IMAGING OVERVIEW: MEDTRONIC DBS FOR EPILEPSY

ANTERIOR NUCLEUS OF THE THALAMUS (ANT)

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.

*neurostimulator, leads, patient and clinician programmers

TODAY'S TOPICS

PRE-OPERATIVE IMAGING

- What sequences are best for ANT imaging?
- What sequences 'should' an account do for ANT?
- Sequence database
- Imaging patients with VNS & DBS

INTRAOPERATIVE IMAGING

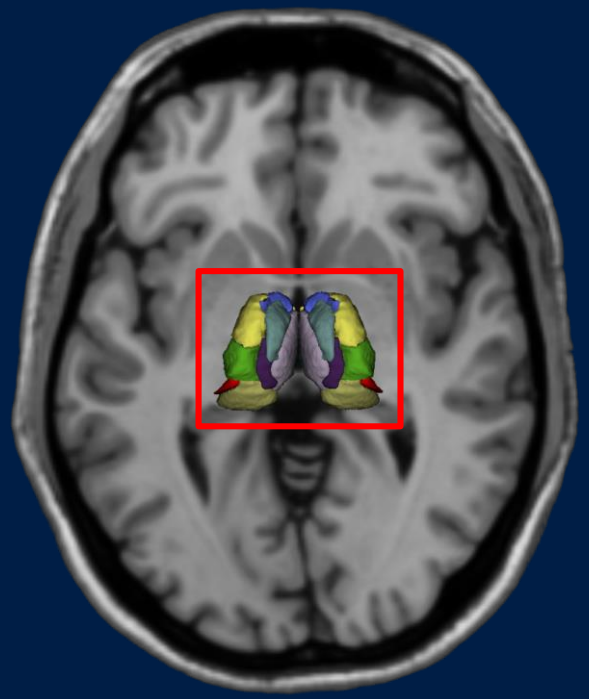
- Value of intraoperative imaging for ANT?
- Benefits of intra-op imaging + StealthStation™ S8 (or Cranial 3.0)

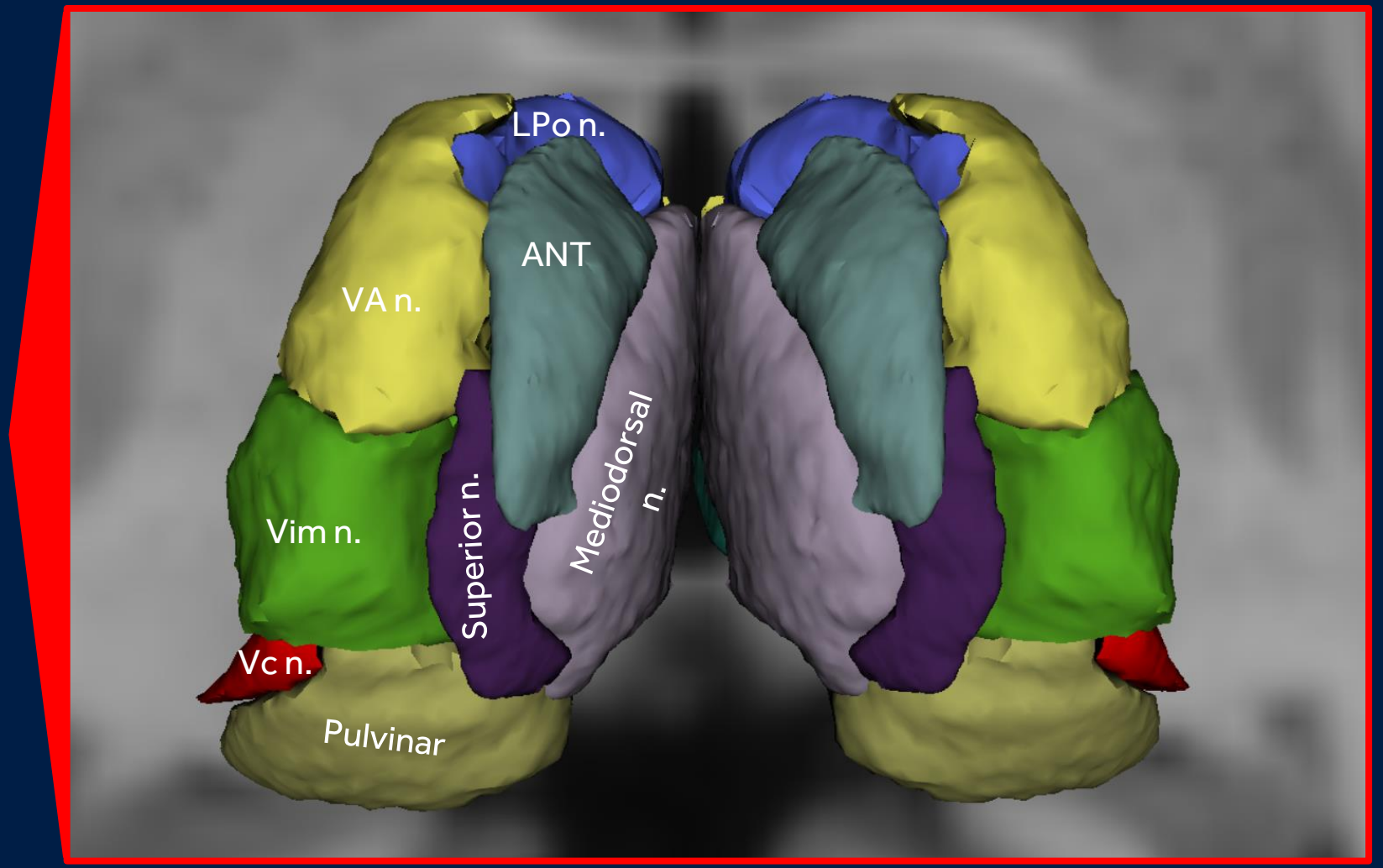
KEY SURGICAL CONSIDERATIONS[1] FOR ANT DBS

- Pre-operative/Intra-operative MR Imaging (with and w/o VNS)
- Trajectory (trans-ventricular approach)
- To-target cannula
- Visualizing and avoiding venous structures
- Performed under general anesthesia
- MER *(value has not been demonstrated)*
- Intra-operative testing *(value has not been demonstrated)*

[1]*Medtronic SANTE Study*

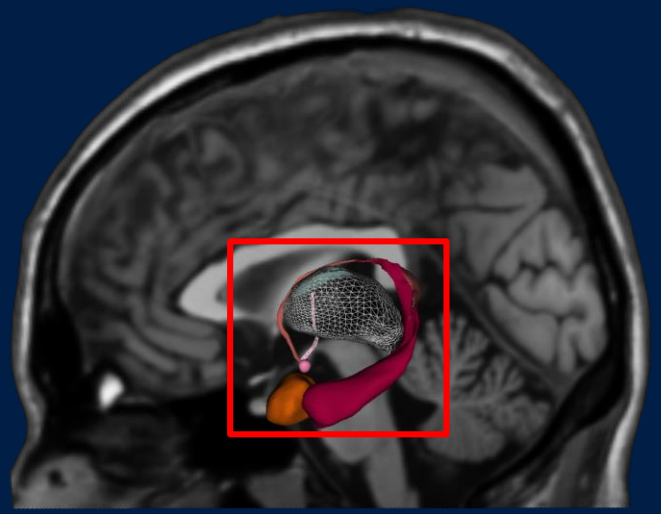
ANATOMICAL LOCATION (AXIAL VIEW)

