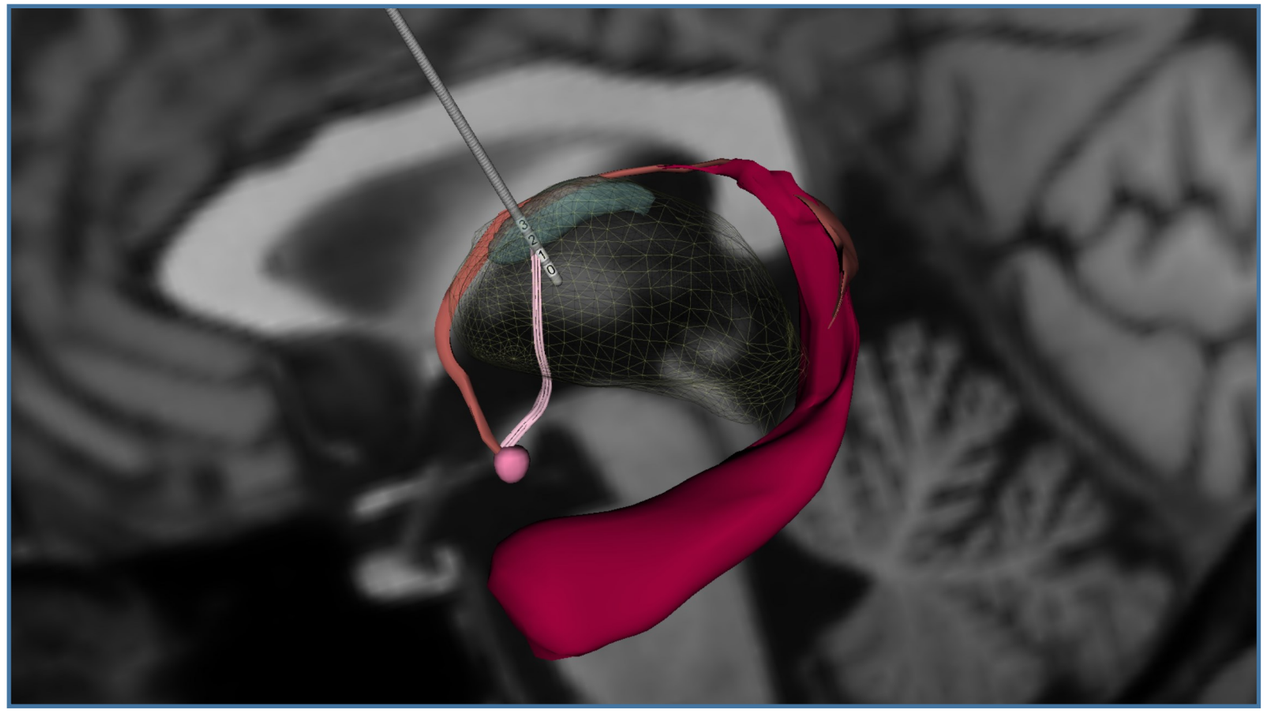
Medtronic DBS
Anterior Nucleus of the Thalamus (ANT)



The purpose of this document is to provide summary technical information related to DBS lead placement within targeted brain nuclei for the approved indication/intended use of Medtronic DBS Therapy for Epilepsy. Implanting physicians should have expertise with functional stereotactic neurosurgical treatment of epilepsy. Such expertise should include knowledge of the anatomical and neurophysiological characteristics of the targeted nucleus, surgical and/or implantation techniques for the Medtronic DBS System, operational and functional characteristics of the Medtronic DBS System, and experience in the continued management of patients by stimulation parameter adjustment. Physicians should use their medical judgment and product labeling to optimize therapy for individual patients.

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Medtronic
Further, Together

1. Example Pre-Operative MRI Sequences with Anatomical Landmarks

Direct visualization of the mammillothalamic tract, internal medullary lamina of the thalamus, the ANT itself and the surrounding veins is critical for successful direct targeting. The following are examples of MRI sequences which may provide superior contrast visualization within the target area. See *MRI Guidelines for Medtronic deep brain stimulation systems* for more information.

