SURGICAL OVERVIEW: MEDTRONIC DBS FOR EPILEPSY

ANTERIOR NUCLEUS
OF THE THALAMUS (ANT)

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MEDTRONIC DBS FOR EPILEPSY INDICATION STATEMENT

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.

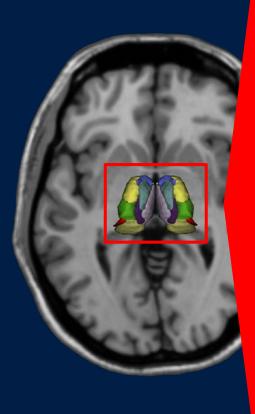
KEY SURGICAL CONSIDERATIONS FOR ANT DBS¹

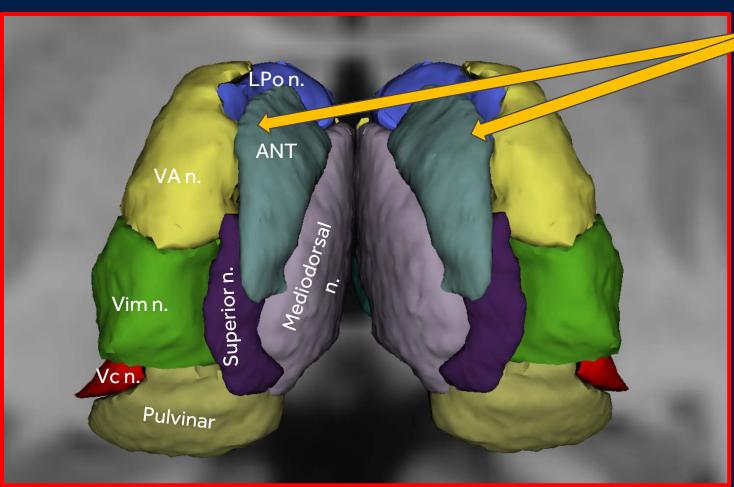
- Pre-operative MR imaging sequences
- Exclusively direct targeting
- Trajectory
- Cannula length
- Visualizing and avoiding venous structures
- Performed under general anesthesia
- MER (value has not been demonstrated)
- Intra-operative confirmation (*value has not been demonstrated*)

¹Medtronic SANTE Study



ANATOMICAL LOCATION (AXIAL VIEW) & OUTPUT FIBERS



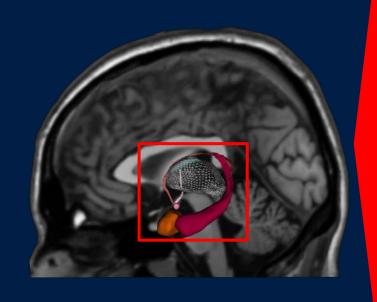


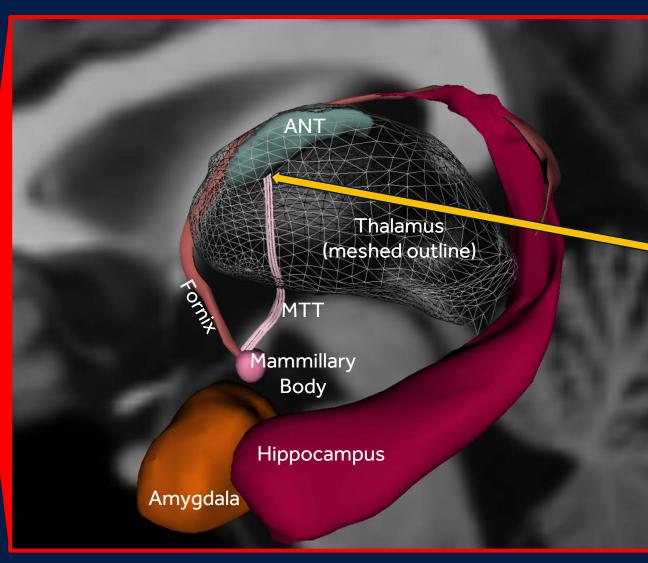
ANT OUTPUT:

Anterior & lateral aspects via:

Anterior Thalamic
Radiation
to
Anterior Limb of the
Internal Capsule
to
cingulate gyrus

ANATOMICAL LOCATION (SAGITTAL VIEW) & INPUT FIBERS





ANT INPUT:

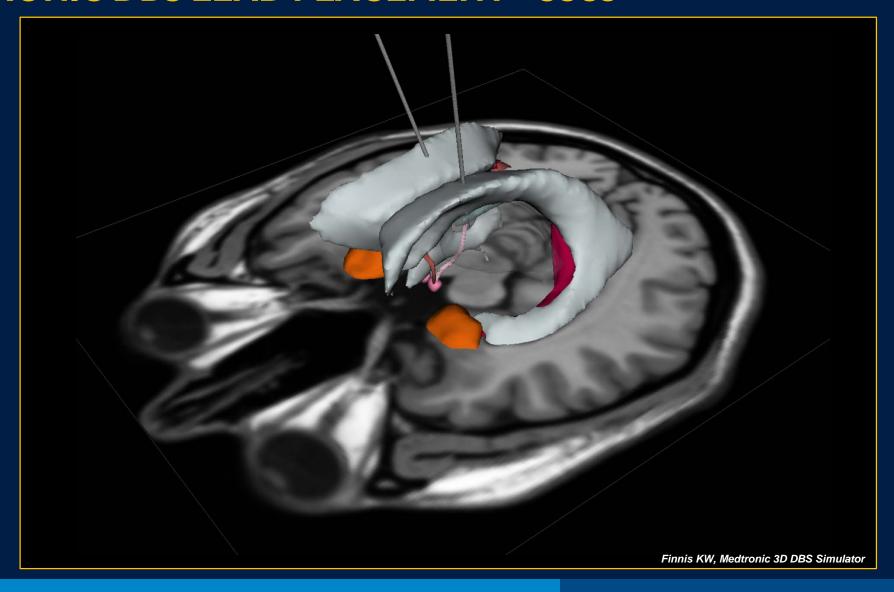
Ventral & anterior aspects via MTT (bidirectional tract) and fornix