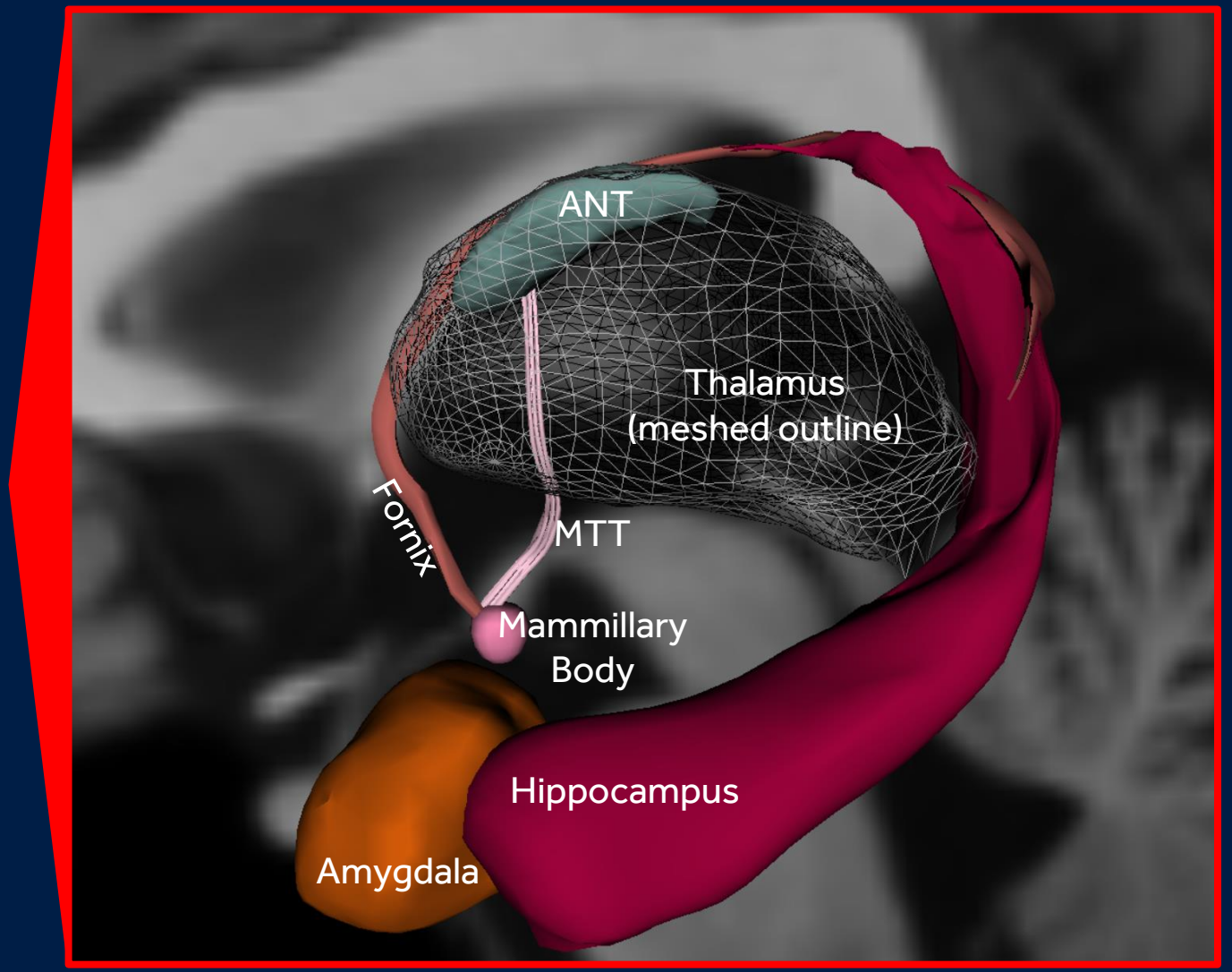




Finnis KW, Medtronic 3D DBS Simulator

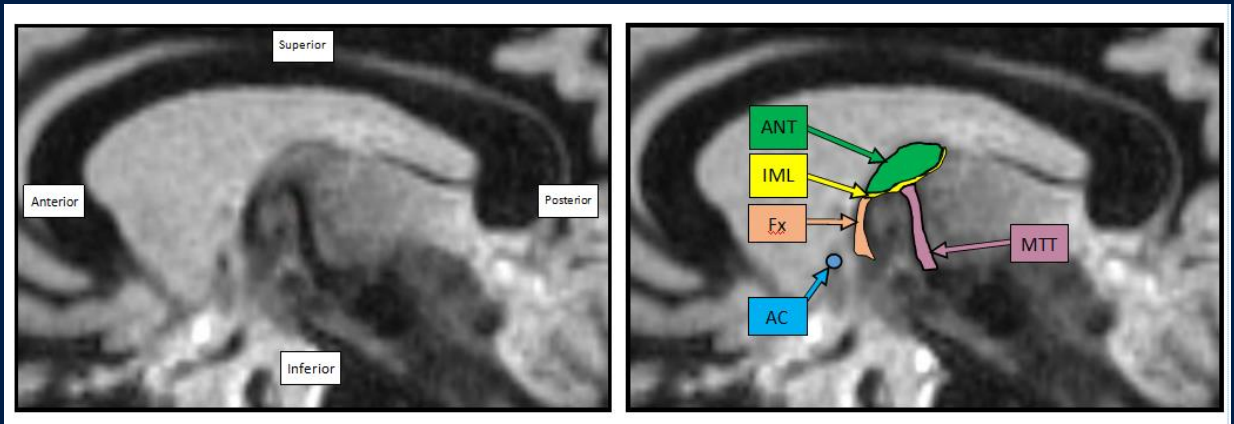
ANATOMICAL LOCATION (SAGITTAL VIEW)





Finnis KW, Medtronic 3D DBS Simulator

SURGICAL CONSIDERATIONS – DIRECT TARGETING

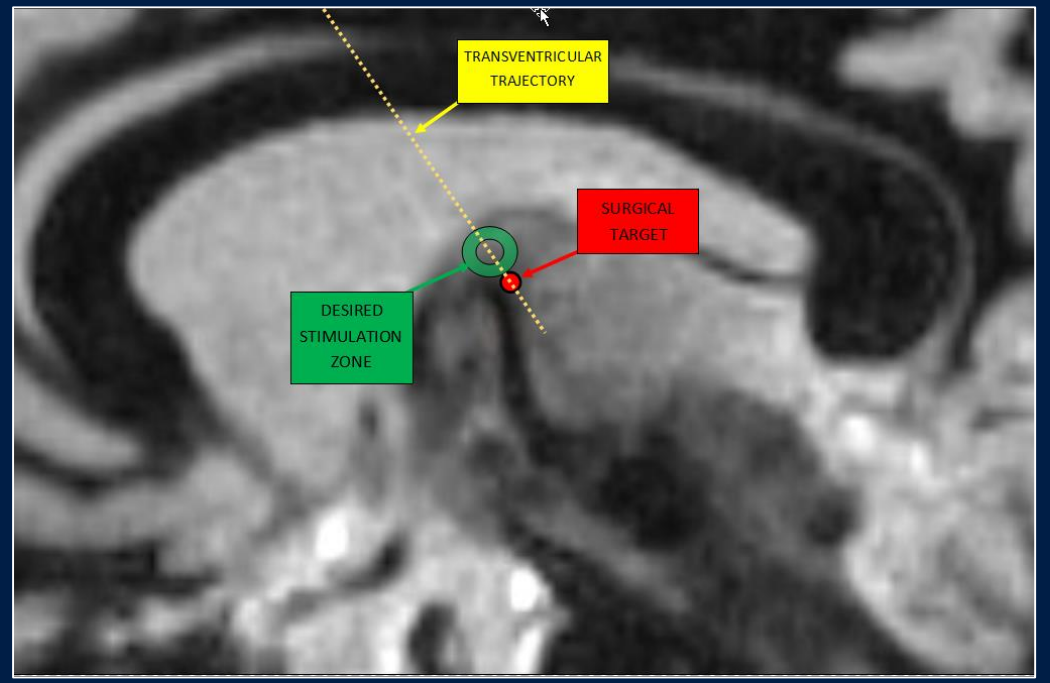


Broad range of ACPC coordinates (anatomical variability)[1]