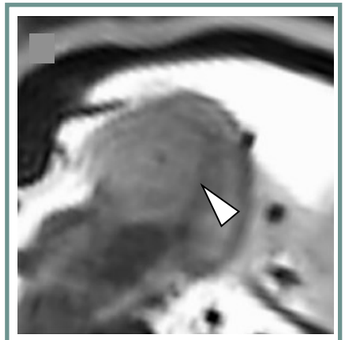

Figure 1.1: 3T STIR MRI. Sagittal view.
Arrowhead marks the MTT (Lehtimäki 2016)

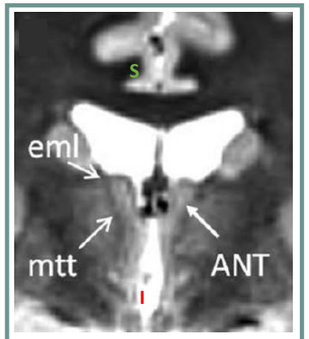

Figure 1.2: 1.5T STIR MRI. Coronal view (Jiltsova 2016)

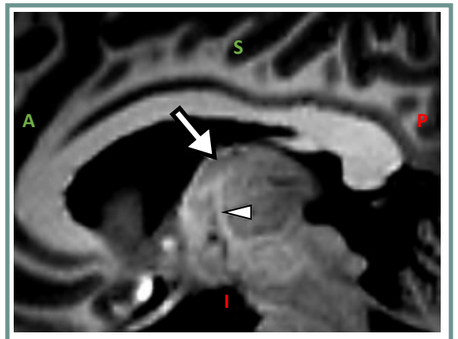

Figure 1.3: 3T MPRAGE MRI. Sagittal view. (Buentjen 2013)
Arrow marks the ANT. Arrowhead marks the MTT

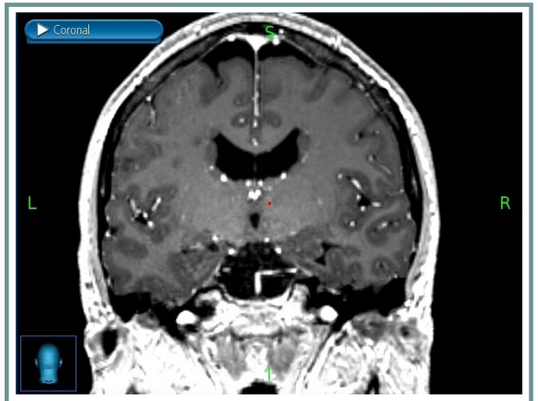

Figure 1.4: 3T T1-weighted MRI with contrast for visualization of adjacent veins within the target zone. Coronal view.

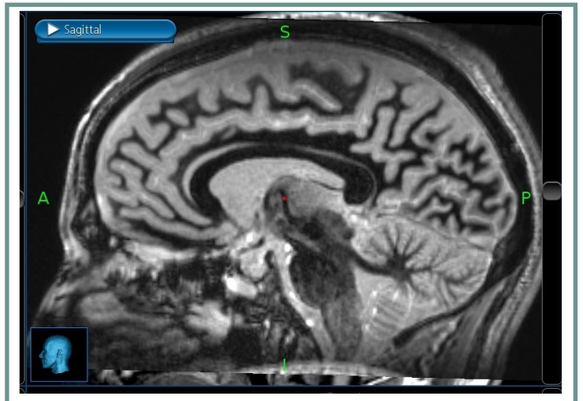

Figure 1.5: 3T FGATIR MRI. Sagittal view.
Red targeting dot placed within MTT

2. AC-PC Coordinates

The morphology of the ANT is subject to normal anatomical variability. Direct anatomical-based targeting on stereotactic MRI is preferable whenever possible.

X: 5.0 — 6.0 mm Lateral from AC-PC Line

Y: 0.0 — 2.0 mm Anterior to MCP

Z: 10.0 —12.0 mm Superior to AC-PC Line

Transventricular Trajectory Angles:

Declination: ~ 50-60° posterior from AC-PC plane (or, equivalently stated as: 30-40° anterior from coronal plane perpendicular to AC-PC plane)

Azimuth: ~ 0-10° lateral from parasagittal plane perpendicular to AC-PC plane

Abbreviations Used Throughout:

AC: *Anterior Commissure* PC: *Posterior Commissure* MCP: *Mid-Commissural Point* ANT: *Anterior Nucleus of the Thalamus* MTT: *Mammillothalamic Tract*
Fx: *Fornix* EML: *External Medullary Lamina (thalamus)* IML: *Internal Medullary Lamina (thalamus)*