MEDTRONIC DBS LEAD PLACEMENT - 3389

Surgical Target:

Anteroventrolateral aspect of ANT

- Bilateral implants
- Transventricular trajectory
- Medtronic 3389 Lead
- Performed under GA
- ANT is subject to significant anatomical variation¹
- ANT may undergo significant and asymmetric atrophy in patients with medically-refractory epilepsy²





SURGICAL CONSIDERATIONS – PRE-OP IMAGING*

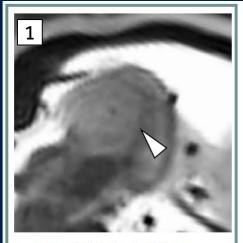


Figure 1.1: 3T STIR MRI. Sagittal view. Arrowhead marks the MTT

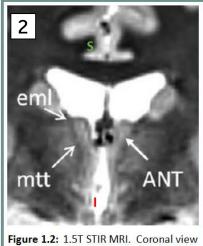




Figure 1.3: 3T MPRAGE MRI. Sagittal view. Arrow marks the ANT. Arrowhead marks the MTT

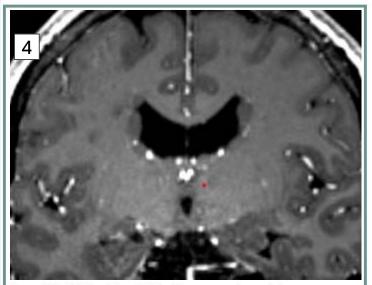


Figure 1.4: 3T T1-weighted MRI with contrast. Coronal view. Red targeting dot placed within MTT

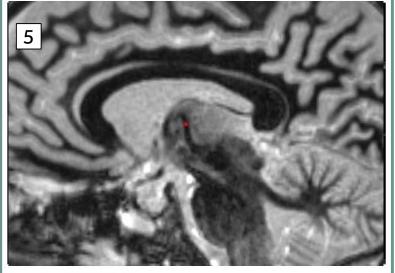


Figure 1.5: 3T FGATIR MRI. Red targeting dot placed within MTT

Visualize 4 key anatomical structures:

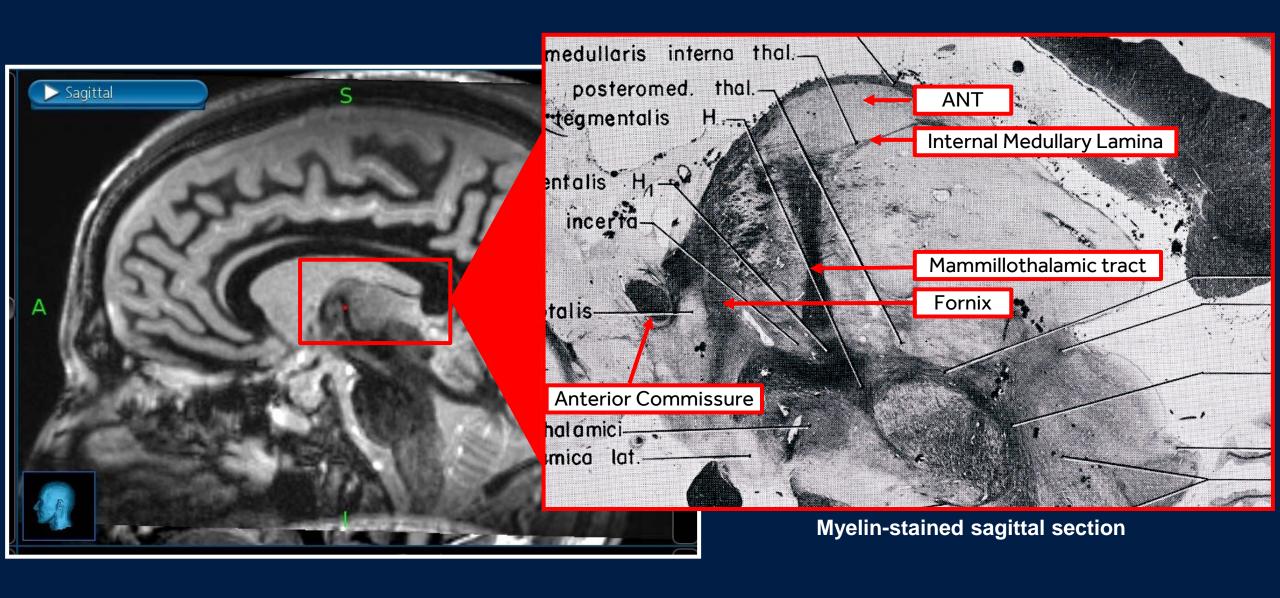
ANT

- Mammillothalamic tract (MTT)
- Internal/external medullary lamina of thalamus (IML/EML)
 - Surrounding veins