X = 4-7mm
Y = 0-5mm anterior
Z = 10-12 superior

ANT: *Anterior nucleus of the thalamus*
IML: *Internal Medullary Lamina of the thalamus*

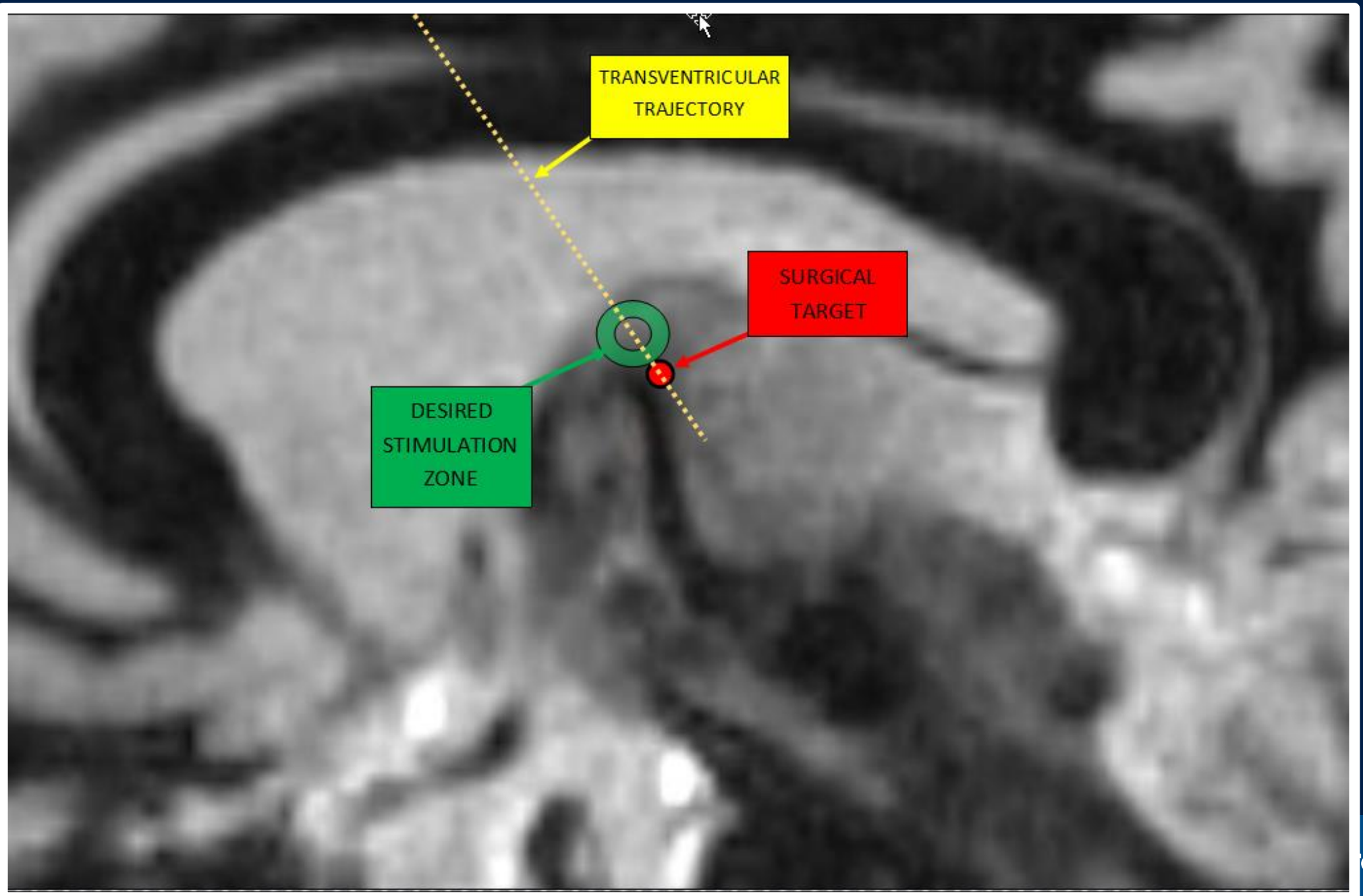
Fx: *Fornix*
AC: *Anterior Commissure*
MTT: *Mammillothalamic Tract*



[1]Medtronic SANTE Study

Medtronic

SURGICAL CONSIDERATIONS – DIRECT TARGETING



SURGICAL CONSIDERATIONS – DIRECT TARGETING

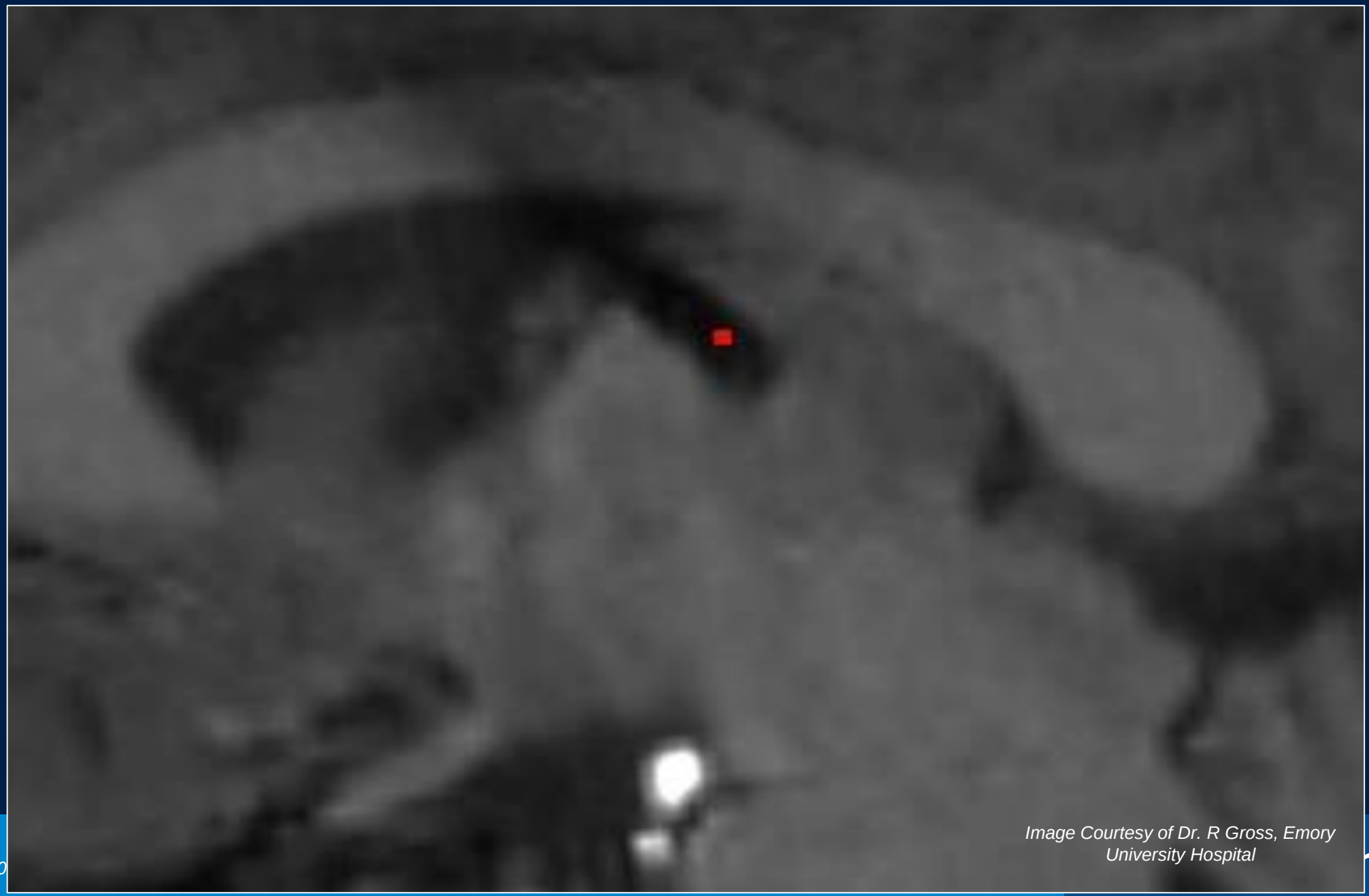


Image Courtesy of Dr. R Gross, Emory University Hospital

SURGICAL CONSIDERATIONS – PRE-OP IMAGING

- Which MRI sequences adequately show ANT and surrounding anatomy?
  - T1 FGATIR
  - T1 STIR
  - MPRAGE
  - STANDARD T1 with Contrast (for vascular visualization)
  - Other Available Sequences?
    - Standard Inversion Recovery?
    - FLAIR?
    - Proton Density?
    - White Matter/Fat-Nulled?

