SURGICAL 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.

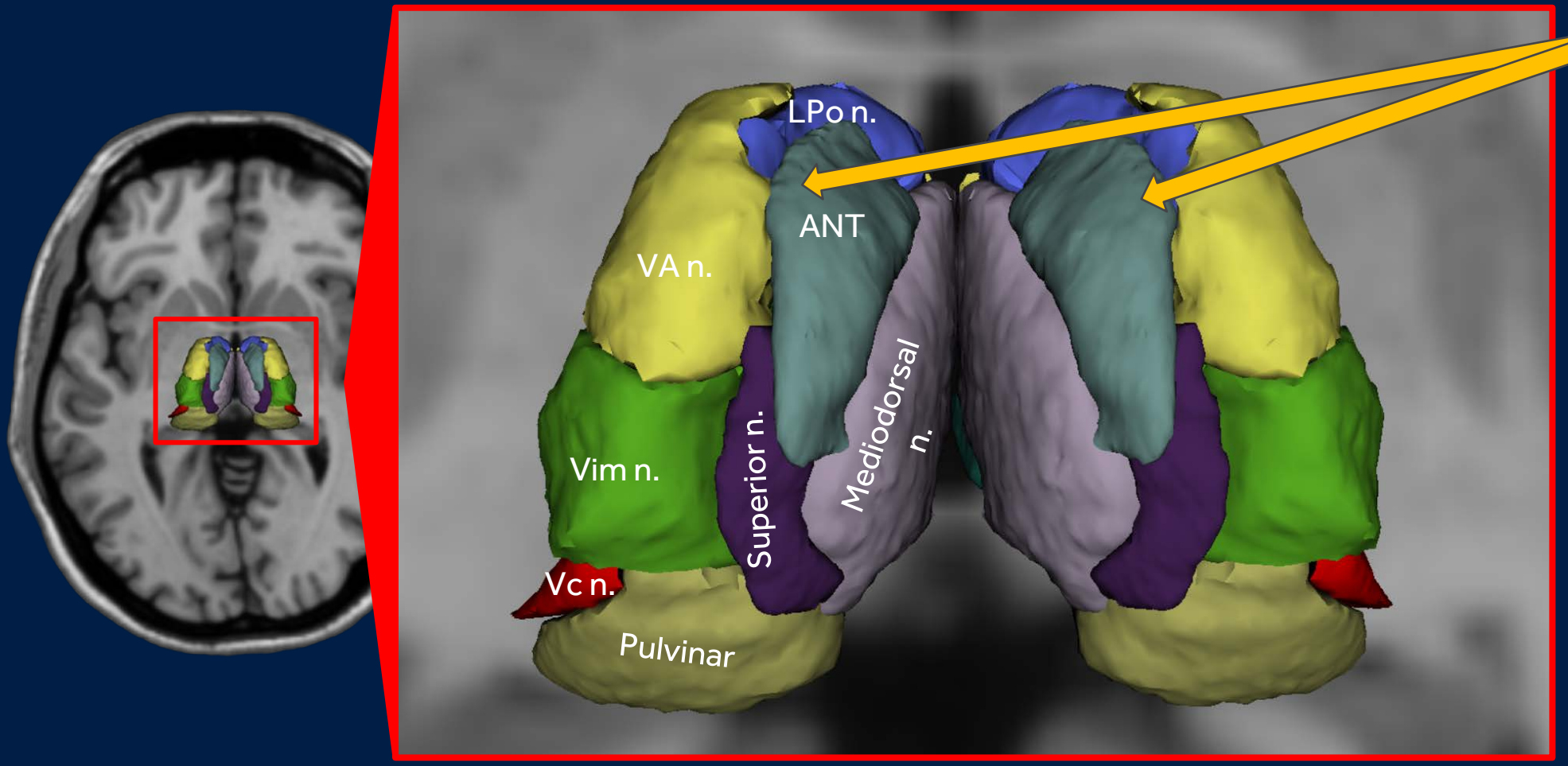
The Medtronic DBS System for Epilepsy has demonstrated safety and effectiveness for patients who average six or more seizures per month over the three most recent months prior to implant of the DBS system (with no more than 30 days between seizures). The Medtronic DBS System for Epilepsy has not been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

KEY SURGICAL CONSIDERATIONS FOR ANT DBS[1]

- 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)*

[1]*Medtronic SANTE Study*

ANATOMICAL LOCATION (AXIAL VIEW) & OUTPUT FIBERS



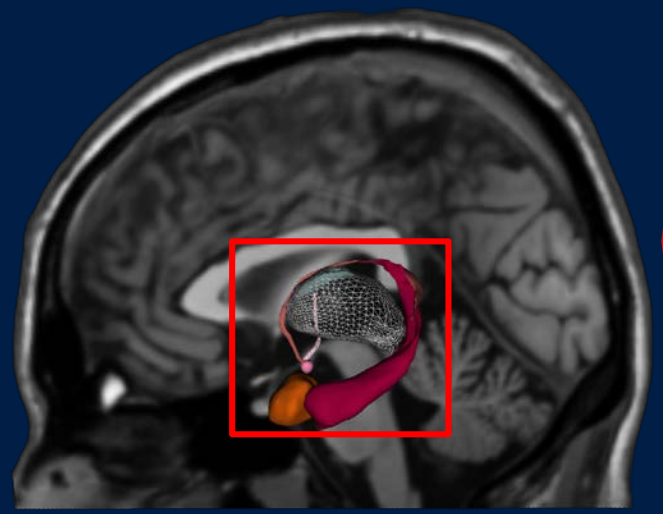
ANT OUTPUT:

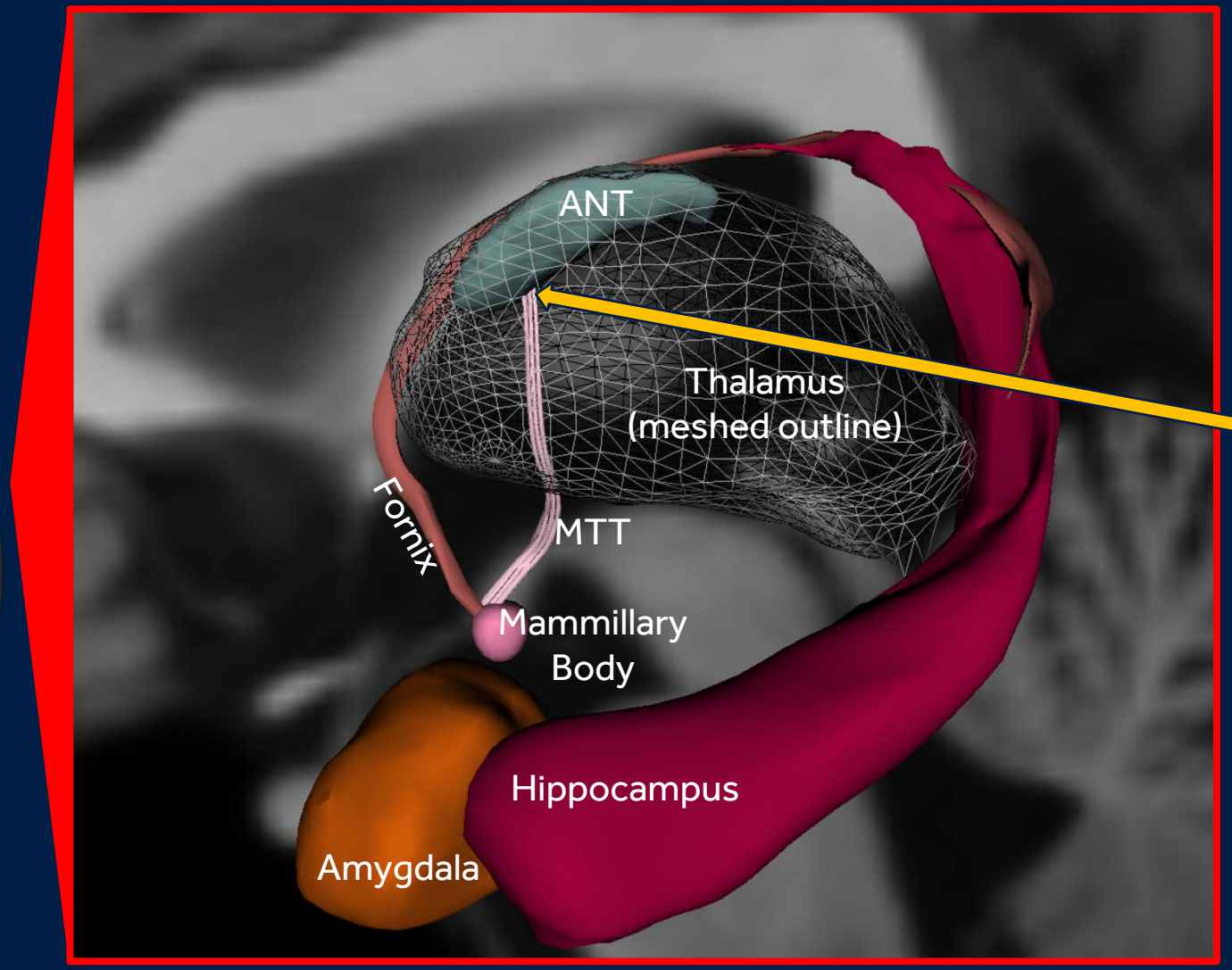
Anterior & lateral aspects via:

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

Finnis KW, Medtronic 3D DBS Simulator

ANATOMICAL LOCATION (SAGITTAL VIEW) & INPUT FIBERS





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

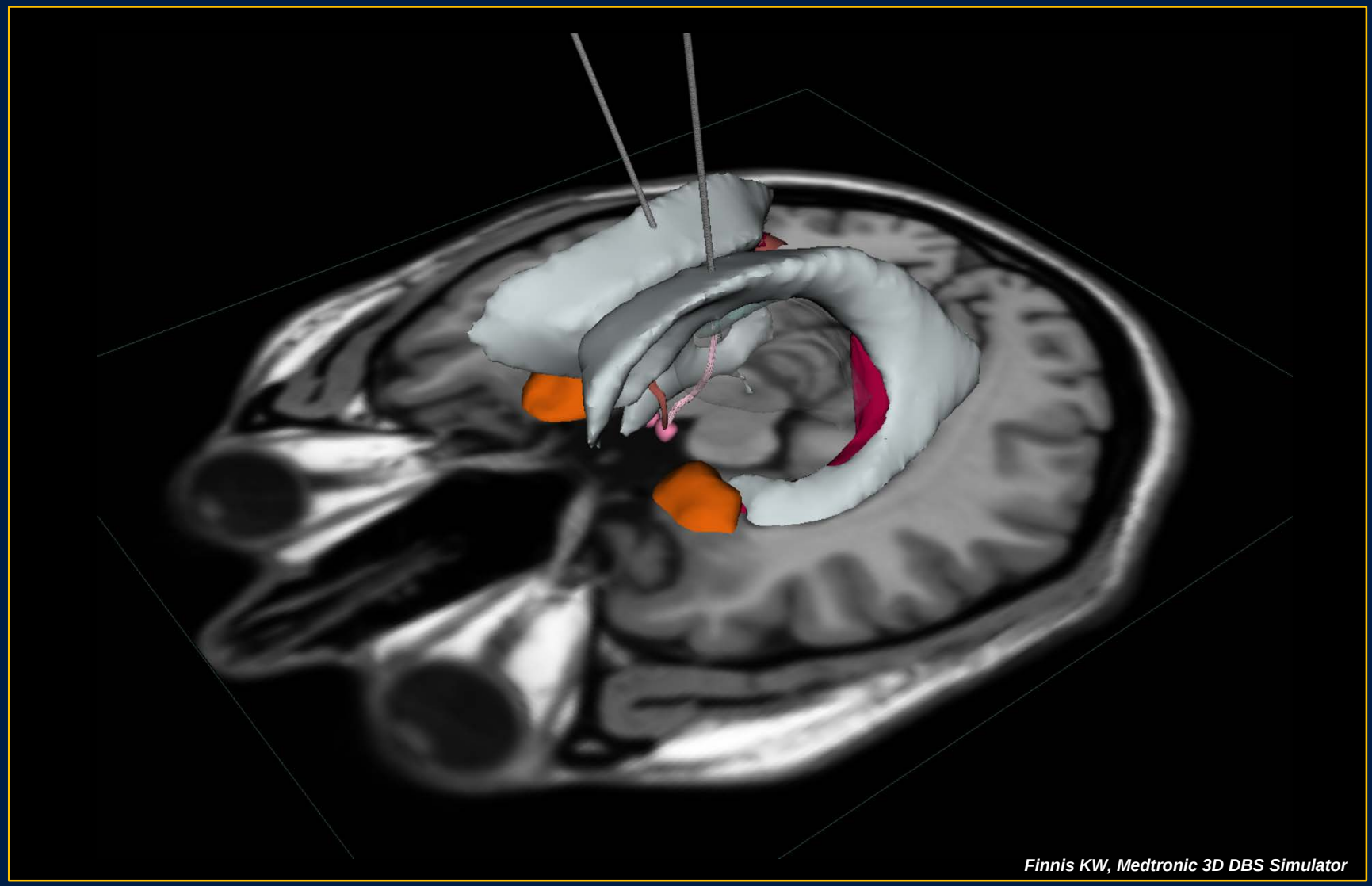
Finnis KW, Medtronic 3D DBS Simulator

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 variation[1]
- ANT may undergo significant and asymmetric atrophy in patients with medically-refractory epilepsy[2]



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[1]Mottonen et al, Neuroimage Clin. 2015;7:823-829
[2]Mueller et al, Epilepsia. 2010;51(8):1436-1445

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SURGICAL CONSIDERATIONS – PRE-OP IMAGING*

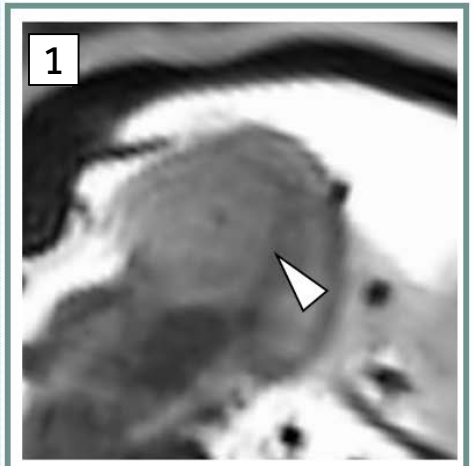


Figure 1.1: 3T STIR MRI. Sagittal view.
Arrowhead marks the MTT

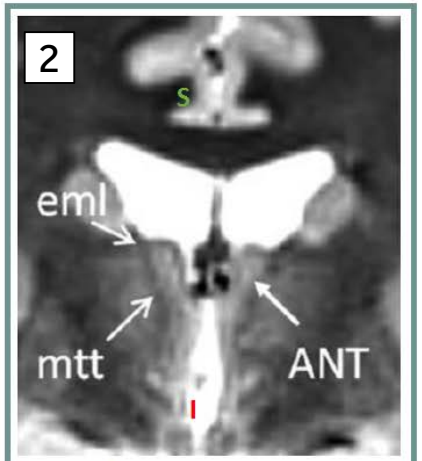


Figure 1.2: 1.5T STIR MRI. Coronal view

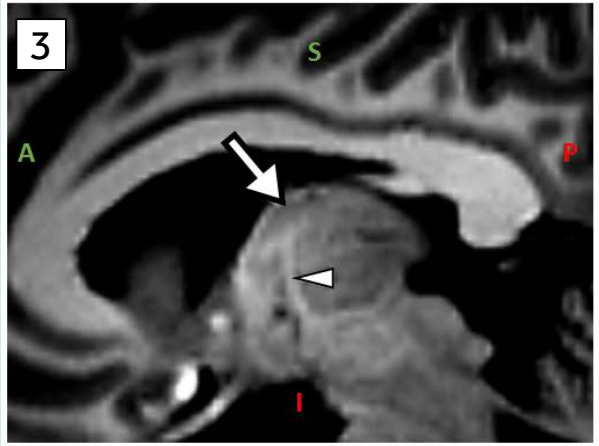


Figure 1.3: 3T MPRAGE MRI. Sagittal view.
Arrow marks the ANT. Arrowhead marks the MTT