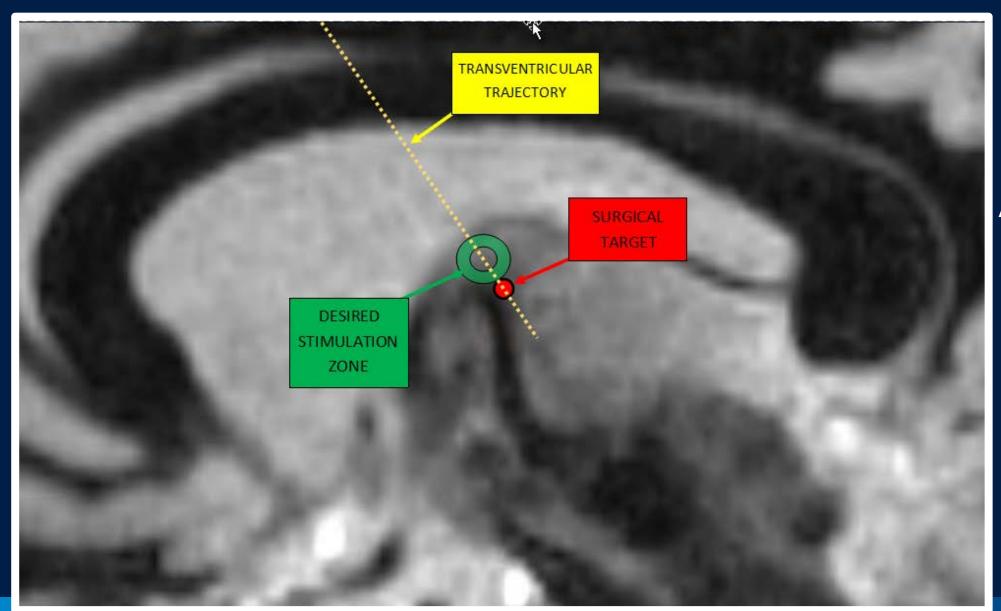
¹Lehtimaki et al, Brain Stim. 2016;9:268-275 ²Jiltsova et al, Neuromodulation. 2016;19(8):812-817 ³Buentjen et al, Stereotact Funct Neurosurg. 2014;92:25-30 4,5 Medtronic

^{*} See Guidelines for Medtronic deep brain stimulation systems for more information

SURGICAL CONSIDERATIONS – PRE-OP IMAGING



SURGICAL CONSIDERATIONS – DIRECT TARGETING VS ACPC



Broad range of ACPC coordinates¹

 $X = 5-6 \, \text{mm lateral}$

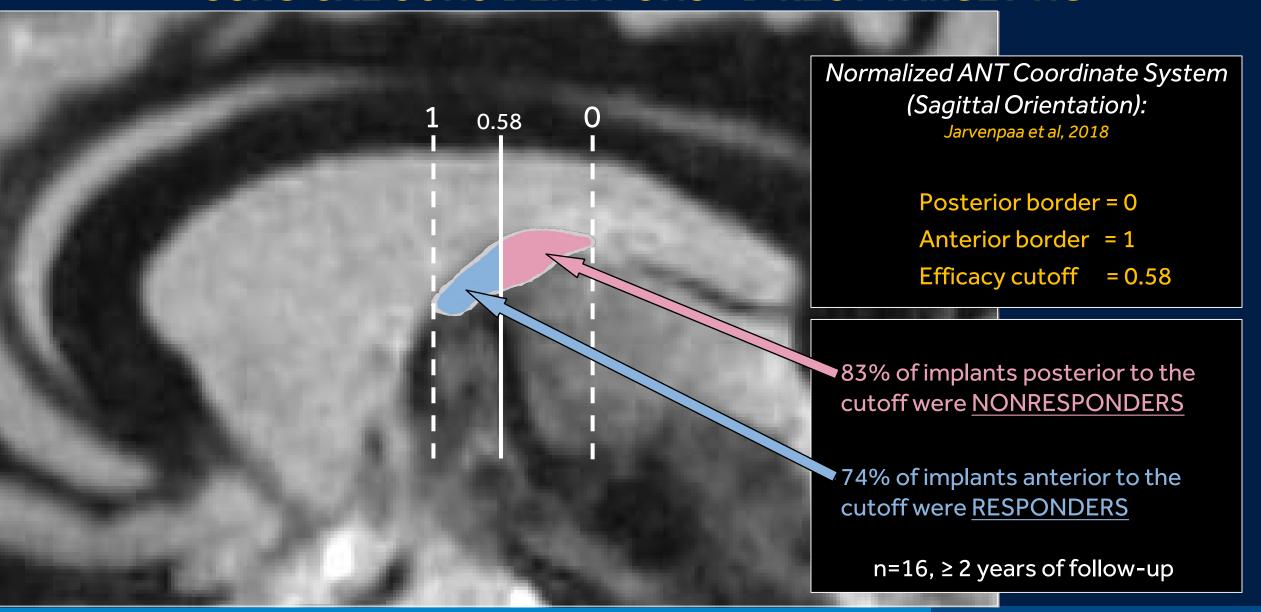
Y = 0-2 mm anterior

Z = 10-12 mm superior

¹Medtronic SANTE Study



SURGICAL CONSIDERATIONS – DIRECT TARGETING



SURGICAL CONSIDERATIONS – TRAJECTORY

Based on 73 implants¹:

90% of transventricular trajectories had at least ONE contact in ANT

VS

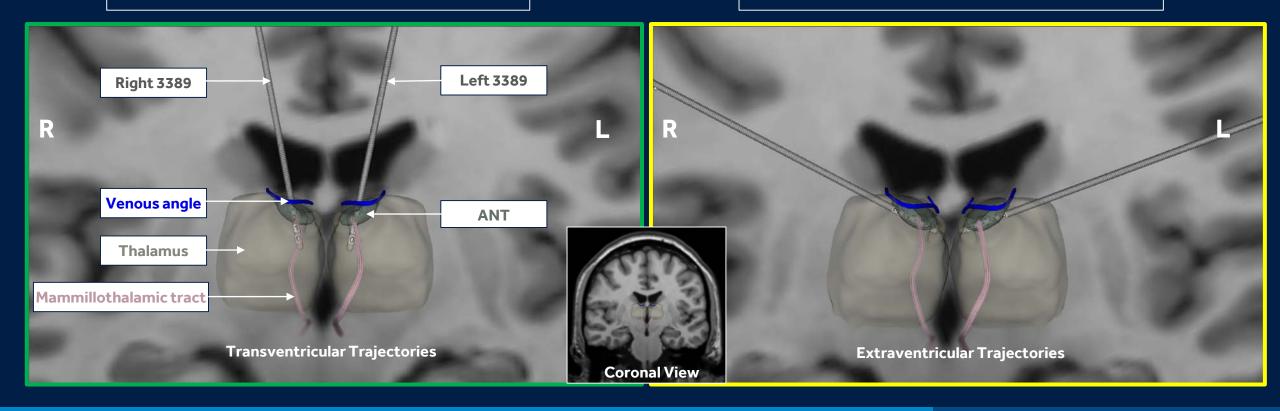
71% of extraventricular trajectories had at least ONE contact in ANT

The success rate for placing at least 1 contact in ANT bilaterally:

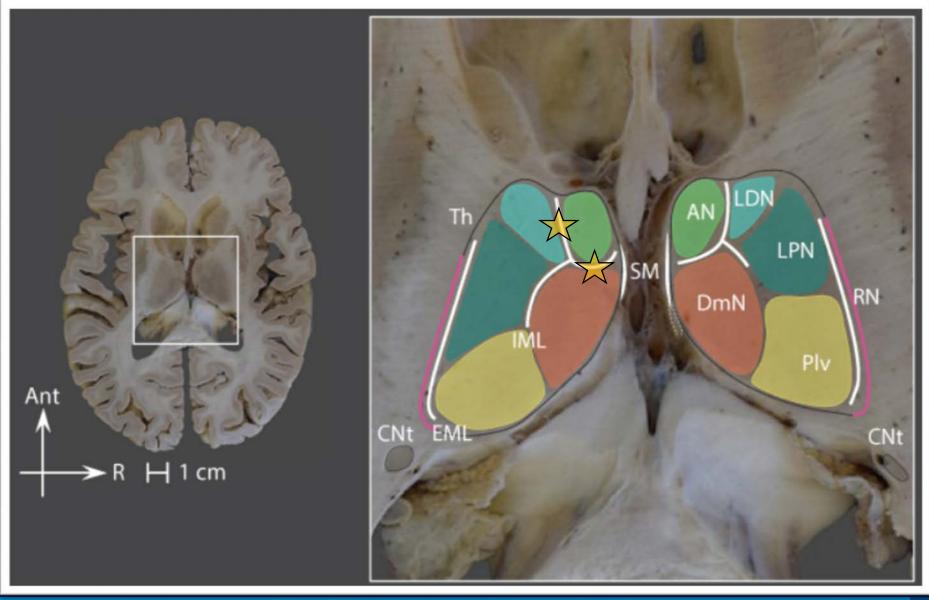
84% Transventricular

VS

58% Extraventricular



SURGICAL CONSIDERATIONS – WHITE MATTER LAMINA



The ANT is enveloped by the internal medullary lamina (white matter), a high impedance structure that may influence current flow.