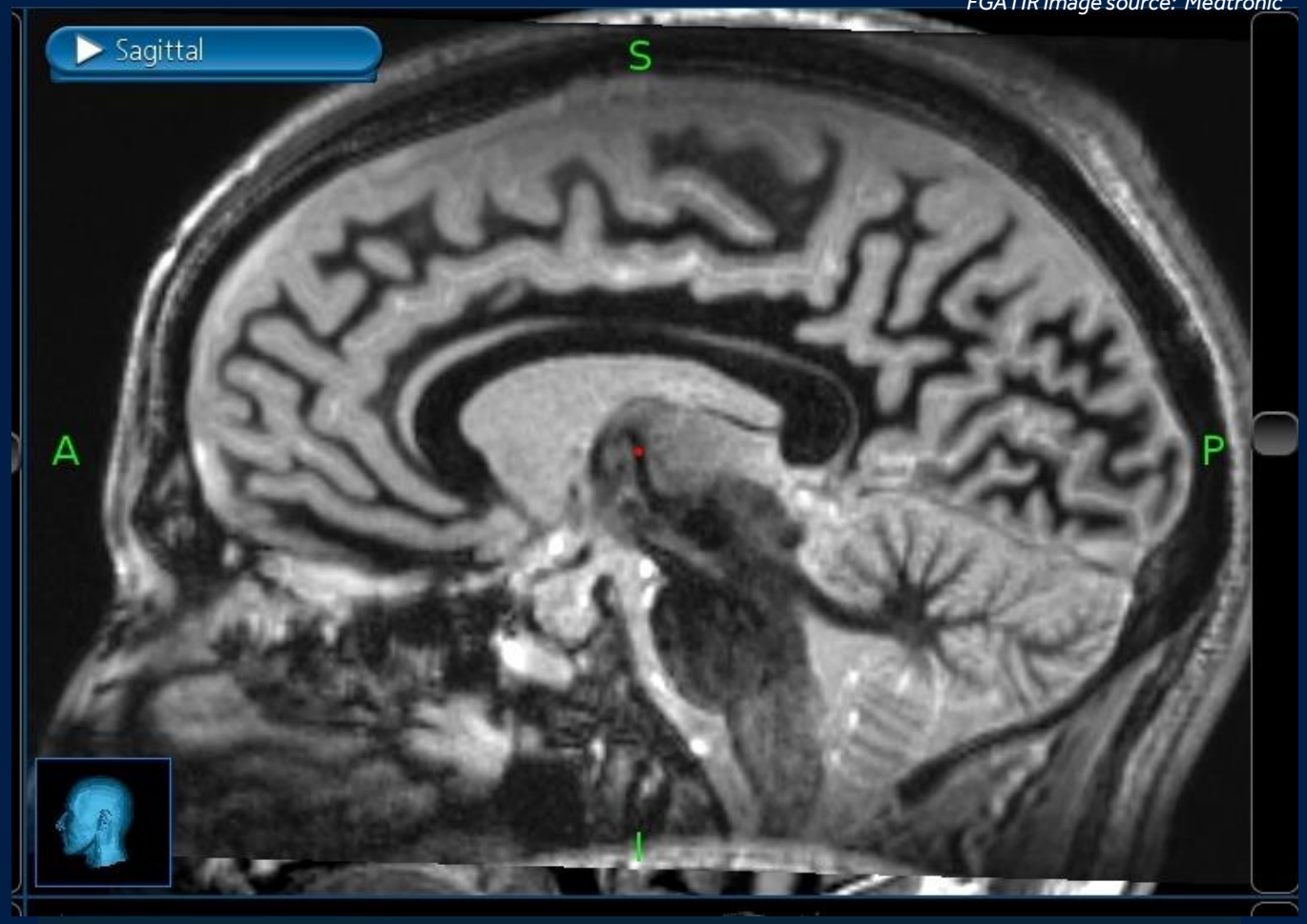
FGATIR Fast Grey matter Acquisition T1 Inversion Recovery

- Superior grey/white matter differentiation

- 1.5T or 3T*

*See *"MRI Guidelines for Medtronic deep brain stimulation systems"* for more information on scanning conditions

FGATIR Image source: Medtronic



"This sequence can be difficult to optimize on GE Scanners – it's far easier with Siemens."

- Personal communication: Dr. Anant Patel, Feb 7, 2019, Hoboken, NJ, **Medtronic DBS Therapy, Foundations for Epilepsy** Course.

See University of Florida FGATIR website for example sequences:
https://movementdisorders.ufhealth.org/research/fgatir-new-scan-for-surgical-targeting/
Parent website: https://movementdisorders.ufhealth.org
Last accessed: Feb 7, 2019

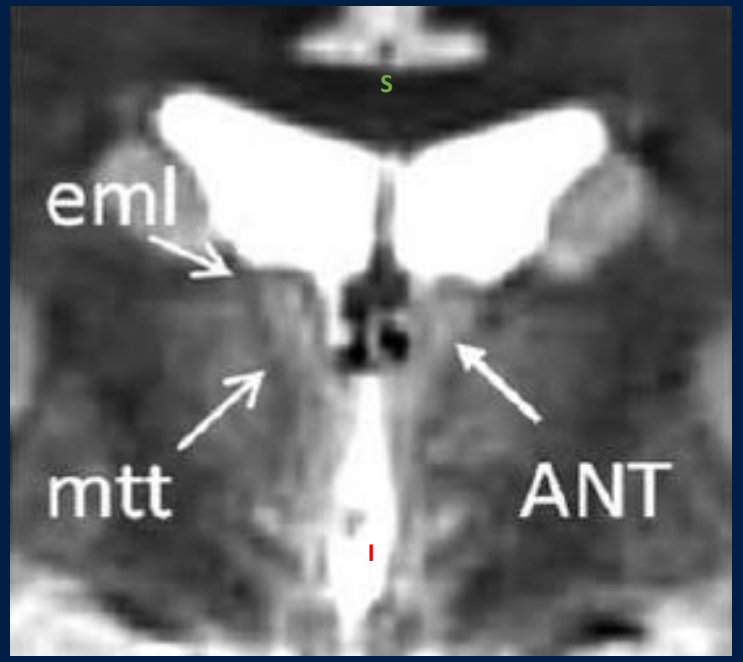
Medtronic

STIR Short Tau Inversion Recovery

- Good grey/white matter differentiation
- Fat signal is nulled
- 1.5T or 3T* (preferable)

