ 0	9	-/-
		Right	X 16.5 Y 9.0 Z 2.0	25.7°/34.3°			X 15.4 Y 7.5 Z −0.4	DM 0 3.6	4 → 1	4→ 1		
11	ET	Left	X 15.7 Y 8.5 Z 2.0	24.5°/40.4°	No	Unknown	X 13.5 Y 7.6 Z −1.0	VM 0 2.4	0 → 0	2→ 1	8	-/-
12	ET	Left	X 15.0 Y 6.5 Z 2.0	16.5°/24.1°	No	Unknown	X 14.1 Y 5.0 Z −2.9	DM 0 3.2	0 → 0	2→ 2	7	-/-
13		Right	X 16.5 Y 8.0 Z 2.0	22.1°/30.6°			X 12.5 Y 5.2 Z −2.4	DM 0 3.2	2 → 0	3→ 3		
	ET	Left	X 11.7 Y 5.3 Z −4.0	38.0°/23.4°	No	9	X 16.6 Y 6.0 Z −0.1	DM 0 0.7	2 → 0	3→ 0	7	-/-
14	ET	Left	X 14.5 Y 7.5 Z 2.0	27.1°/35.3°	General anesthesia	14	X 12.2 Y 4.6 Z −0.4	VM 0 4.5	2 → 0	4→ 2	6	-/-
		Right	X 15.0 Y 7.0 Z 2.0	23.6°/32.5°			X 13.6 Y 6.2 Z −0.8	VM 0 3.5	3 → 0	4→ 1		

CP, contact point; DM, dorsomedial; M, moderate; VM, ventromedial.