AN: Anterior nucleus

LDN: Lateral dorsal nucleus

LPN: Lateral posterior nucleus

DmN: Dorsomedian nucleus

Plv: Pulvinar

RN: Reticular nucleus

CNt: Caudate nucleus (tail)

EML: External medullary lamina

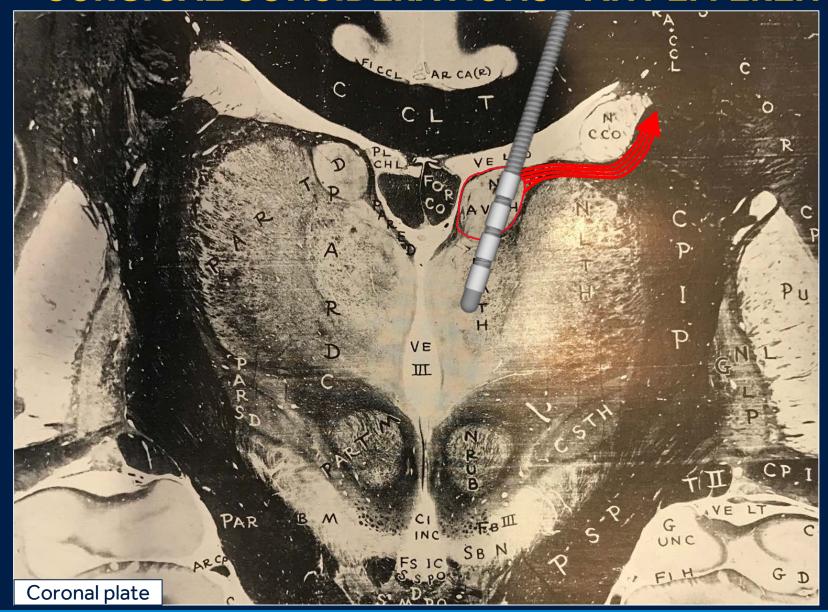
IML: Internal medullary lamina

SM: Stria medularis

Th: Thalamus



SURGICAL CONSIDERATIONS – ANT EFFERENT PATHWAY

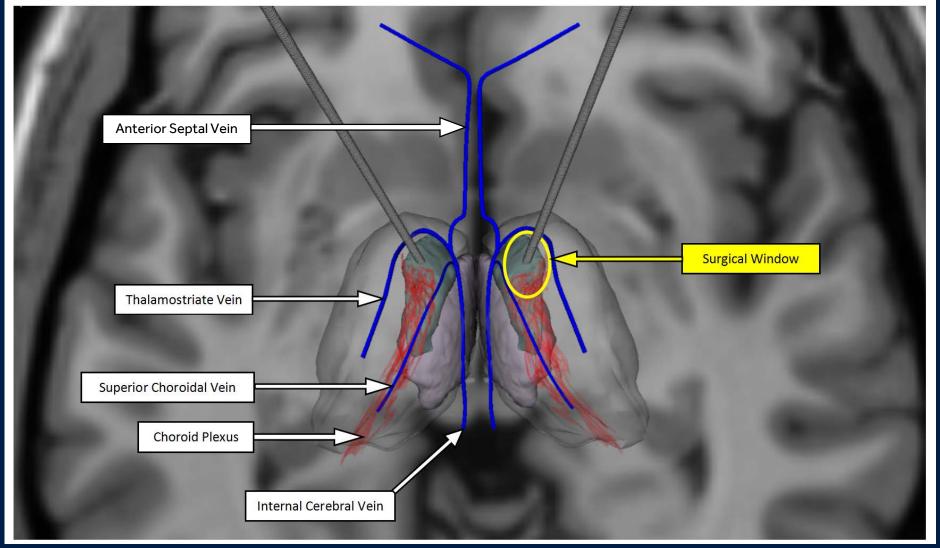


Outflow pathway from ANT exits on lateral border via the anterior thalamic radiation.

A Medtronic lead biased slightly laterally within ANT may have greater potential for influencing these axons.

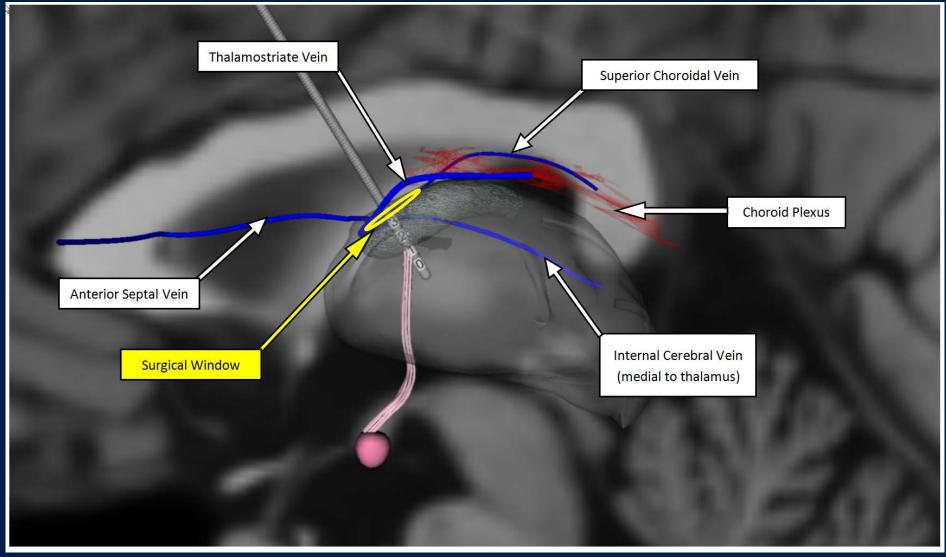
An Atlas Of The Basal Ganglia, Brain Stem And Spinal Cord (Based On Myelin-Stained Material) Riley HA, Baltimore: Williams and Wilkins Co., 1943