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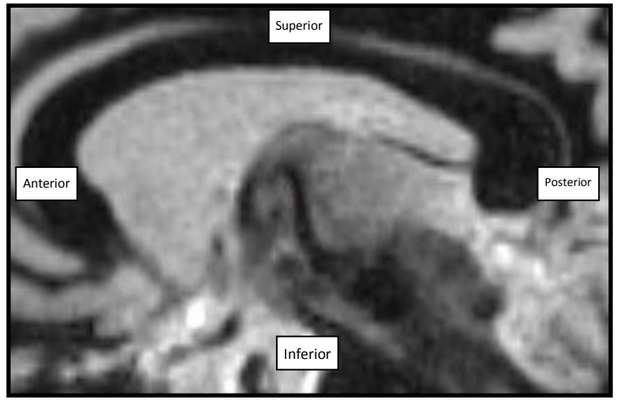
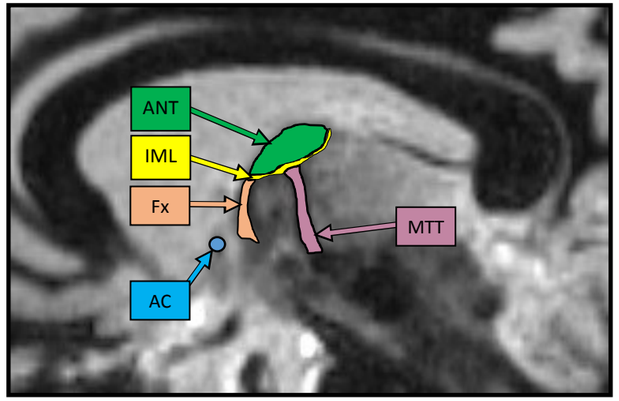
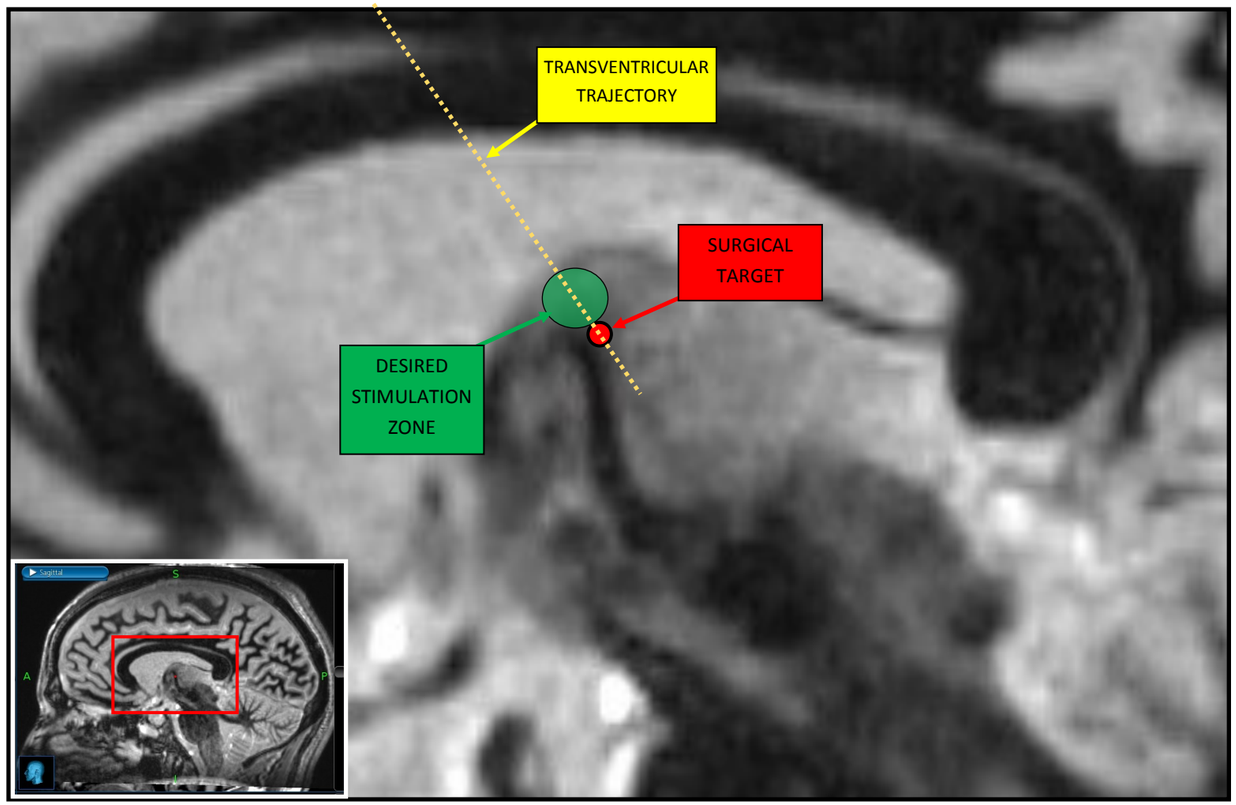
3. ANT Direct Targeting

Successful localization of the surgical target relies upon direct visualization of the ANT, mammillothalamic tract and adjacent structures. The desired zone for stimulation lies directly above and slightly anterior to this surgical target.