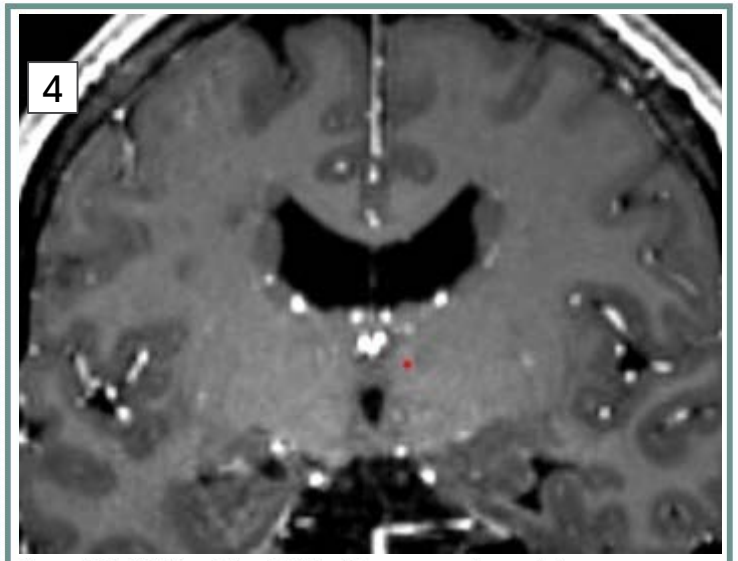


Figure 1.4: 3T T1-weighted MRI with contrast. Coronal view.
Red targeting dot placed within MTT

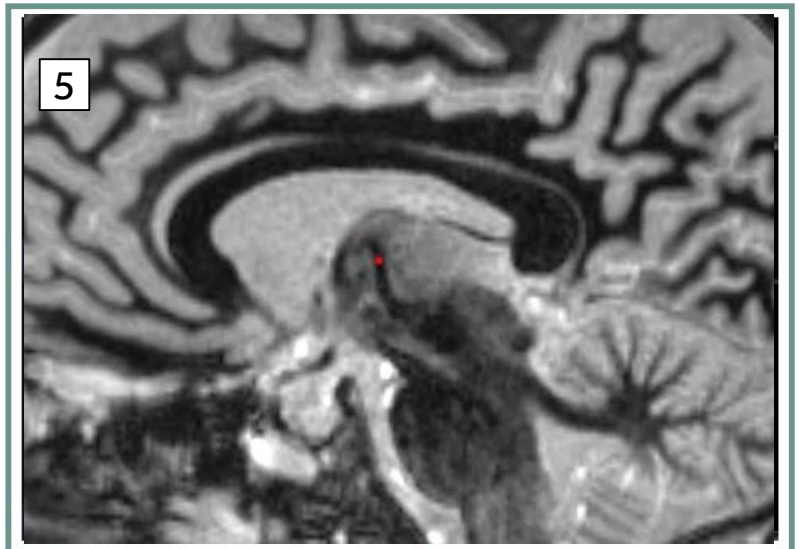


Figure 1.5: 3T FGATIR MRI.
Red targeting dot placed within MTT

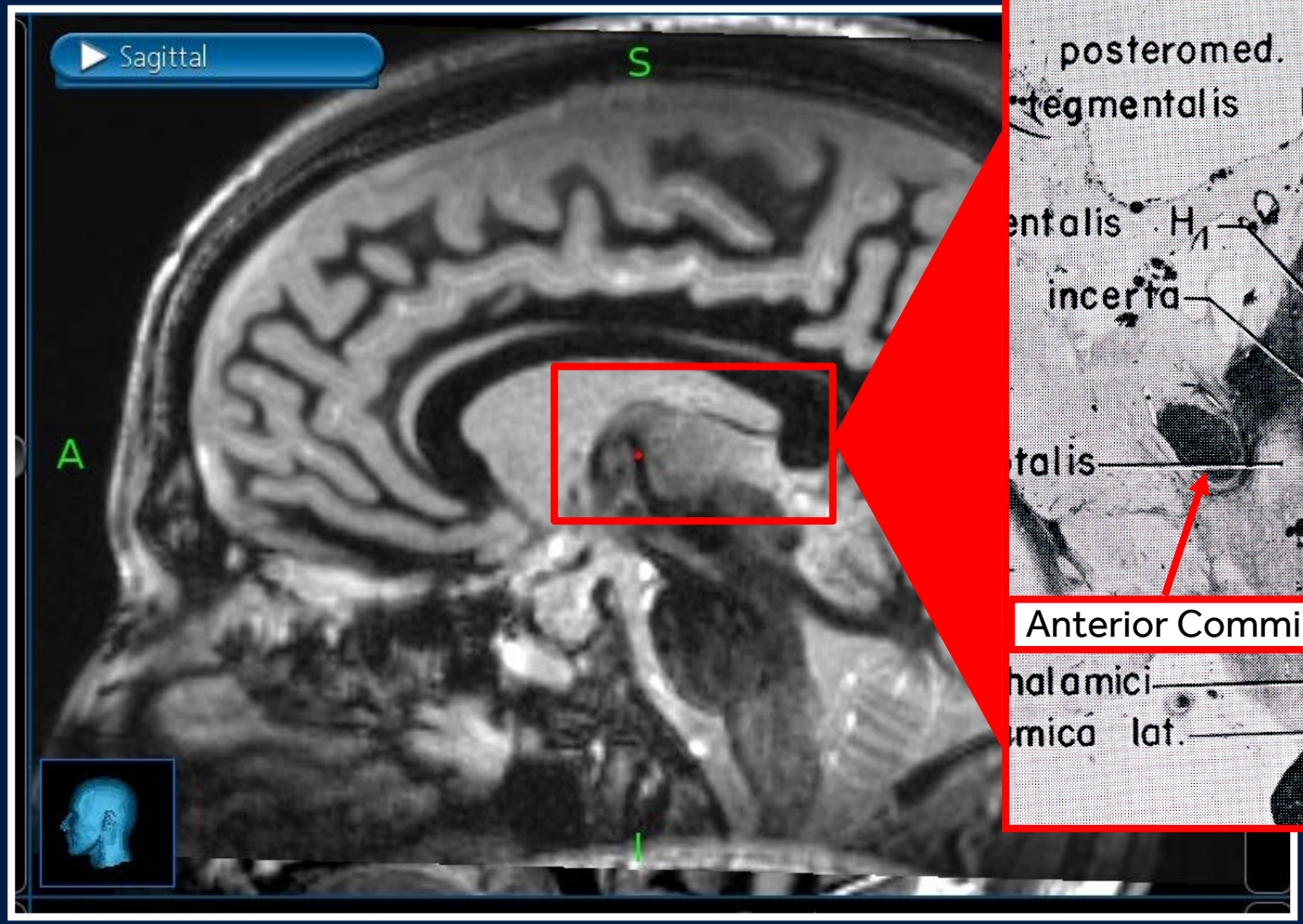
Visualize 4 key anatomical structures:

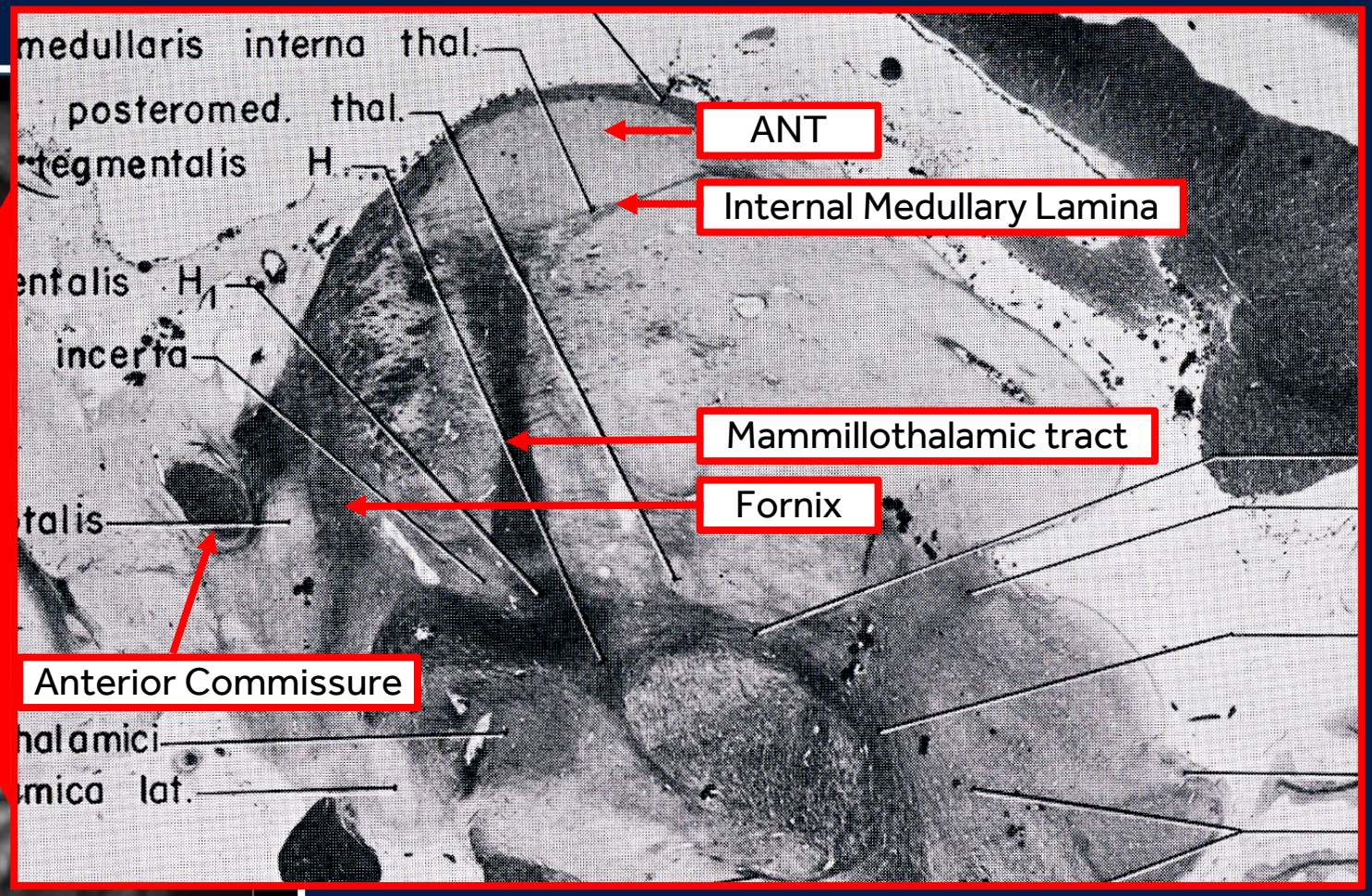
- ANT
- Mammillothalamic tract (MTT)
- Internal/external medullary lamina of thalamus (IML/EML)
- Surrounding veins

[1]*Lehtimaki et al, Brain Stim. 2016;9:268-275*
[2]*Jiltsova et al, Neuromodulation. 2016;19(8):812-817*
[3]*Buentjen 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

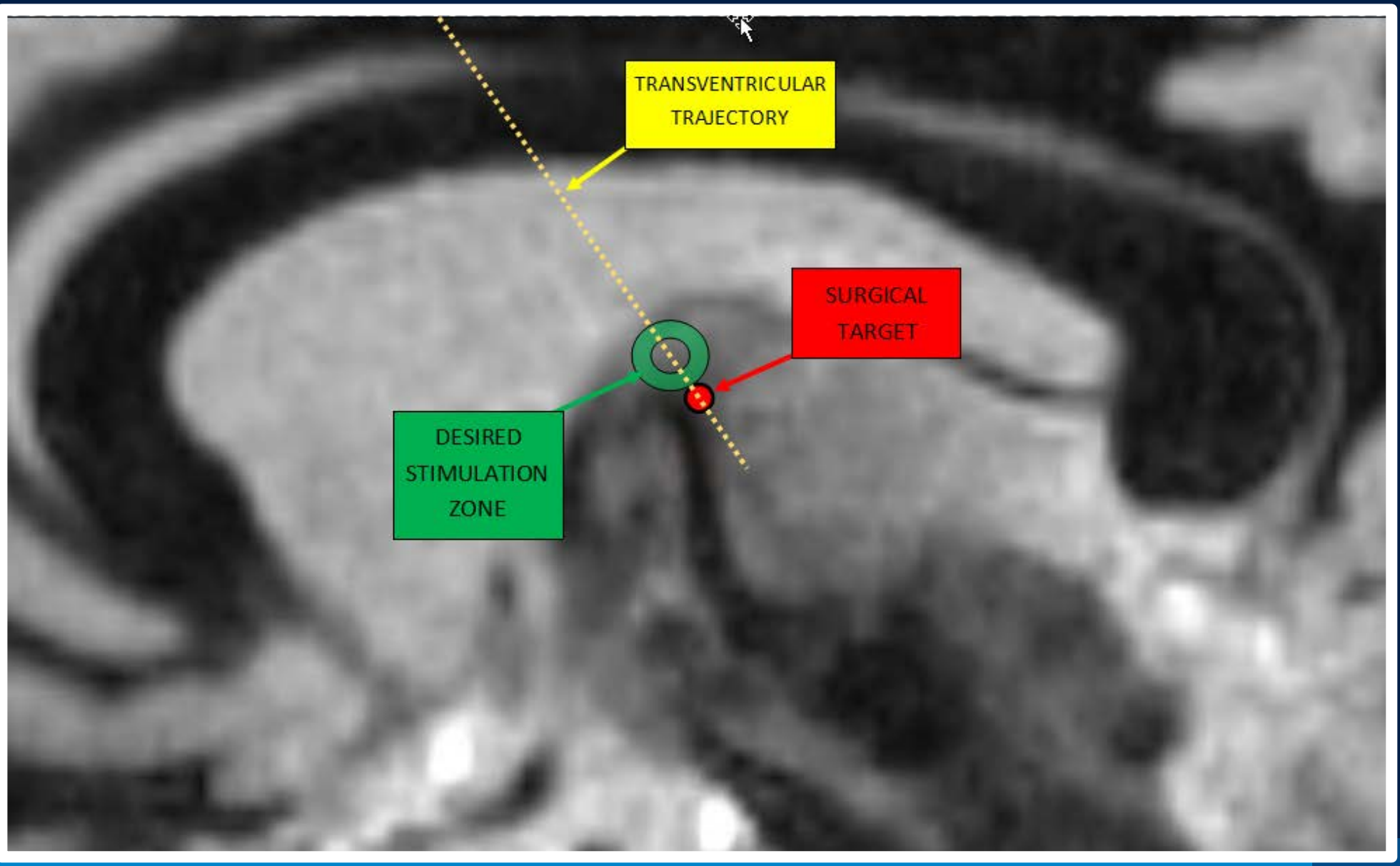




Myelin-stained sagittal section

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 – DIRECT TARGETING VS ACPC



Broad range of ACPC coordinates[1]