SURGICAL CONSIDERATIONS – VASCULATURE



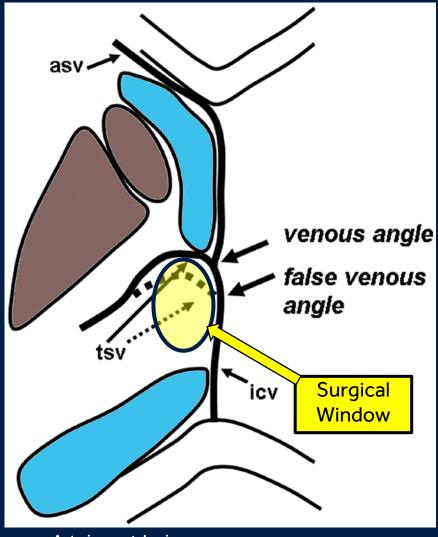
Axial View (superior aspect)

SURGICAL CONSIDERATIONS – VASCULATURE

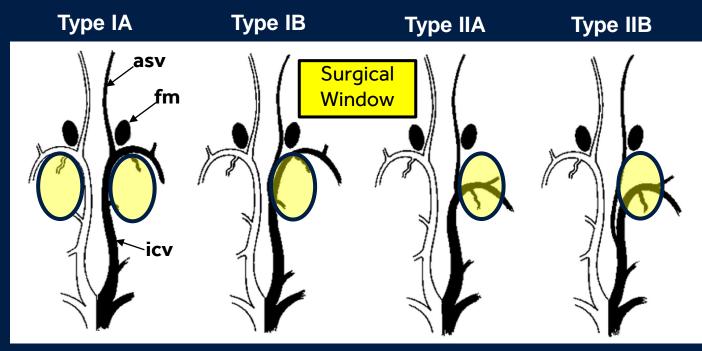


Sagittal View (lateral aspect)

SURGICAL CONSIDERATIONS – VENOUS VARIABILITY



asv: Anterior septal vein tsv: Thalamostriate vein icv: Internal cerebral vein



Variations in venous angle & asv-icv junction relative to the Foramen of Monro (fm)

Left Hemisphere: Typical venous anatomy (white)

Right Hemisphere: Variations (black)