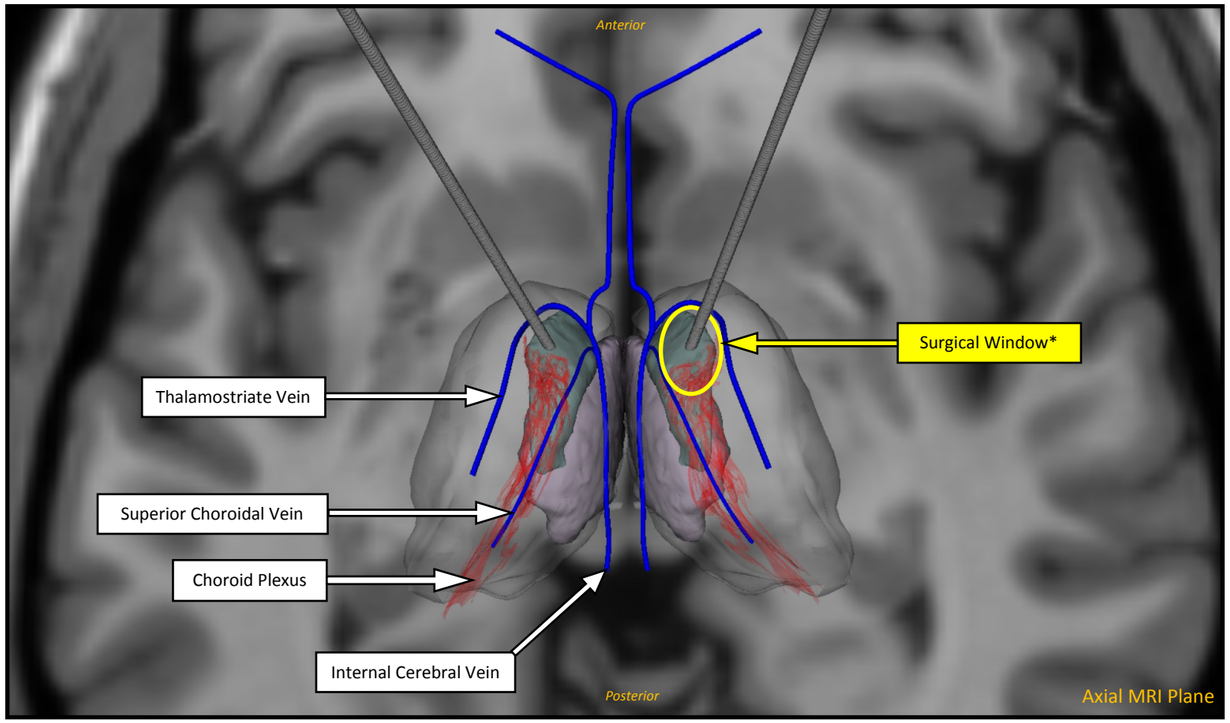


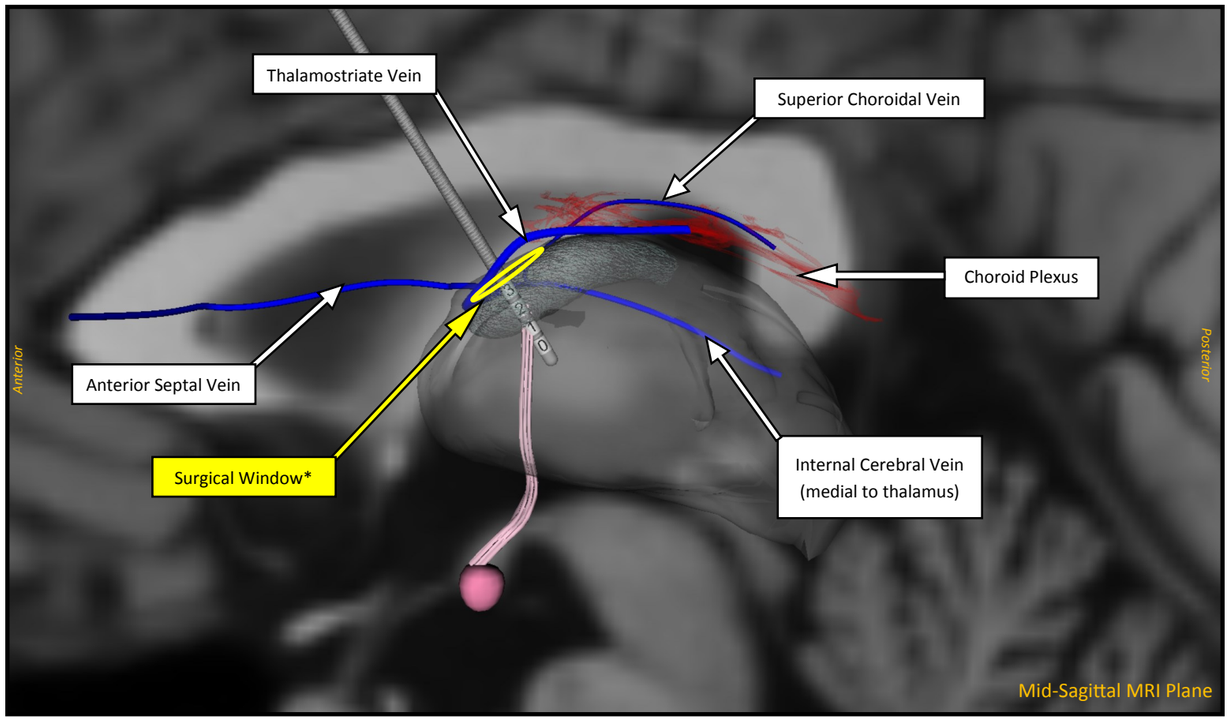




Top Left: Sagittal 3T FGATIR image centered through the long axis of the mammillothalamic tract. ***Top Right:*** Labelled relevant anatomical landmarks. ***Bottom:*** Surgical trajectory shown as a dotted yellow line. Desired zone of DBS stimulation (green) encompasses ANT dorsally and anteriorly to surgical target (red). Stereotactic target is located at the posterior aspect of the MTT where it terminates at the ANT.