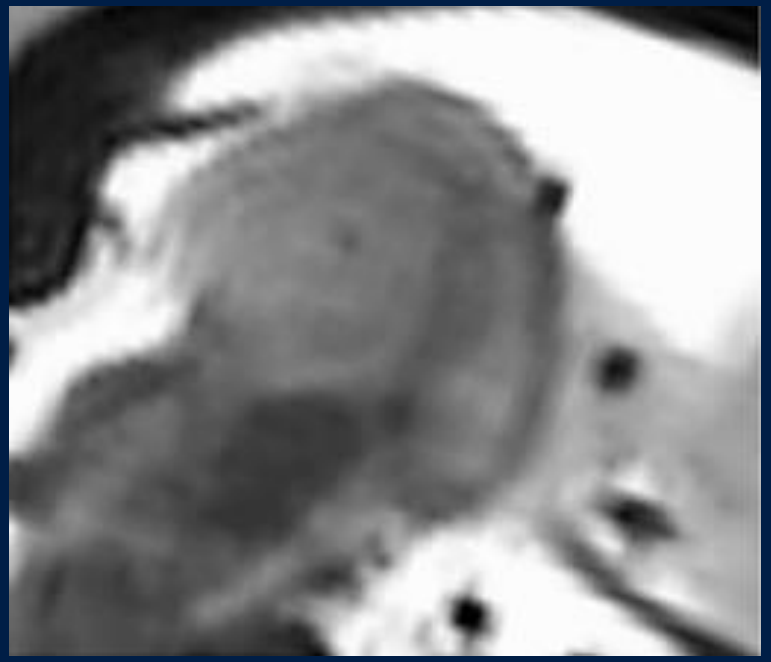
  * See *"MRI Guidelines for Medtronic deep brain stimulation systems"* for more information on scanning conditions

- Many centers do these scans in addition to FGATIR or MPRAGE (next slide)



1.5 T

Jiltsova et al, Neuromodulation. 2016;19(8):812-817



3 T

Lehtimaki et al, Brain Stim. 2016;9:268-275

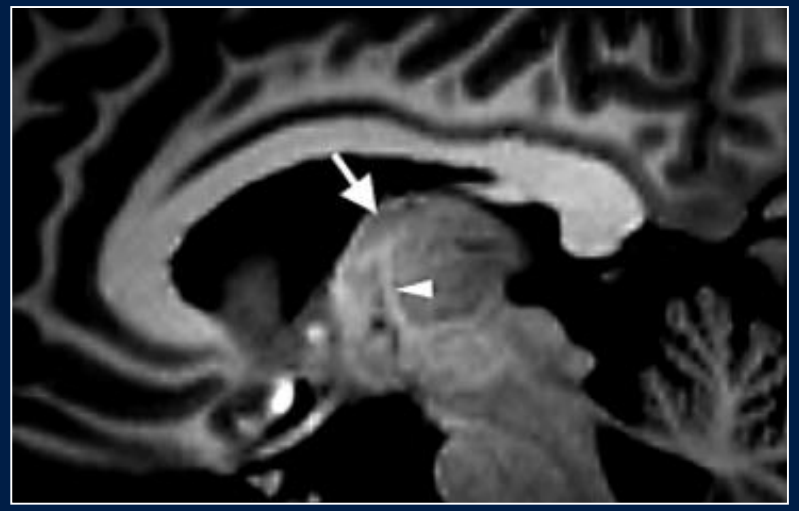
"2 mm slice thickness is recommended over 1 mm for STIR images to preserve grey/white tissue contrast. This may necessitate acquiring three separate datasets in axial, coronal and sagittal orientations as out-of-plane reconstructions may be of insufficient quality." - Dr. Kai Lehtimaki, Feb 7, 2019, Hoboken, NJ, **Medtronic DBS Therapy, Foundations for Epilepsy** Course.

MPRAGE

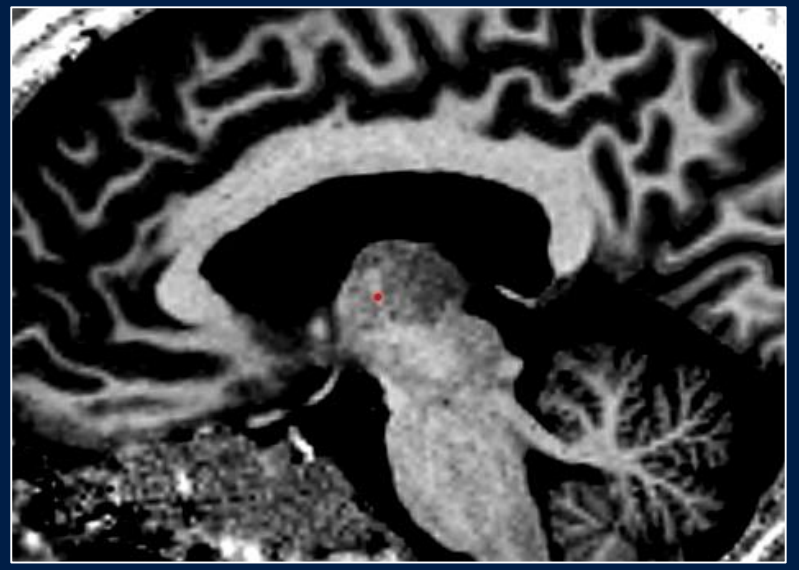
Magnetization Prepared RApid Gradient Echo

- Often used for accentuating lesions (such as those found in MS)
- Will provide excellent visualization of mammillothalamic tract and ANT
- MP2RAGE is a similar sequence although often used at higher field strengths (3T and higher) *

*See *"MRI Guidelines for Medtronic deep brain stimulation systems"* for more information on scanning conditions



MPRAGE[1]



MP2RAGE[2]

[1]*Buentjen et al, Stereotact Funct Neurosurg. 2014;92:25-30*
[2]*Image Source: Medtronic*

T1 WITH CONTRAST (BLOOD VESSELS)

- Same T1 that we use for movement disorders*

  * See "*MRI Guidelines for Medtronic deep brain stimulation systems*" for more information on scanning conditions