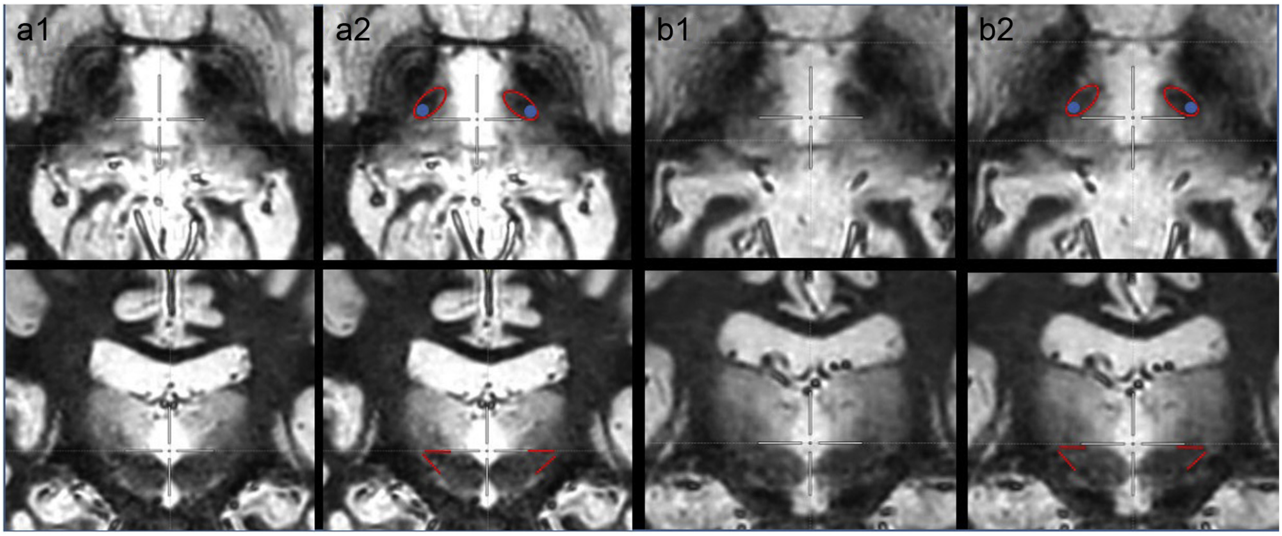

Figure 3. Overview of thalamic and subthalamic region on T2 and FGATIR MRI and identification of rubro-thalamic fibers on FGATIR. Imaging is aligned to the commissural line, the left side of the panel represents the right side of the hemisphere, and axial represented depth is at the posterior commissural line. The panels show an axial and corresponding coronal view on 3T FGATIR MRI. Panels a1/a2 and b1/b2 each represent one patient. Panels a1/b1 and a2/b2 are equal, and except in a2/b2, outlining is added for clarification. A hypointense white matter tract within the thalamus, generally visible from the level of the PC, is distinguishable in both axial and coronal projections. In coronal plane, this tract was most readily recognizable as a rubral wing, with the round RN as base and lateral triangular convergence (indicated in red in coronal sections of panels a2 and b2). In axial plane, this resulted in an oval, oblique orientation, hypointense area (indicated in red in axial sections of panels a2 and b2). The location of the DRT in this area is indicated by the blue circle. [Color figure can be viewed at www.neuromodulationjournal.org]

grade 4 to a grade 2; postural tremor improved to a grade 0 in both. For all patients, the DBS electrodes were situated in DRT depiction.

Standardized implementation of DRT depiction during target planning and long-term follow-up (covering both effect and side effect) is needed for evaluation of optimal (stimulation) target selection, ie, section, within the DRT. Previous studies, including from our group, concluded that the most optimal contact points were situated in the region between VIM and PSA.[12,14,18] In this study, we again found this area to show optimal tremor response.

In awake DBS for tremor, the rubral wing serves as an anatomical landmark that can be used for targeting and/or for guiding depiction of the DRT. In these surgeries, the FGATIR sequence may reduce the need for additional trajectories to obtain complete intraoperative tremor control and a suitable therapeutic window.