4. Important Vasculature





** Standard transventricular approach*

Abbreviations Used Throughout:

AC: *Anterior Commissure* ANT: *Anterior Nucleus of the Thalamus* MER: *Microelectrode Recording* IPG: *Implantable Pulse Generator* MTT: *Mammillothalamic Tract*
IML: *Internal Medullary Lamina* DM: *Dorsomedial Nucleus of the Thalamus* VA: *Ventral Anterior Nucleus of the Thalamus*

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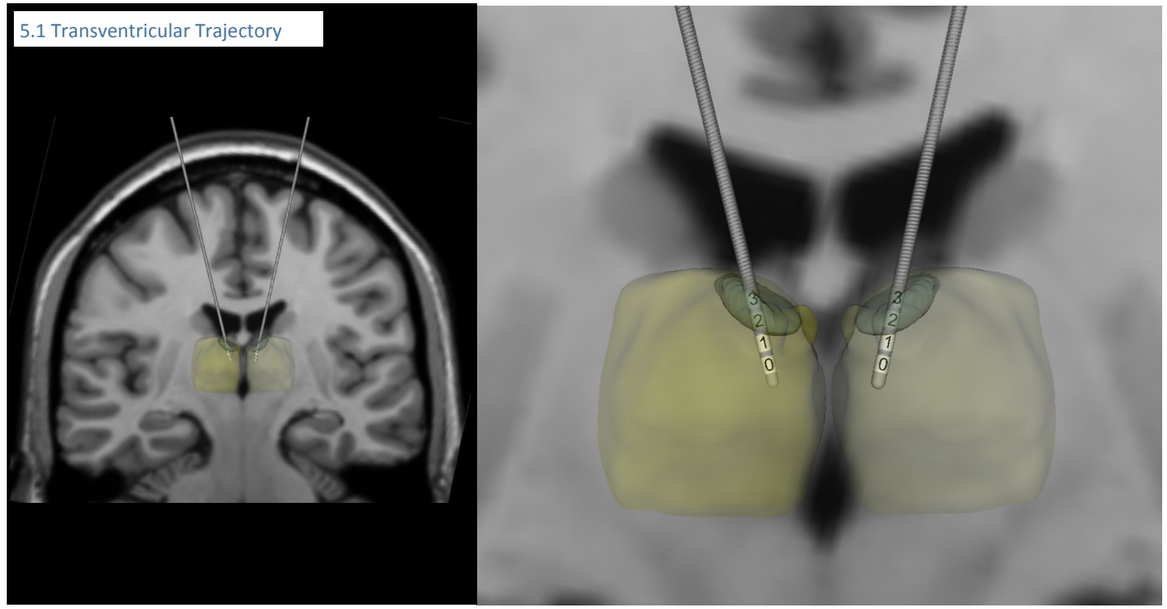
5. Surgical Trajectory