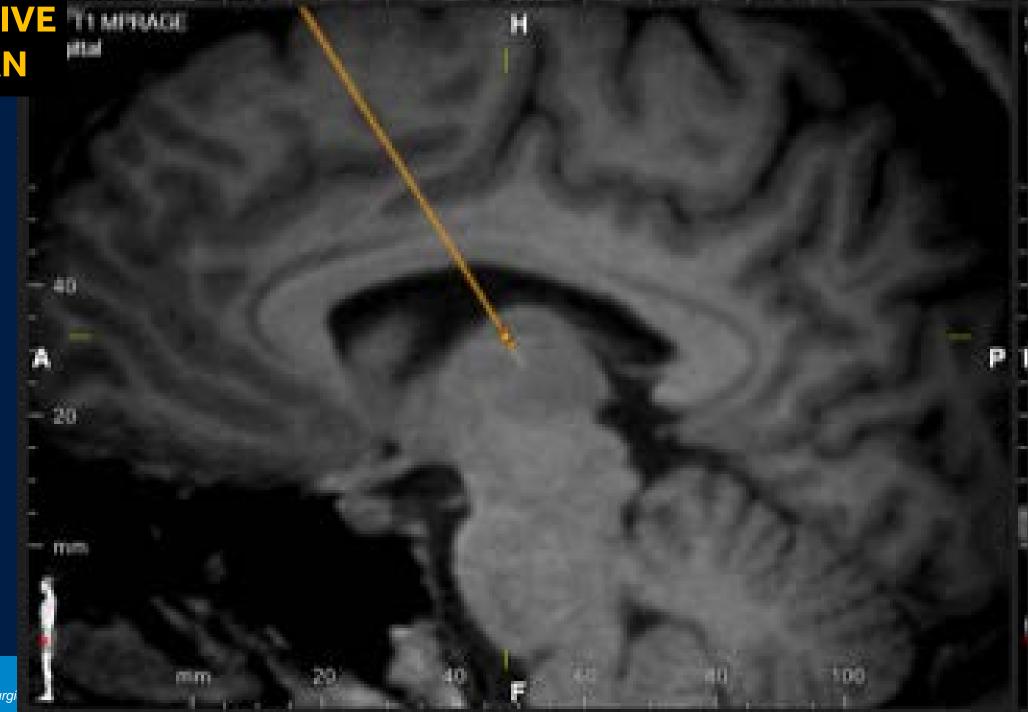
REPRESENTATIVE TO A SURGICAL PLAN

Planes centered at contact 2

LH

3389

MPRAGE image



REPRESENTATIVE DESPER POST SURGICAL PLAN

Planes centered at contact 3

LH

3389

T1 w/c image



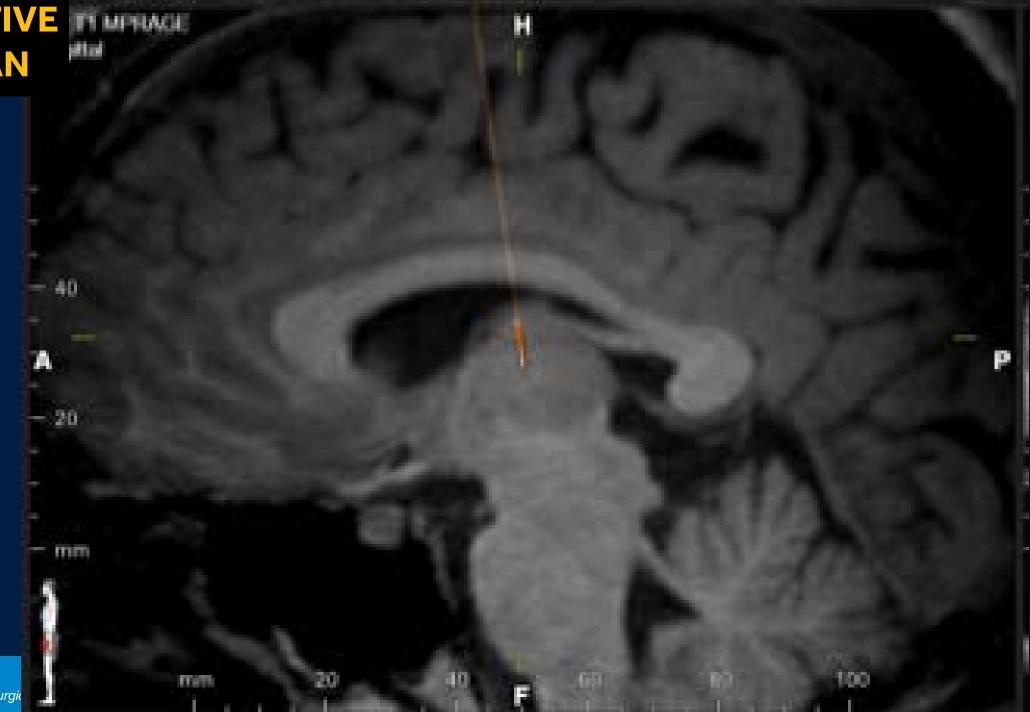
REPRESENTATIVE TO THE SURGICAL PLAN

Planes centered at contact 2

RH

3389

MPRAGE



REPRESENTATIVE 30 FSPGR POST
SURGICAL PLAN

Planes centered at contact 3

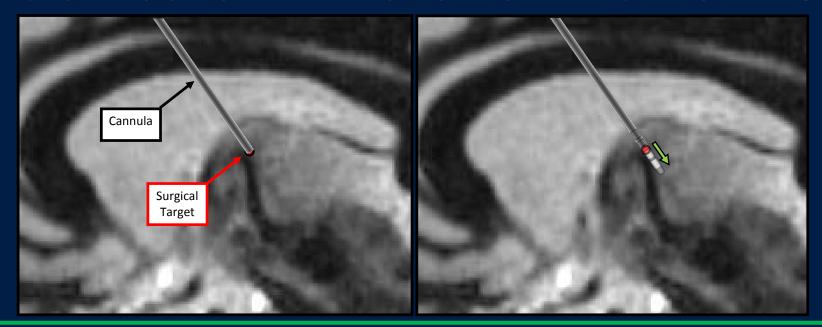
RH

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T1 w/c

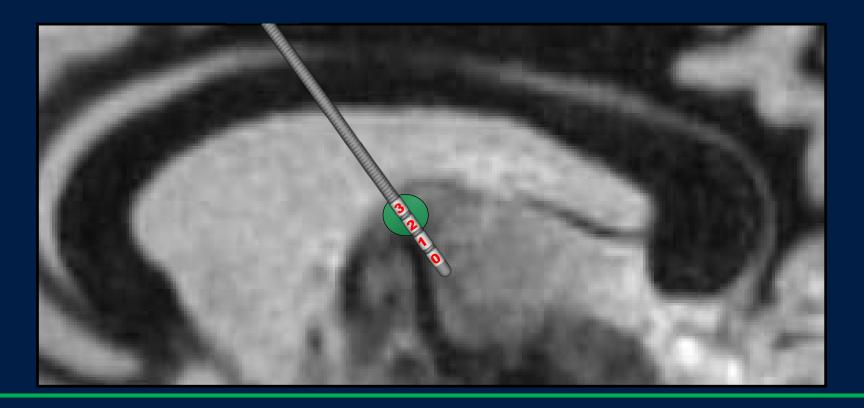


SURGICAL CONSIDERATIONS: TO-TARGET CANNULA



- A cannula that extends to target (or one positioned to just penetrate the ANT) may help reduce deflection of lead into third ventricle
- Some adjustment of the lead position along the trajectory will be necessary to accommodate anatomical variability and to ensure the chosen contacts are within the ANT and not within the ventricle
- The use of intra-operative volumetric imaging, such as the Medtronic O-Arm[™] O2 Imaging System or intraoperative CT, is highly recommended to ensure appropriate lead placement.