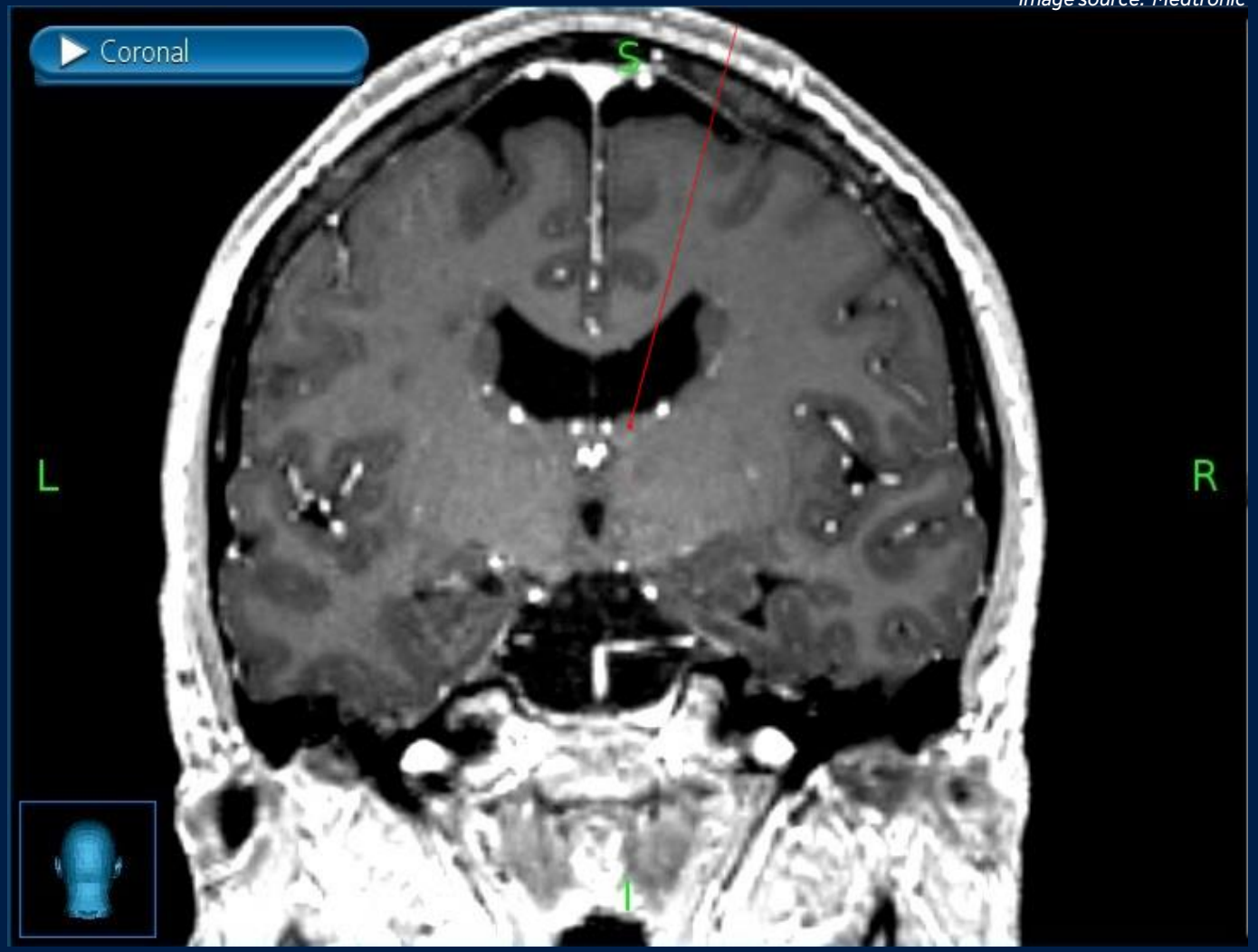
- Addition of gadolinium for contrast

- Enhances blood vessels (veins)

- Multiple trade names* for contrast:
  - Omniscan™
  - Magnevist™
  - Gadovist™
  - OptiMARK™
  - ProHance™
  - Dotarem™

  And more....

Image source: Medtronic



Medtronic

OTHER SEQUENCES? "STANDARD INVERSION RECOVERY (IR)"

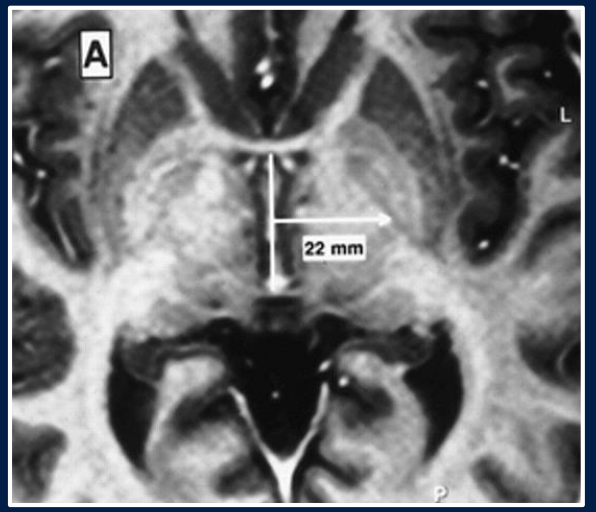
- Often referred to as a "Standard inversion recovery scan"
  - May also be described as "White matter-nulled" or "Fat-nulled"

- What is an inversion recovery scan?

  Inversion recovery pulse sequences are a type of MRI sequence used to selectively null the signal for certain tissues (e.g. fat or fluid).
  IR scans can generate excellent grey-white matter contrast.

- Inversion recovery scans have been used since the early days of MRI (late 80s) so experienced centers should be familiar with the sequence

- Often already done for planning GPi cases



IR-FSE (*fast spin echo*) scan for direct targeting of the GPi (Circa 2000)

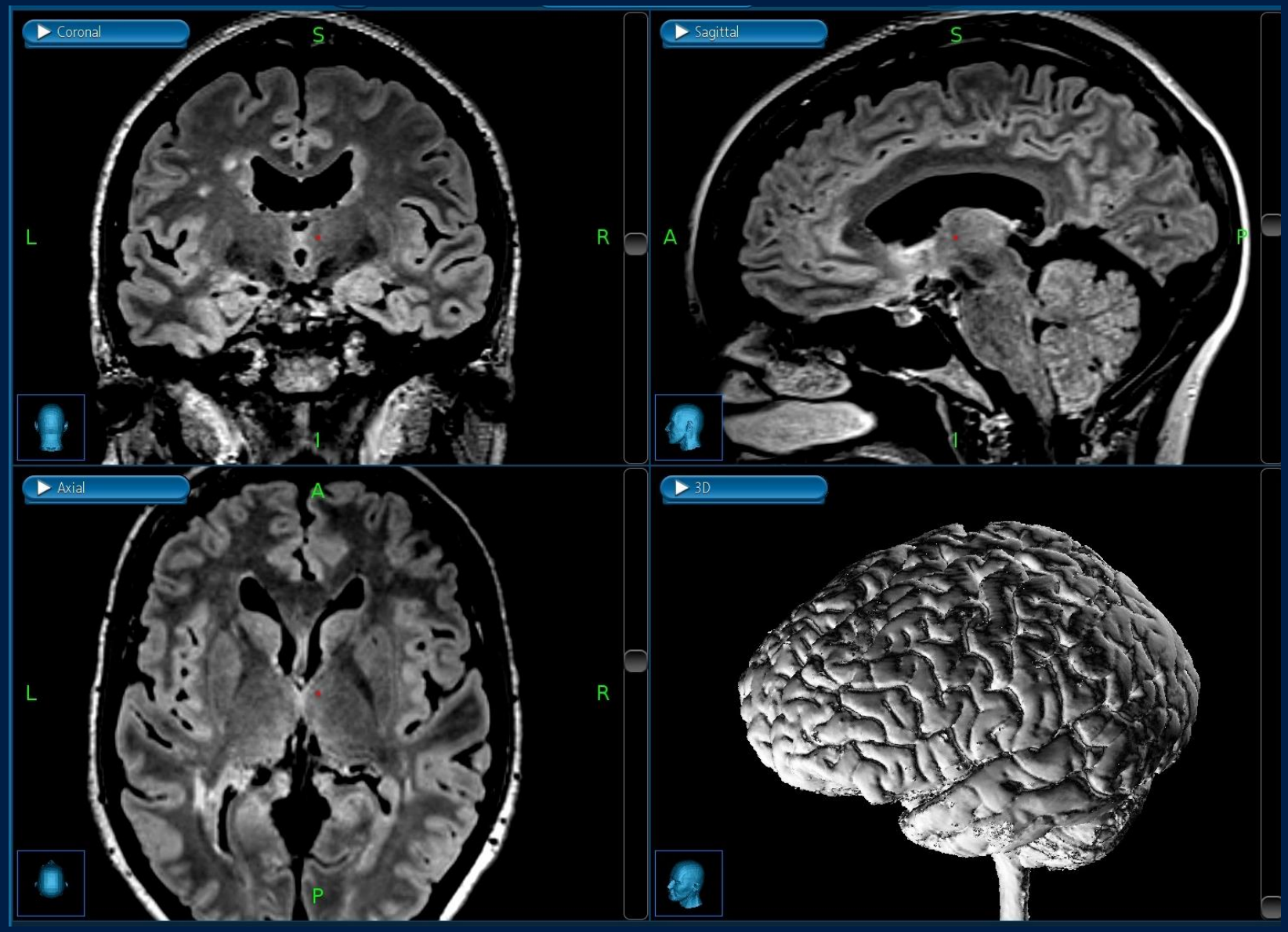
Reich et al, AJNR. 2000;21:928-931

OTHER SEQUENCES? FLAIR

FLAIR

Fluid attenuated inversion recovery

- Inversion recovery set to null fluids (CSF is dark)
- Often used for white matter lesions, inflammation