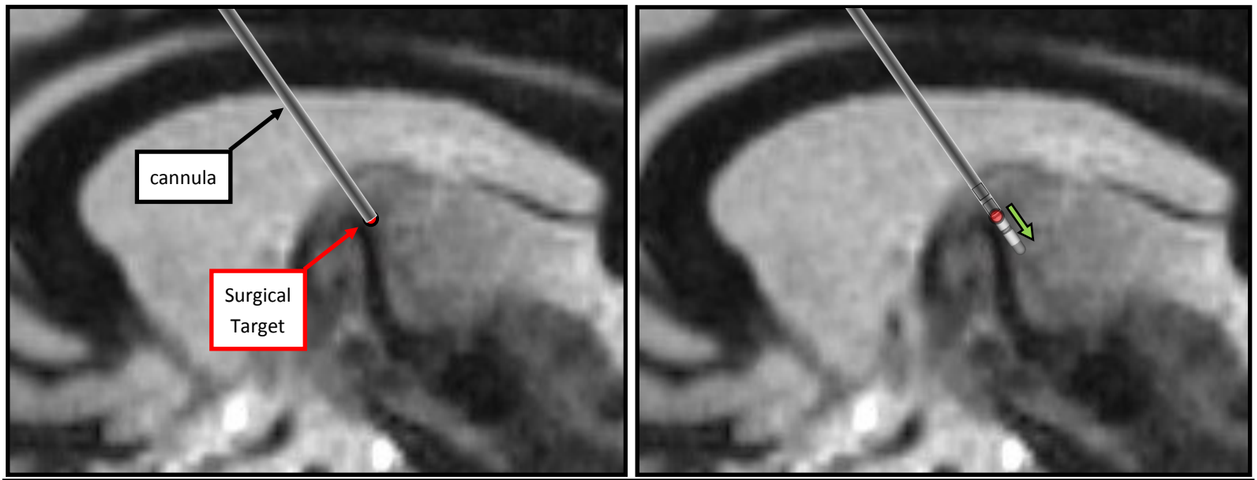


5.3 Other Trajectories

Efficacy data and implant success rates are only available for the transventricular (5.1) and extraventricular (5.2) approaches (Lehtimäki 2018). Other ANT trajectory approaches are possible and may need to be considered in patients presenting with complex vascular arrangement and/or anatomical variability.

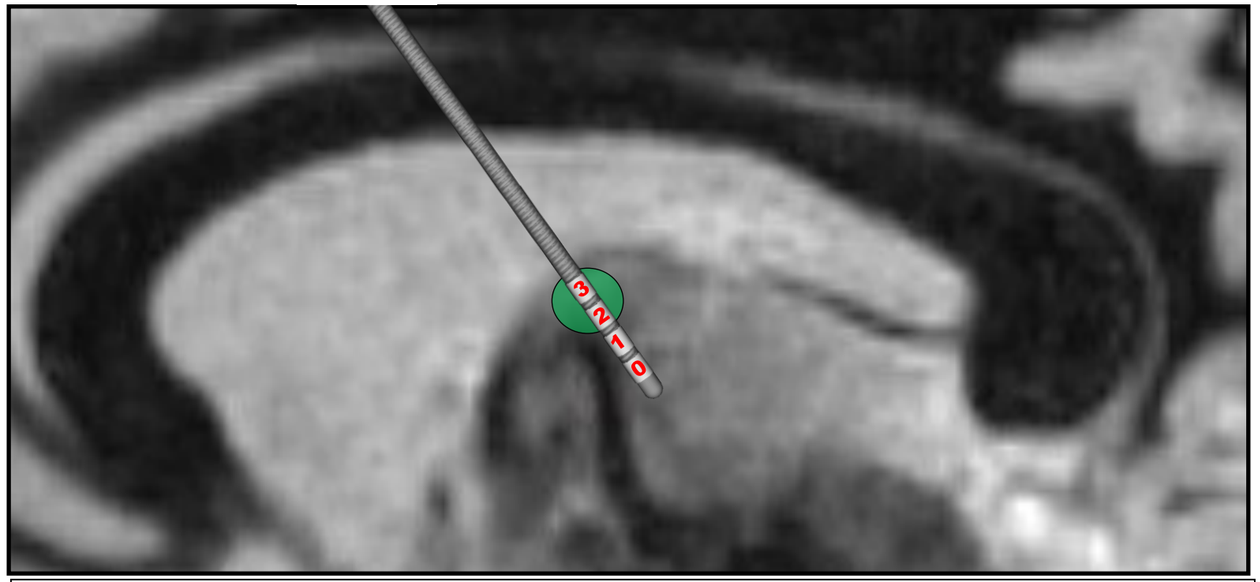
Point to Consider: *In one study (Lehtimäki 2018) analyzing 73 ANT-DBS implants (53% of these trajectories were extraventricular), approximately 90% of the transventricular trajectories had at least 1 contact in the ANT, verses 71% of the extraventricular trajectories. The success rate for placing at least 1 contact in ANT bilaterally was 84% for transventricular and 58% for extraventricular. No intracranial bleeds were observed with either method but 1 cortical infarct was reported following extraventricular trajectory*