SURGICAL CONSIDERATIONS – CONTACT PLACEMENT



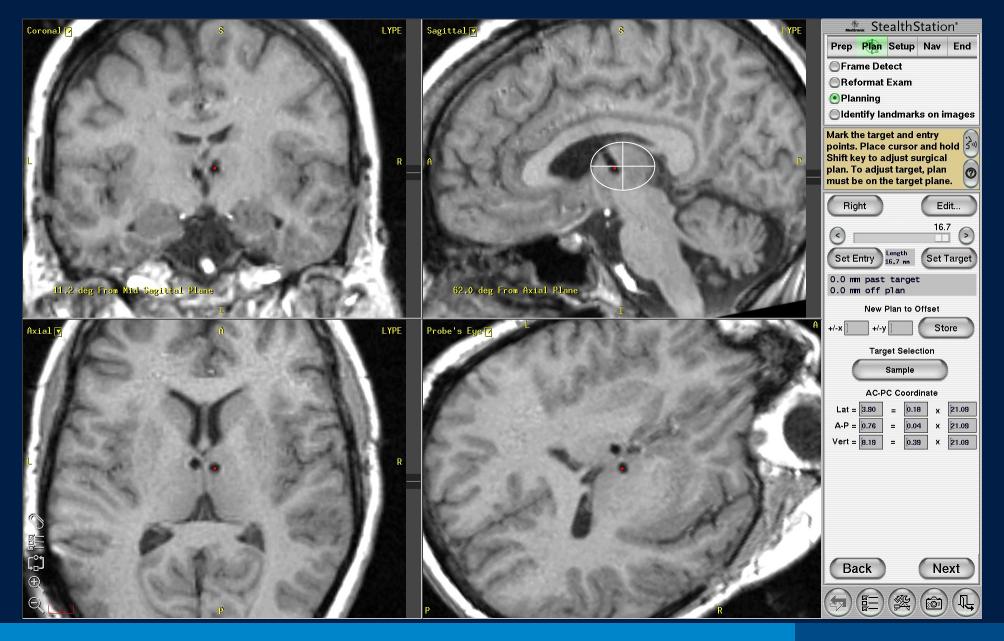
- Contacts 2 & 3 are placed within the ANT to overlap the desired area for DBS stimulation (green)
- Contact 3 is completely within the ANT and does not extend into the ventricle
- Contacts 0 & 1 in this example would likely not be used for stimulation.

LEAD PLACEMENT EXAMPLES (POST-OP MRI*, SANTE STUDY)

* See $\underline{\textit{Guidelines for Medtronic deep brain stimulation systems}}$ for more information



GOOD PLACEMENT



SLIGHT POSTERIOR



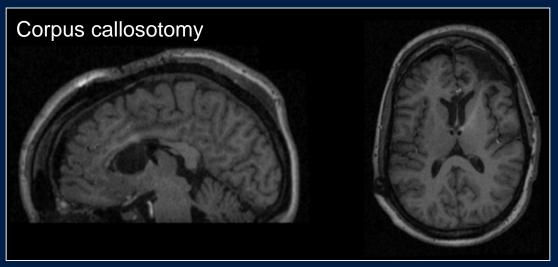
POSTERIOR



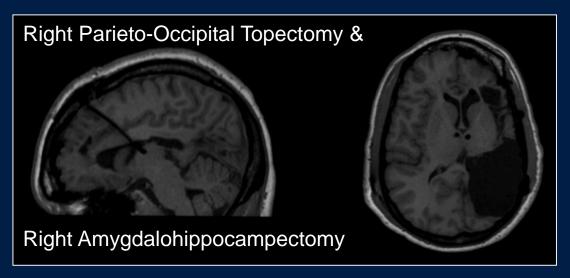
MEDIAL

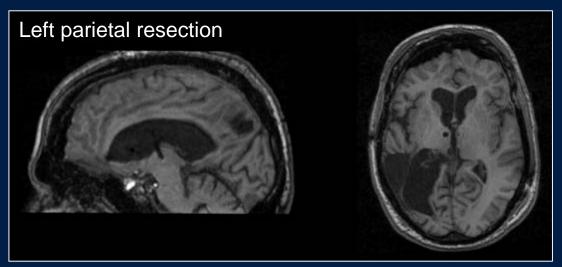


SUCCESSFUL LEAD IMPLANTATIONS WITH DISORDERED ANATOMY









Images Courtesy of Dr. R Gross, Emory University Hospital



ANT Surgical White Paper

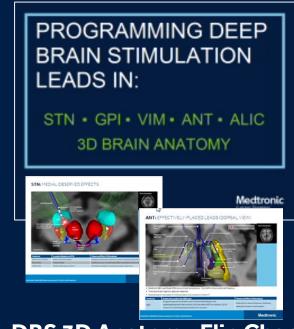
PHYSICIAN RESOURCES:



Example ANT MRI Sequences



Surgical Target Fact Brief (Vim, GPi, STN, ANT)



DBS 3D Anatomy Flip Chart

Post-Op MRI Guidance (SAR vs B1+RMS)





Learn more about DBS therapy for Epilepsy (Brochure)

BRIEF STATEMENT: MEDTRONIC DBS 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, sultrasonic 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 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 epilepticulation 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 ca

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.

USA Rx Only Rev 06/18



BIBLIOGRAPHY

In order of citation:

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- Web Reference for Brain Atlas image [Slide 10]:

https://www.braininteratlas.be/en/chapter/dorsal-thalamus#slideshow-13

Parent Page: https://www.braininteratlas.be/en

Last Accessed: Jan 30, 2019

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- Fuju S, Kanasaki Y, Matsusue E, Kakite S, Kminou T, Ogawa T. Demonstration of cerebral venous variations in the region of the third ventricle on phase-sensitive imaging. AJNR. 2010;31:55-59