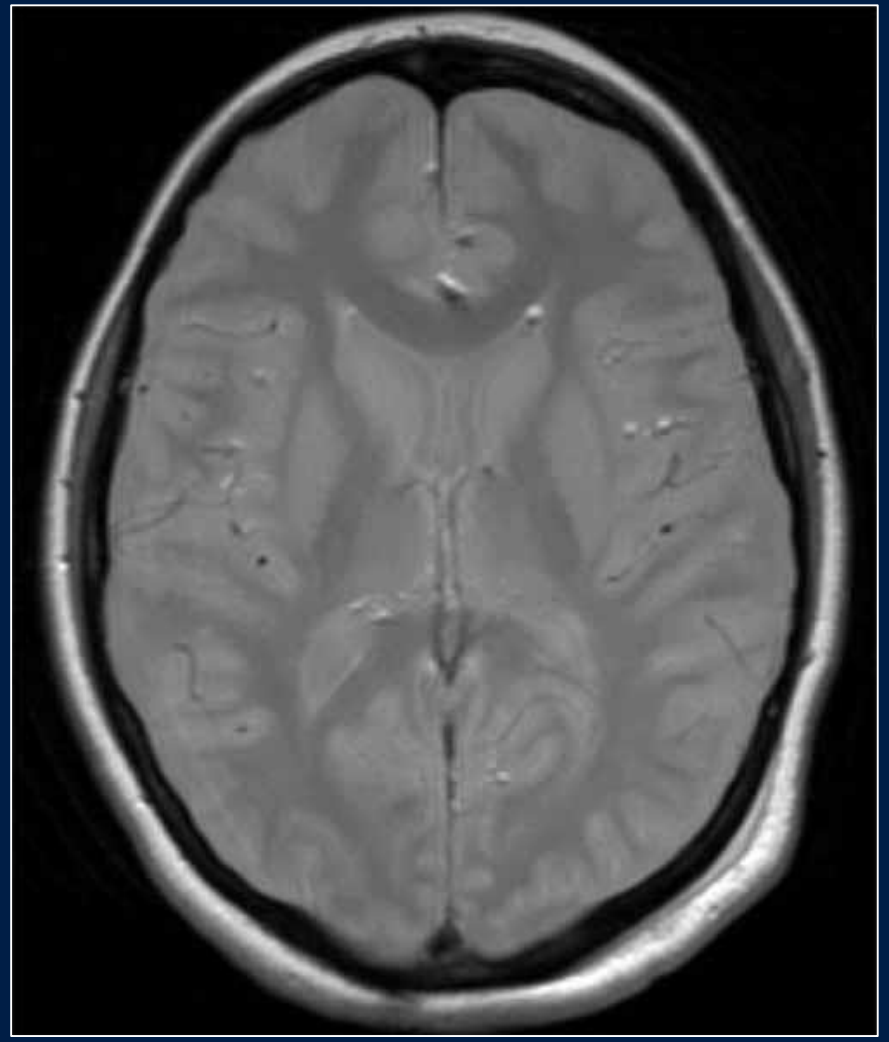


FLAIR Image source: Medtronic

OTHER SEQUENCES? PD SCAN

Proton Density Scan

- Often used for muscle, cartilage, joint imaging and for imaging pathology in the brain
- Nulls fluid so vessels appear darker
- Images quantitatively demonstrate density of protons in the brain
- Good for ANT? Possibly....



Proton Density MR Image[1]

Web Page: ***https://www.radiologycafe.com/radiology-trainees/frcr-physics-notes/t1-t2-and-pd-weighted-imaging***
Parent Site: ***https://www.radiologycafe.com***
Last Accessed: ***Feb 7, 2019***

SO WHICH SCANS SHOULD WE CONSIDER?

Anatomical Image

Stereotactic full head T1 with contrast

Target Visualization

FGATIR ≥ MPRAGE or STIR ≥ Inversion Recovery scan with white matter/fat-nulled signal > FLAIR, PD, T1 (without contrast), Others?

CONSIDERATIONS FOR PATIENTS WITH VNS

Post-op MRI with both DBS and VNS implants ***may*** be possible provided all safety conditions are met. Several questions must be answered by the physician prior to scanning:

1. Determine what model of DBS system is implanted and if full-body or head-only MRI eligible*
   * See "*MRI Guidelines for Medtronic deep brain stimulation systems*" for more information on scanning conditions

2. Determine what brand/model of VNS system is implanted

3. Determine if the VNS is complete, active or inactive, or partially excised

4. If the VNS system is complete (leads & IPG), determine if VNS IPG is to be excised or left in place prior to MRI scan

5. If the VNS IPG has previously been removed, physician must determine:
   a. If > 2 cm of VNS lead length remains, or
   b. If < 2 cm of VNS lead length remains

6. Follow the most restrictive manufacturer's guidelines

HIGHLIGHT OF CYBERONICS' VNS (LIVANOVA) MRI LABELING

Refer your physician to consult Cyberonics labeling &/or representative

Table 2. Summary of Conditional MR Use

VNS Device		Group A	Group B
Scanner Type		Horizontal field, cylindrical closed-bore, clinical system for hydrogen proton imaging	
Scanner Characteristics	**Static magnetic field strength**	1.5 or 3 T	
	Spatial field gradient	**Models 100C and 101:** ≤ 720 Gauss/cm **Models 102 through 1000:** ≤ 3000 Gauss/cm	
	Maximum slew rate	200 T/m/s	
Scanner Operation	**Operating mode**	Normal Operating Mode	
	Transmit RF coil	**Head or extremity coils:** Scan (placement of entire coil) must be outside of C7 - T8 **Body coil:** Iso-center of scan (center of the MRI bore) must be outside of C7 - L3. This may be accomplished by landmarking above C7 or below L3.	**Transmit/receive head or extremity coils only:** Scan (placement of entire coil) must be outside of C7 - T8
	Maximum Specific Absorption Rate (SAR)	**Transmit head coil:** 3.2 W/kg **Transmit body coil:** 2.0 W/kg	**Transmit/receive head coil:** 3.2 W/kg
	Exposure time	**Transmit head or extremity coil:** No restriction **Transmit body coil:** ≤ 15 minutes of active scan time within a 30 minute window	**Transmit/receive head or extremity coil:** No restriction
	Additional Restriction(s)	**Transmit head or extremity coil:** None **Transmit body coil:** Circularly Polarized (CP) mode only (i.e., no shimming)	none

Table 3. Scan Conditions for Partially Explanted VNS Therapy Systems or Damaged Leads

Implant Configuration	Scan Conditions	
	1.5T or 3T with transmit/receive Head Coil or transmit/receive Extremity Coil, with C7-T8 exclusion zone (i.e., Group B Scan Conditions)	1.5T or 3T with transmission of RF with the Body Coil, any landmark, no exclusion zones
VNS Therapy System with a suspected lead break (IPG is still connected)		
Lead length > 2 cm remains (No IPG)		
≤ 2 cm of lead (i.e. electrodes remain implanted)		

MRI with the VNS Therapy. Oct 2017 publication, LivaNova USA Inc. 100 Cyberonics Blvd, Houston, Texas, 77058. http://www.livanova.com

INTRA-OP IMAGING & MEDTRONIC SURGICAL SYNERGY

O-Arm™ O2 Imaging System

- Useful for assessing:
  - if contacts are positioned in ventricles following implant
  - if any medial lead deflection has occurred

StealthStation™ S8 Cranial Software (or Cranial 3.0 software for S7/i7)

- 3D lead modeling is very useful for:
  - customizing lead depth along the surgical plan
  - maximizing the number of contacts in ANT (vs CSF)