6. Medtronic DBS Lead Implant Considerations: Cannula



Using A To-Target Canula:
A to-target (0 mm above target) cannula may help prevent deflection of the lead when penetrating the dorsal surface of the ANT. Some adjustment of the lead position along the trajectory will be necessary to accommodate anatomical variability and to ensure the appropriate contacts are within the ANT and not within the ventricle. The use of intra-operative volumetric imaging, such as the Medtronic O-Arm O2 or intraoperative CT, is highly recommended to ensure appropriate lead placement. Sagittal FGATIR image shown.

7. Medtronic DBS Lead Implant Considerations: Contact Locations



Placement of 3389 Contacts within ANT:
Contacts 2 & 3 are placed within the ANT to overlap the desired area for DBS stimulation (green). Contact 3 is completely within the ANT and does not extend into the ventricle. Contacts 0 & 1 in this example would likely not be used for stimulation. Sagittal FGATIR image shown.

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EML: *External Medullary Lamina (thalamus)* IML: *Internal Medullary Lamina (thalamus)* IPG: *Implantable Pulse Generator*

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8. Microelectrode Recording

The value of MER for ANT DBS has not been established.

9. Intra-operative DBS Lead Testing

This procedure should be performed with the patient asleep as lead efficacy cannot be adequately evaluated under standard awake operative conditions. Furthermore, there are no known side-effects that can be elicited through acute stimulation testing on an appropriately-placed lead in an awake patient.

Checking contact impedances prior to lead fixation may indicate if a DBS contact is within cerebrospinal fluid (low impedance).

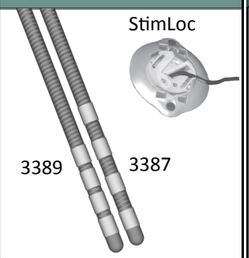
10. Assessment of Implant Position

Intra-operative assessment of lead position is best achieved through volumetric intra-operative imaging, such as the Medtronic O2 O-ARM.

11. Medtronic DBS System Implant & Peripherals

The following implants and peripherals are approved for Medtronic ANT DBS therapy:

IMPLANTS

DBS LEAD KIT	DBS EXTENSIONS	DBS IPG
		
Medtronic 3389s DBS Lead Kit or Medtronic 3387s DBS Lead Kit	Medtronic 37086	Medtronic 37601 Activa PC

PERIPHERALS

PATIENT PROGRAMMER	CLINICIAN PROGRAMMER
	
Medtronic 37441 Intercept	Medtronic A610 Activa Clinician Programmer Application

Images are not to scale

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Buentjen L, Kopitzki K, Schmitt FC, Voges J, Tempelmann C, Kaufmann J, Kanowski M. Direct targeting of the thalamic anteroventral nucleus for deep brain stimulation by T1-weighted magnetic resonance imaging at 3T. *Stereotact Funct Neurosurg*, 2014; 92:25-30

Finnis KW. 3D DBS Simulator, Medtronic 2006

Jiltsova E, Mottonen T, Fahlstrom M, Haapasalo J, Tahtinen T, Peltola J, Ohman J, Larsson EM, Kiekara T, Lehtimaki K. Imaging of anterior nucleus of thalamus using 1.5T MRI for deep brain stimulation targeting in refractory epilepsy. *Neuromodulation*, 2016;19(8):812-817

Lehtimaki K, Mottonen T, Jarventausta K, Katisko J, Tahtinen T, Haapasalo J, Niskakangas T, Kiekara T, Ohman J, Peltola J. Outcome based definition of the anterior thalamic deep brain stimulation target in refractory epilepsy. Brain Stim. 2016; 9:268-275

Lehtimaki K, Coenen VA, Ferreira AG, Boon P, Elger C, Taylor RS, Ryvlin P, Gil-Nagel A, Gielen F, Brionne TC, Abouihia A, Beth G. The surgical approach to the anterior nucleus of thalamus in patients with refractory epilepsy: Experience from the international multicenter registry (MORE). *Neurosurgery*. 2018:0:1-10

Brief Statement: Medtronic DBS Therapy for Epilepsy

Medtronic DBS Therapy for Epilepsy: Product labeling must be reviewed prior to use for detailed disclosure of risks.

Indications: Bilateral stimulation of the anterior nucleus of the thalamus (ANT) using the Medtronic DBS System for Epilepsy is indicated as an adjunctive therapy for reducing the frequency of seizures in individuals 18 years of age or older diagnosed with epilepsy characterized by partial-onset seizures, with or without secondary generalization, that are refractory to three or more antiepileptic medications.