X = 5-6 mm lateral
Y = 0-2 mm anterior
Z = 10-12 mm superior

[1]*Medtronic SANTE Study*

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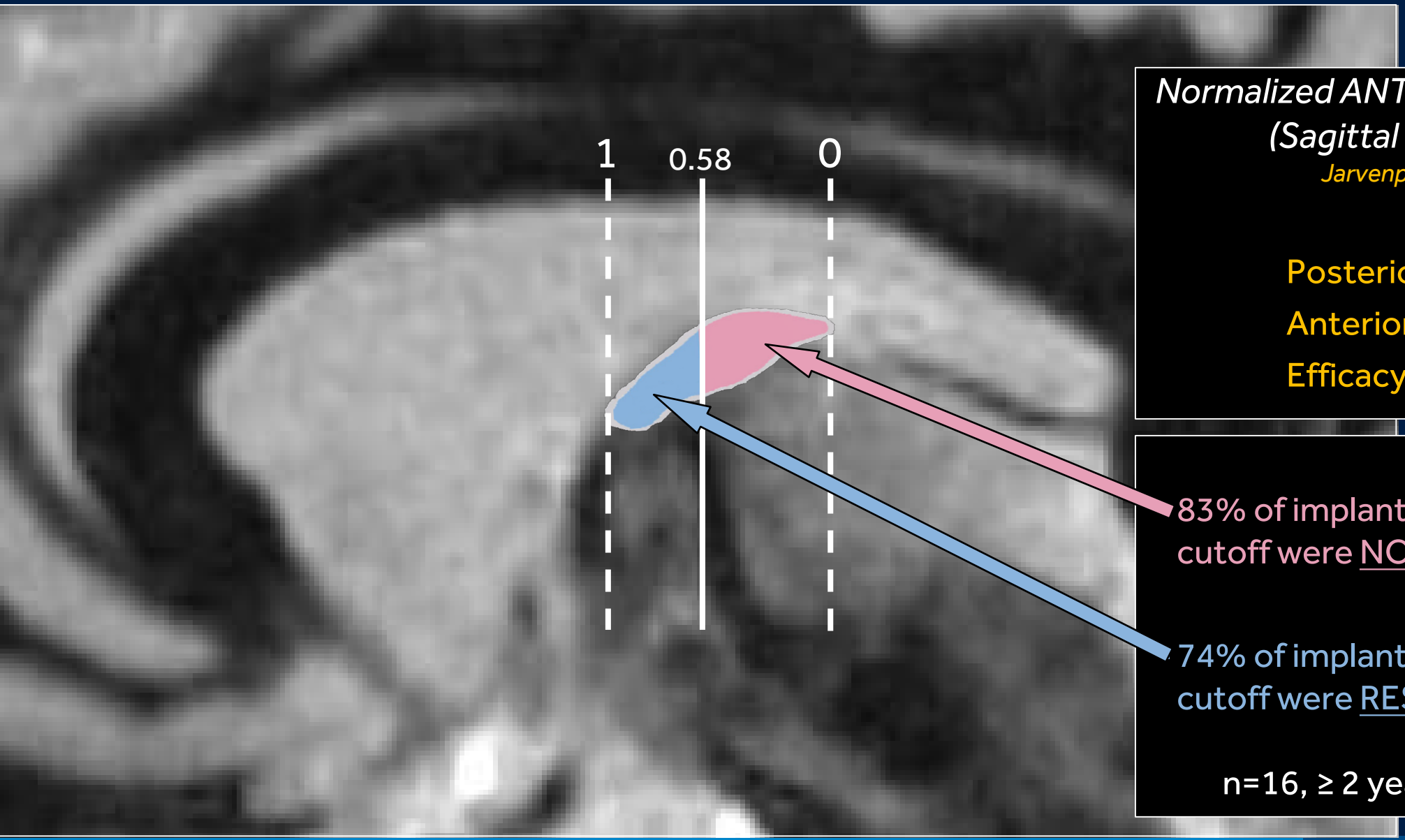
SURGICAL CONSIDERATIONS – DIRECT TARGETING



Normalized ANT Coordinate System (Sagittal Orientation):
Jarvenpaa et al, 2018

Posterior border = 0
Anterior border = 1
Efficacy cutoff = 0.58

83% of implants posterior to the cutoff were NONRESPONDERS

74% of implants anterior to the cutoff were RESPONDERS

n=16, ≥ 2 years of follow-up

Jarvenpaa et al. Front Neurol. 2018;9(May):1-8

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SURGICAL CONSIDERATIONS – TRAJECTORY

Based on 73 implants[1]:

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

vs

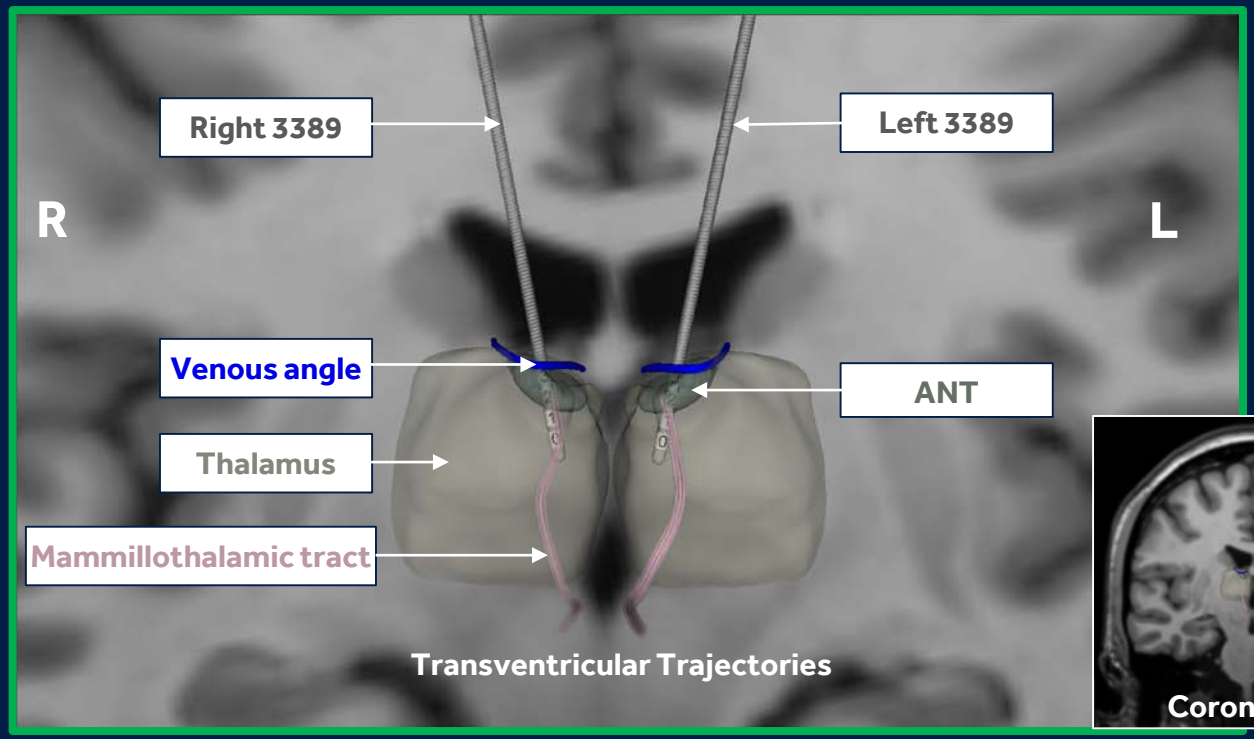
71% of extraventricular trajectories had at least ONE contact in ANT

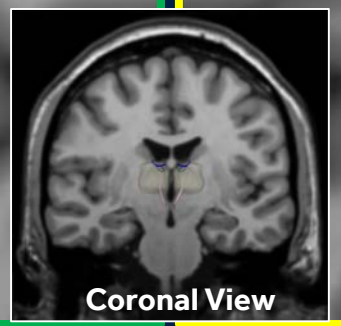
The success rate for placing at least 1 contact in ANT bilaterally:

84% Transventricular

vs

58% Extraventricular





[1]*Lehtimaki K et al, Neurosurgery 2018, Mar 15*

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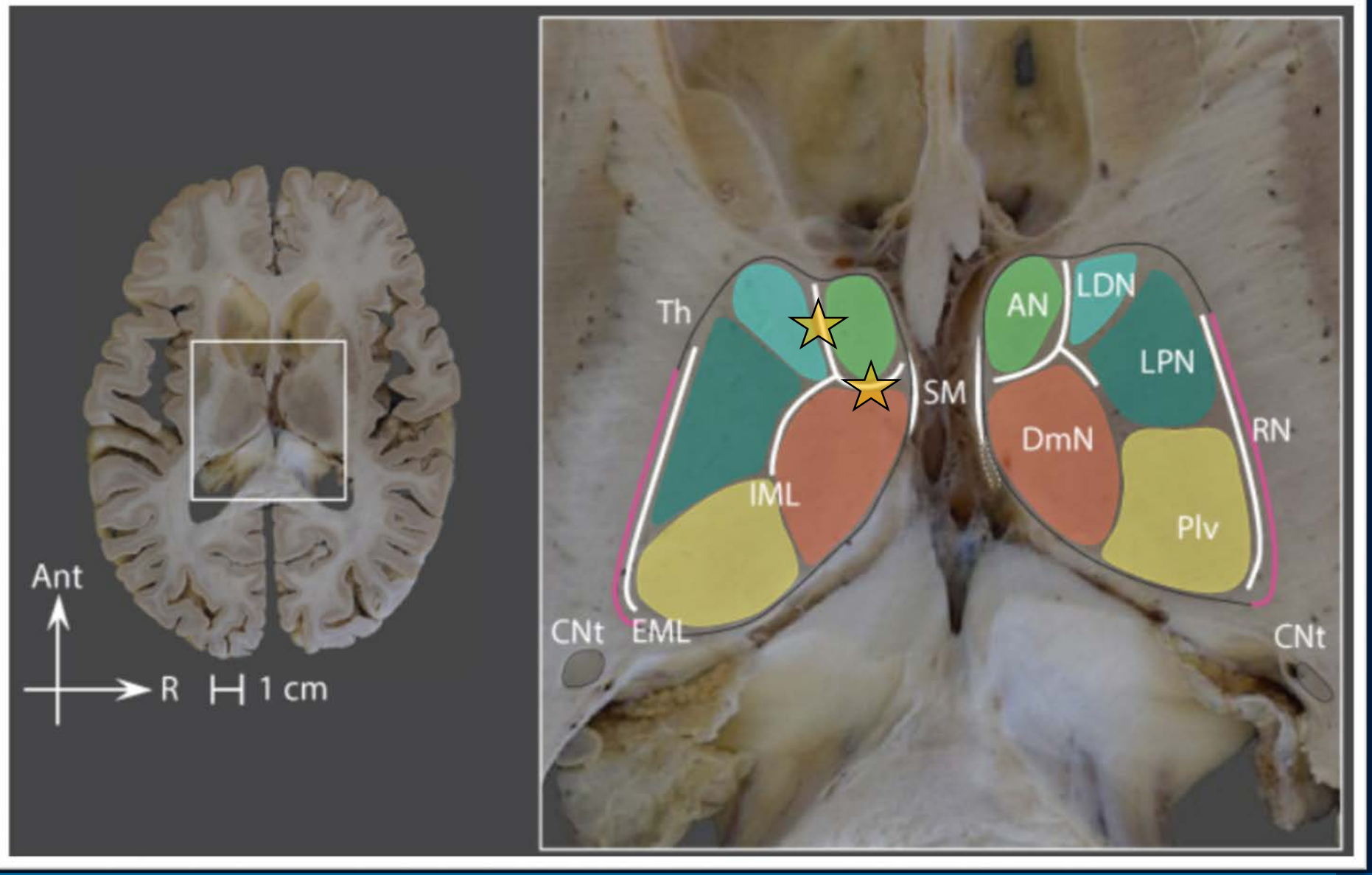
SURGICAL CONSIDERATIONS – WHITE MATTER LAMINA



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*

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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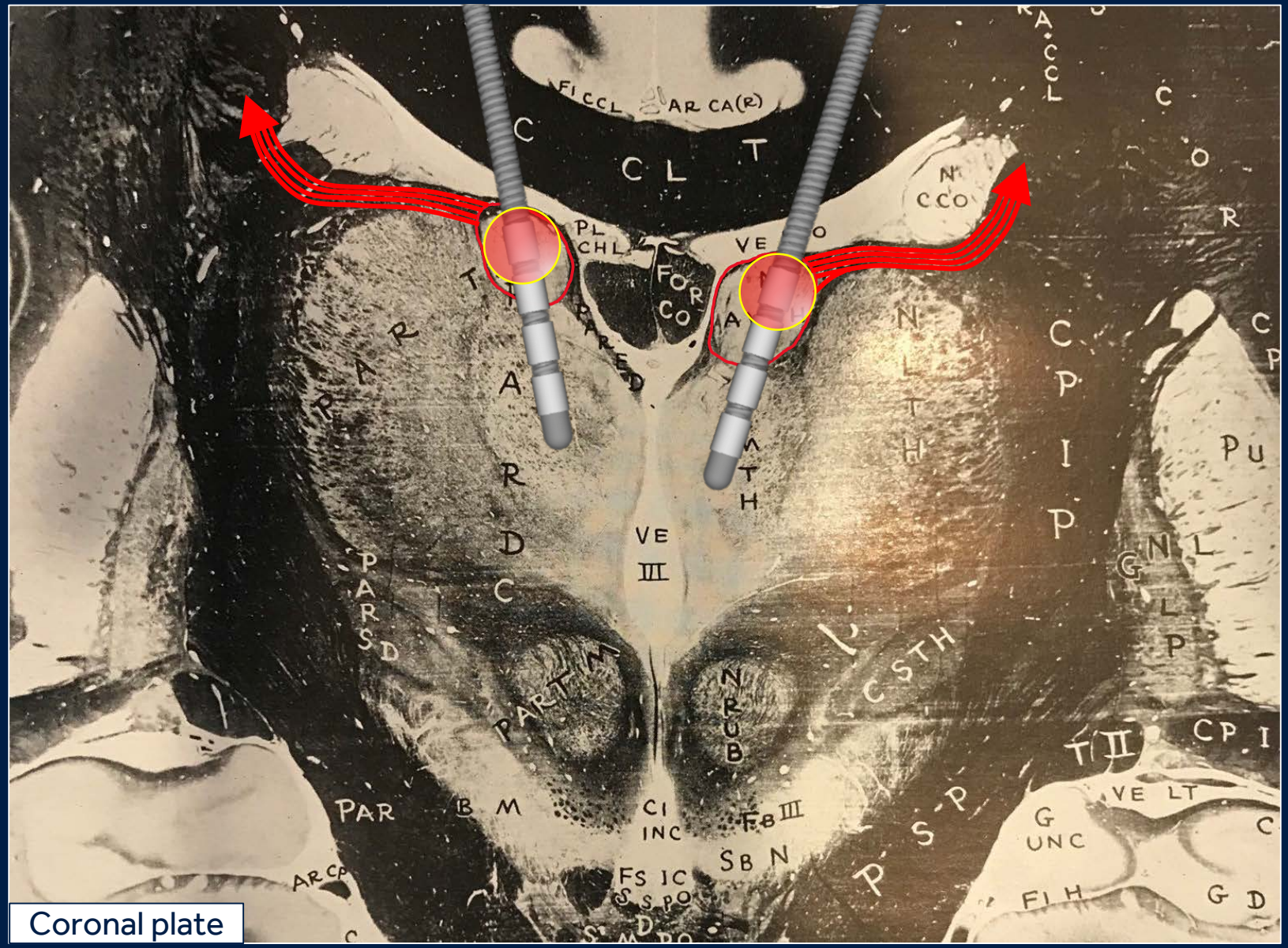
SURGICAL CONSIDERATIONS – ANT EFFERENT PATHWAY