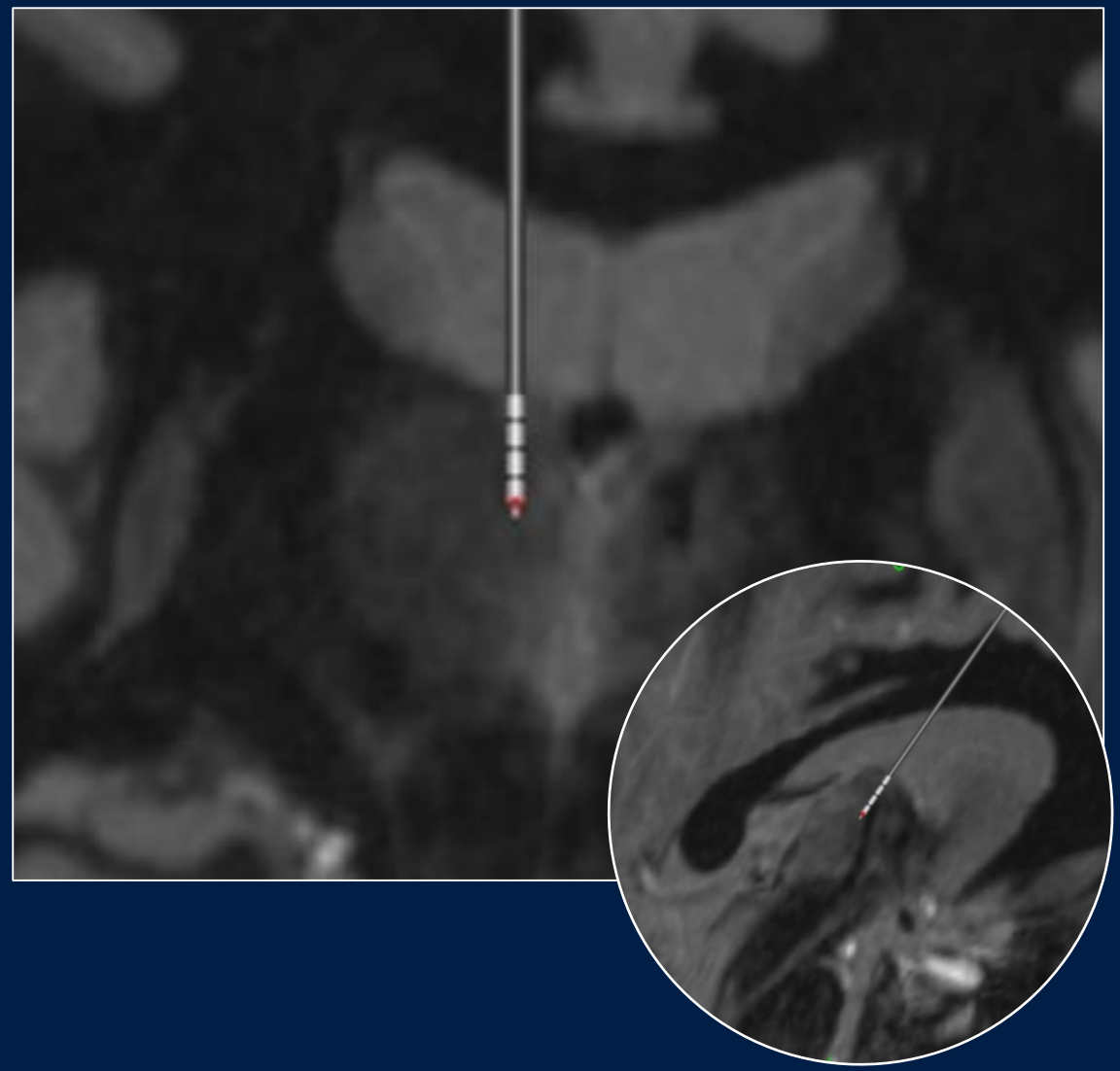
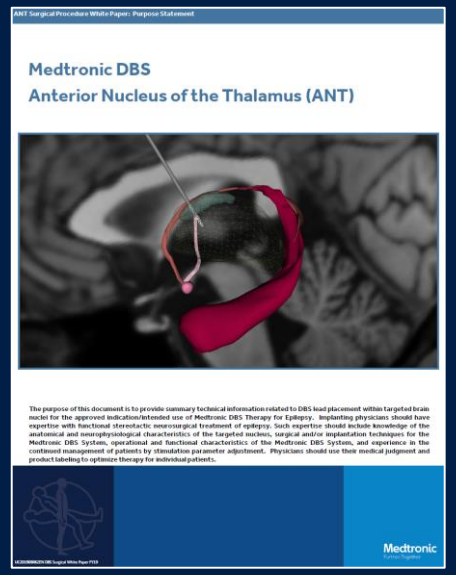
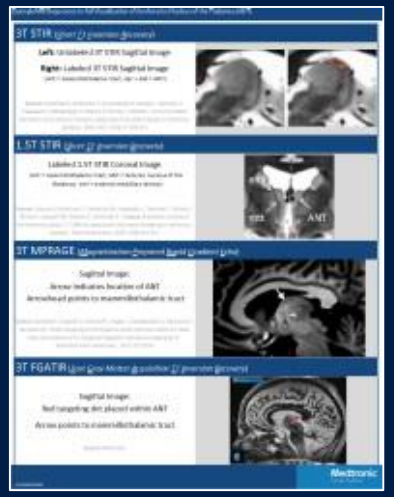


Image source: Medtronic

PHYSICIAN RESOURCES:

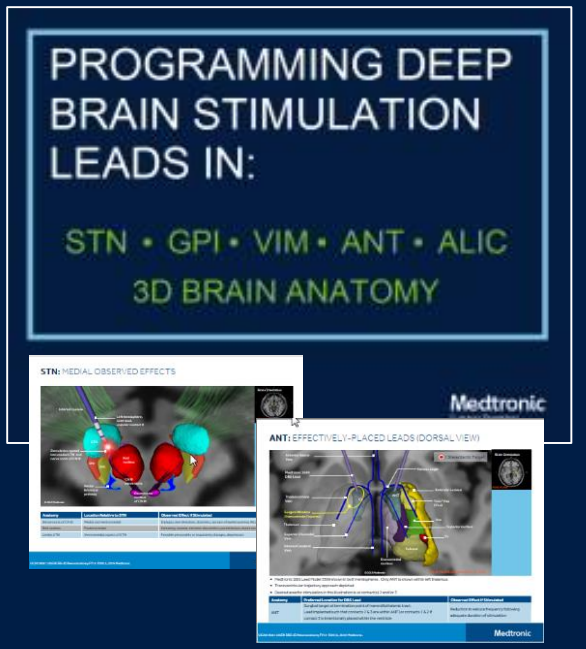


ANT Surgical White Paper



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)

QUESTIONS?

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, 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.

USA Rx Only Rev 06/18

BRIEF STATEMENT: *StealthStation System™* and *O-arm™ Imaging System*

StealthStation System™
Rx only. Refer to product instruction manual/package for instructions, warning, precautions and contraindications. For further information regarding StealthStation System™ and O-arm™ Imaging System, please contact Medtronic at 800-595-9709 and/or consult Medtronic's website at www.medtronic.com/for-healthcare-professionals/products-therapies/neurological/surgical-navigation-and-imaging/o-arm-surgical-imaging-system/index.htm

O-arm™ Imaging System
Rx only. Refer to product instruction manual/package for instructions, warning, precautions and contraindications.
For further information regarding StealthStation System™ and O-arm™ Imaging System, please contact Medtronic at 800-595-9709 and/or consult Medtronic's website at www.medtronic.com/for-healthcare-professionals/products-therapies/neurological/surgical-navigation-and-imaging/o-arm-surgical-imaging-system/index.htm

BIBLIOGRAPHY

In order of citation:

- Finnis KW, Medtronic DBS Simulator
- 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
- 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(1):25-30
- Reich A, Hudgins PA, Sheppard SK, et al. A high-resolution fast spin-echo inversion-recovery sequence for preoperative localization of the internal globus pallidus. AJNR. 2000; 21:928-931.
- Web Page:
  https://www.radiologycafe.com/radiology-trainees/frcr-physics-notes/t1-t2-and-pd-weighted-imaging
  Parent Site:
  https://www.radiologycafe.com
  Last Accessed: Feb 7, 2019
- *MRI with the VNS Therapy,* Oct 2017, LivaNova USA Inc. 100 Cyberonics Blvd, Houston, Texas, 77058. http://www.livanova.com