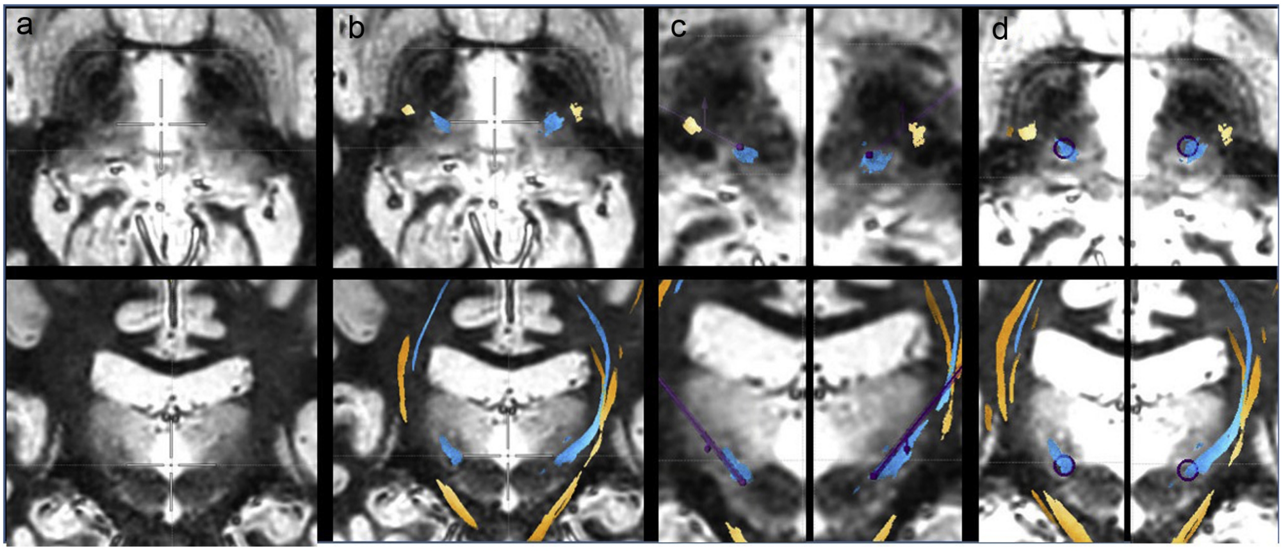

Figure 4. Comparison of rubro-thalamic visualization by FGATIR and diffusion MRI, supported with DBS electrode position. Imaging is aligned to the commissural line; the left side of the panel represents the right side of the hemisphere. a. Thalamic and subthalamic area in axial and corresponding coronal oriented 3T FGATIR MRI. b. The same axial and coronal orientation as (a) but with deterministic DRT (blue) and CST (orange) depiction. The DRT is situated within the rubral wing, and CST runs lateral of the DRT and in internal capsule as depicted by FGATIR. c. Split into four subpanels; the implanted DBS electrode (purple). Right- and left-sided thalamic areas are visualized at the bottom electrode contact (splitting enabled depicting the different electrode depths). d. The right and left locations of electrode contact used for stimulation (purple circle). CST, corticospinal tract. [Color figure can be viewed at www.neuromodulationjournal.org]

For asleep DBS, because an anatomical landmark is needed and without the possibility of test stimulation, combining both FGATIR and diffusion MRI may allow for direct DRT targeting.

Limitations

This study has several limitations. First, the FGATIR evaluation was not set up in a prospective manner. Second, only one type of deterministic tractography software was used, hindering application for DBS groups using other modules. Third, the Brainlab software thus far does not allow anatomical segmentation using the FGATIR sequence, hampering comparison with software-provided VIM depiction. Fourth, because this represents a pilot study, no external validation has been sought. Fifth, as mentioned, findings in recent studies suggest that there is both a crossing and a noncrossing branch of the DRT on DWI that can be used for DBS target planning; we did not evaluate the possibility of depicting a crossing DRT in this study. Finally, using deterministic tractography, we could not differentiate between other fibers as the medial lemniscus, hyperdirect pathway, or fasciculus lenticularis that could form part of the rubral wing.

CONCLUSION

The FGATIR sequence offers visualization of rubro-thalamic connections that form the DRT, most readily recognizable as a "rubral wing" in coronal plane. This sequence contributes to tractographic depiction of DRT and provides a direct anatomical DBS target area for tremor control.

Authorship Statements

Rik Pauwels was responsible for the conceptualization, methodology, validation, preparation, writing, and editing. Maartje de Win was responsible for performing data/3T scans, writing, and editing. Joke Dijk was responsible for the writing and editing. Vincent J.J. Odekerken, Martijn Beudel, Rob M.A. de Bie, Pepijn van den Munckhof, and P. Richard Schuurman were responsible for writing and editing. Maarten Bot was responsible for the conceptualization, methodology, validation, preparation, writing, editing, software, and visualization. All authors approved the final version of the manuscript.

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COMMENTS

Bot and colleagues presented an anatomical landmark "rubral wing" as a potential target for deep brain stimulation (DBS) lead implantation. The tractography with the high-resolution anatomical images has been used in recent publications, and the usefulness has been increasingly recognized. Even though the "rubral wing" on the fast gray matter acquisition T1 inversion recovery sequence may have been intuitively recognized by DBS practitioners, this article makes us aware of the importance of this slide anatomical landmark. I believe that this article will help DBS practitioners to identify the thalamic target for tremor.

Takashi Morishita, MD, PhD
Fukuoka, Japan

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Targeting the optimal area for deep brain stimulation (DBS) procedures in the field of essential tremor is an ongoing matter of discussion with multiple previously suggested approaches. Readily identifiable and reliable magnetic resonance imaging (MRI)–based landmarks are highly warranted. The authors describe an MRI-based landmark (the rubral wing) in the subthalamic area based on fast gray matter acquisition T1 inversion recovery sequences that coincides with the tractographic course of cerebellothalamic fibers. Although the latter approach will produce different results depending on 1) the chosen parameters of the diffusion-weighted images, 2) the applied fiber-orientation model, 3) applied tractography algorithm, and 4) selected tracking parameters by the user, the "rubral wing" sign seems readily identifiable and as a matter of fact less user- and center-dependent. It therefore constitutes an invariant landmark that will help DBS surgeons during their target planning for DBS lead placement for essential tremor.

Andreas Nowacki, MD
Bern, Switzerland