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

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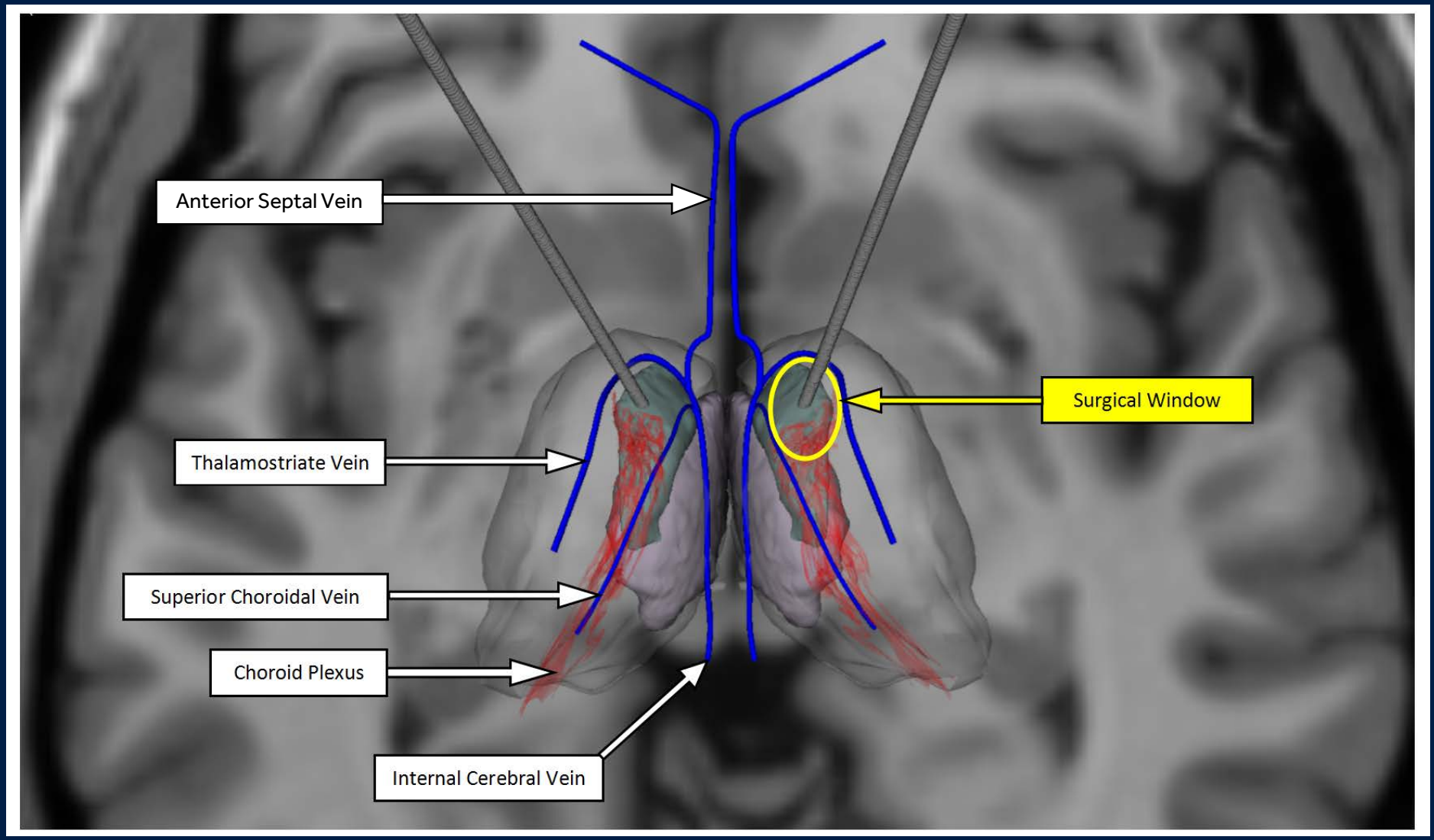
SURGICAL CONSIDERATIONS – VASCULATURE



Axial View (superior aspect)

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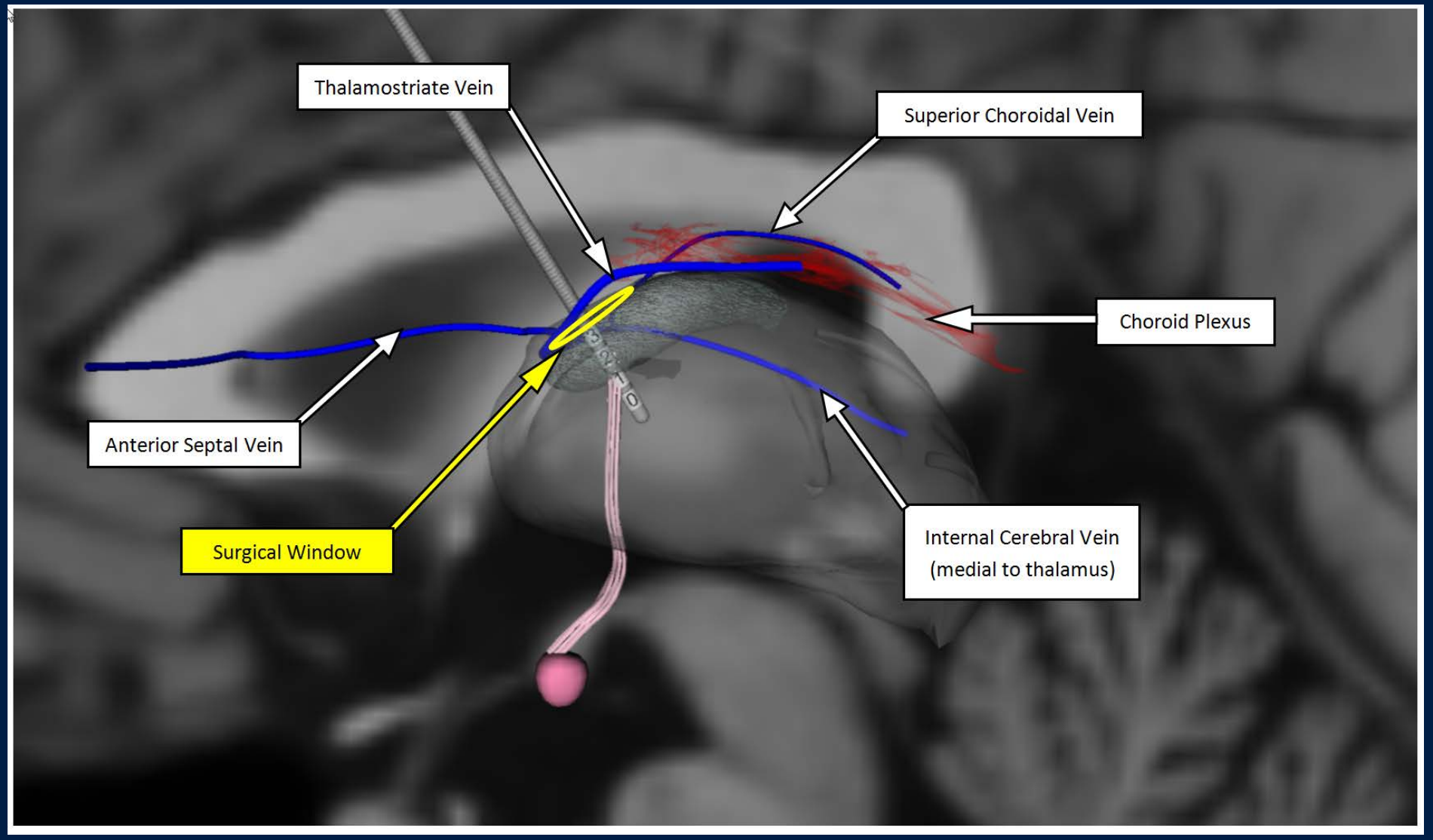
SURGICAL CONSIDERATIONS – VASCULATURE



Sagittal View (lateral aspect)