The Medtronic DBS System for Epilepsy has demonstrated safety and effectiveness for patients who average six or more seizures per month over the three most recent months prior to implant of the DBS system (with no more than 30 days between seizures). The Medtronic DBS System for Epilepsy has not been evaluated in patients with less frequent seizures.

Contraindications: Medtronic DBS Therapy is contraindicated for patients who are unable to properly operate the neurostimulator. The following procedures are contraindicated for patients with DBS systems: diathermy (e.g., shortwave diathermy, microwave diathermy or therapeutic ultrasound diathermy), which can cause neurostimulation system or tissue damage and can result in severe injury or death; Transcranial Magnetic Stimulation (TMS); and certain MRI procedures using a full body transmit radio-frequency (RF) coil, a receive-only head coil, or a head transmit coil that extends over the chest area if the patient has an implanted Soletra™ Model 7426 Neurostimulator, Kinetra™ Model 7428 Neurostimulator, Activa™ SC Model 37602 Neurostimulator, or Model 64001 or 64002 pocket adaptor.

Warnings and Precautions: There is a potential risk of brain tissue damage using stimulation parameter settings of high amplitudes and wide pulse widths. Extreme care should be used with lead implantation in patients with a heightened risk of intracranial hemorrhage. Sources of electromagnetic interference (EMI) may cause device damage or patient injury. Theft detectors and security screening devices may cause stimulation to switch ON or OFF and may cause some patients to experience a momentary increase in perceived stimulation. The DBS System may be affected by or adversely affect medical equipment such as cardiac pacemakers or therapies, cardioverter/defibrillators, external defibrillators, ultrasonic equipment, electrocautery, or radiation therapy. MRI conditions that may cause excessive heating at the lead electrodes which can result in serious injury, including coma, paralysis, or death, or that may cause device damage, include: neurostimulator implant location other than pectoral and abdominal regions; unapproved MRI parameters; partial system explants ("abandoned systems"); misidentification of neurostimulator model numbers; and broken conductor wires (in the lead, extension or pocket adaptor). The safety of electroconvulsive therapy (ECT) in patients receiving DBS Therapy has not been established. Tunneling the extension too superficially or too deeply may result in nerve or vascular injury, or tunneling through unintended anatomy. The lead-extension connector should not be placed in the soft tissues of the neck due to an increased incidence of lead fracture. Cessation, reduction, or initiation of stimulation may potentially lead to an increase in seizure frequency, severity, and new types of seizures. Symptoms may return with an intensity greater than was experienced prior to system implant, including the potential for status epilepticus. Loss of coordination in activities such as swimming may occur. Depression, suicidal ideations and suicide have been reported in patients receiving Medtronic DBS Therapy for Epilepsy, although no direct cause-and-effect relationship has been established. Preoperatively, assess patients for depression and carefully balance this risk with the potential clinical benefit. Postoperatively, monitor patients closely for new or changing symptoms of depression and manage these symptoms appropriately. Patients should be monitored for memory impairment. Memory impairment has been reported in patients receiving Medtronic DBS Therapy for Epilepsy, although no direct cause and effect relationship has been established. The consequences of failing to monitor patients are unknown. When stimulation is adjusted, monitor patients for new or increased seizures, tingling sensation, change in mood, or confusion.

Adverse Events: Adverse events related to the therapy, device, or procedure can include intracranial hemorrhage, cerebral infarction, CSF leak, pneumocephalus, seizures, surgical site complications (including pain, infection, dehiscence, erosion, seroma, and hematoma), meningitis, encephalitis, brain abscess, cerebral edema, aseptic cyst formation, device complications (including lead fracture and device migration) that may require revision or explant, extension fibrosis (tightening or bowstringing), new or exacerbation of neurological symptoms (including vision disorders, speech and swallowing disorders, motor coordination and balance disorders, sensory disturbances, cognitive impairment, and sleep disorders), psychiatric and behavioral disorders (including psychosis and abnormal thinking), cough, shocking or jolting sensation, ineffective therapy and weight gain or loss.

The safety and effectiveness of this therapy has not been established for patients without partial-onset seizures, patients who are pregnant or nursing, patients under the age of 18 years, patients with coagulopathies, and patients older than 65 years.

Medtronic DBS systems are MR Conditional which means they are marked to indicate they are safe in the MR environment as long as certain conditions are met. Read and fully understand the *MRI Guidelines for Medtronic deep brain stimulation systems* before conducting the MRI examination. Go to www.medtronic.com/mri or contact Medtronic at 1-800-707-0933 for a copy. Also review current MRI manufacturer labeling before conducting the MRI.

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