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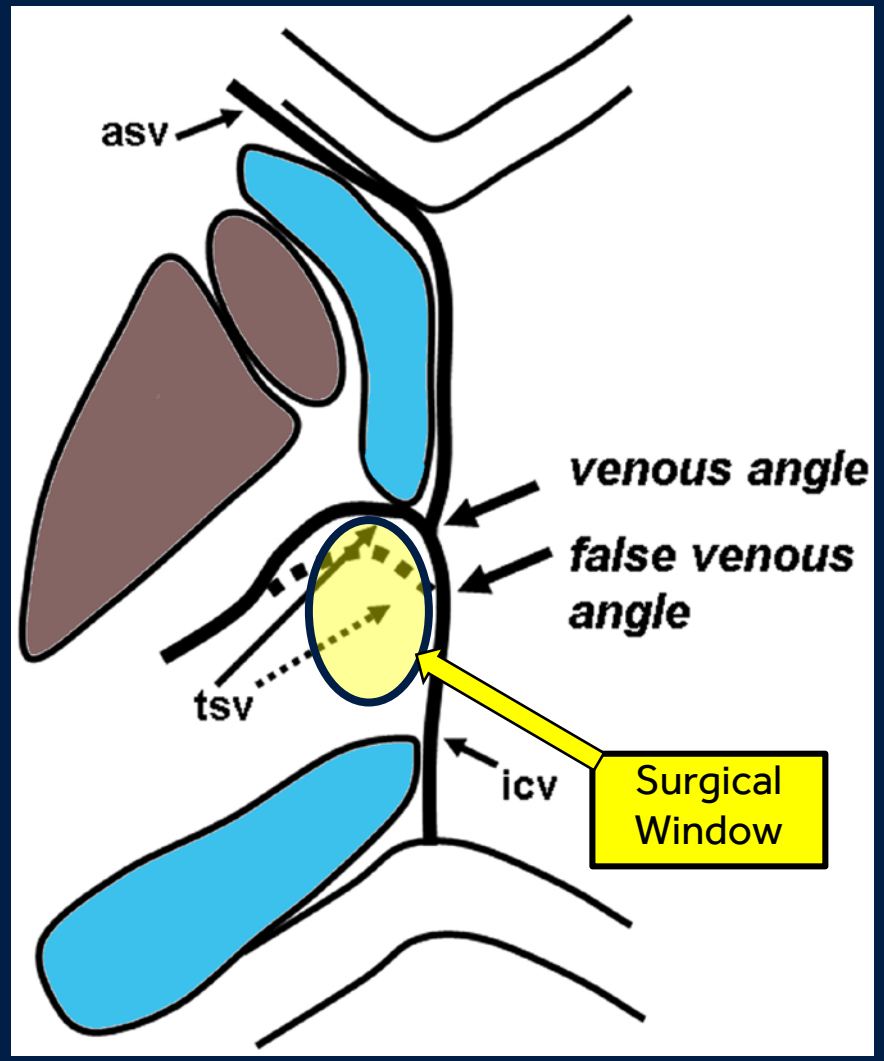
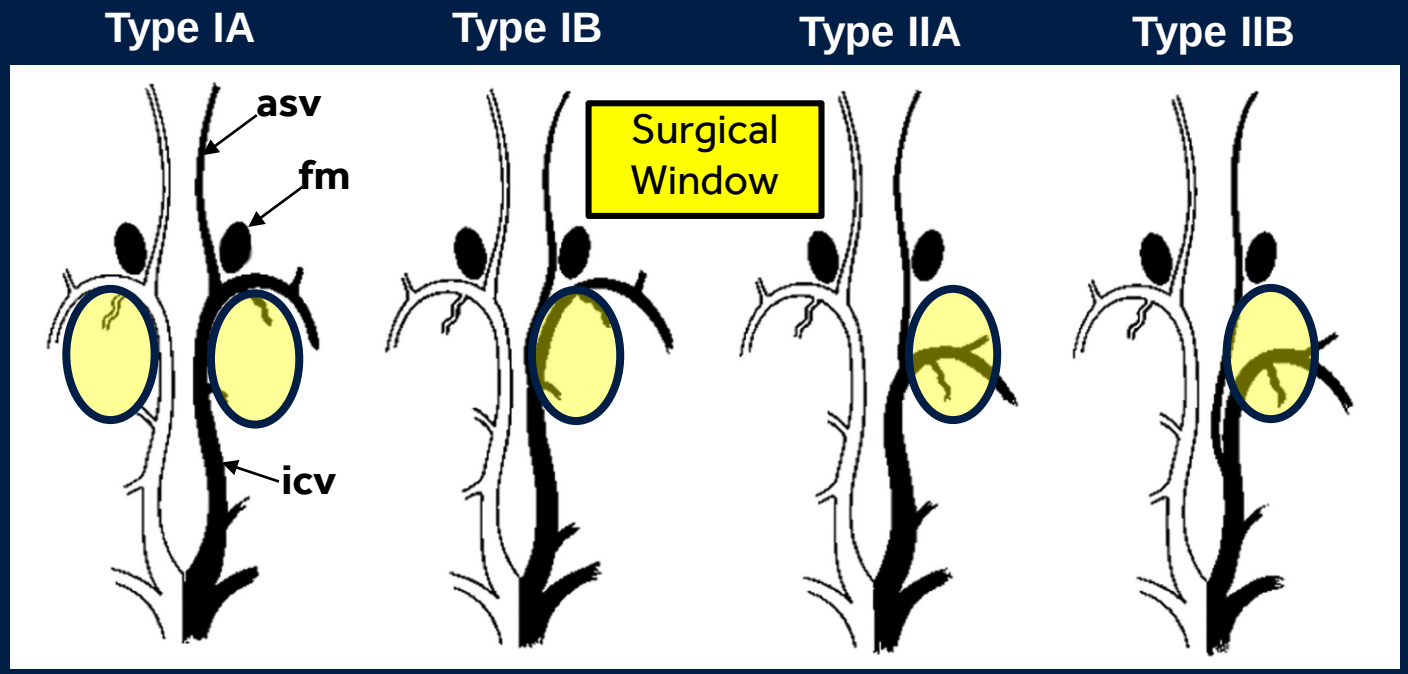
SURGICAL CONSIDERATIONS – VENOUS VARIABILITY



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)

Fuju et al. AJNR. 2010;31:55-59

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REPRESENTATIVE SURGICAL PLAN

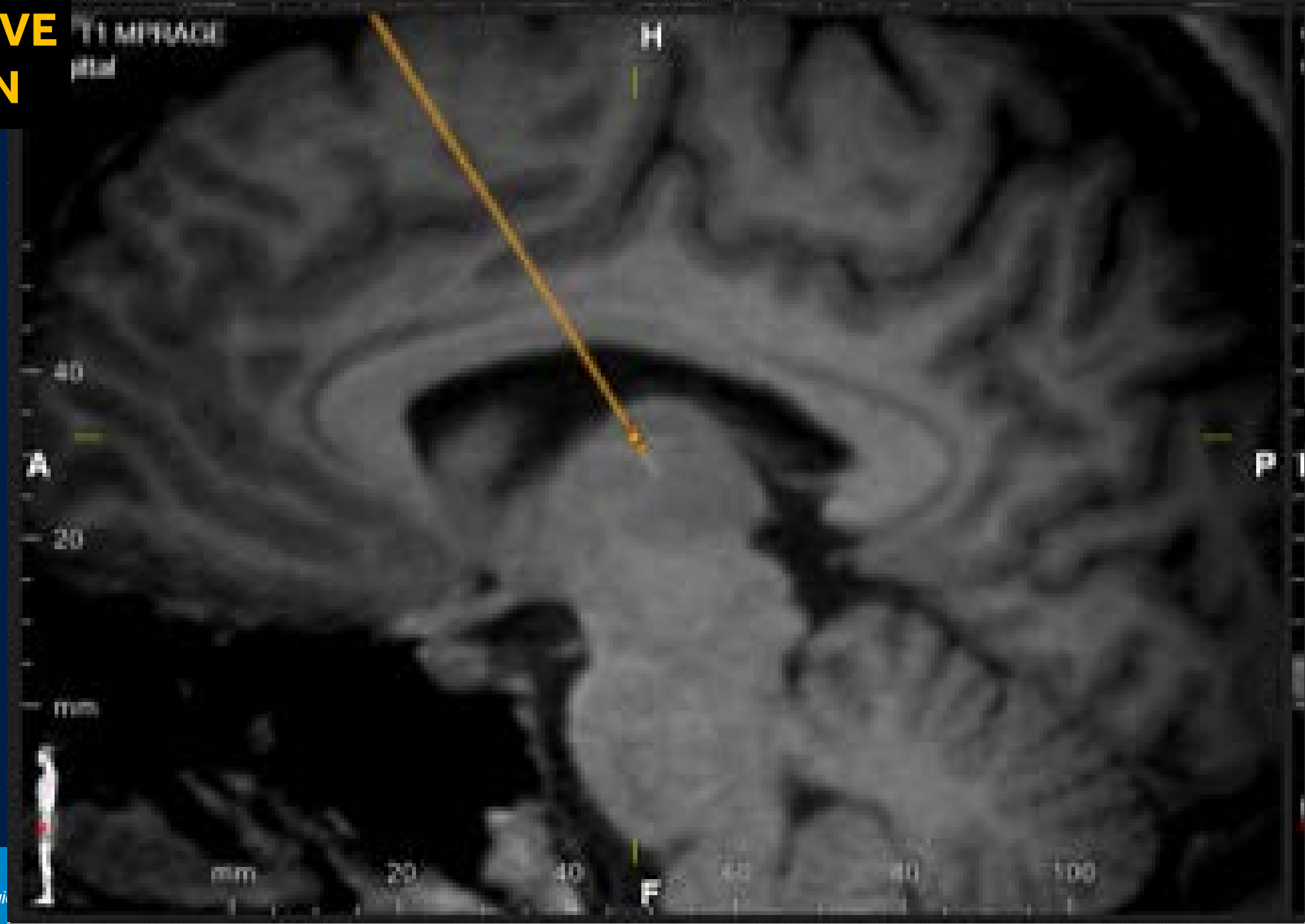
Planes centered at contact 2

LH

3389

MPRAGE image

Image Courtesy of Dr. A Bari, UCLA



REPRESENTATIVE SURGICAL PLAN

Planes centered at contact 3

LH

3389

T1 w/c image

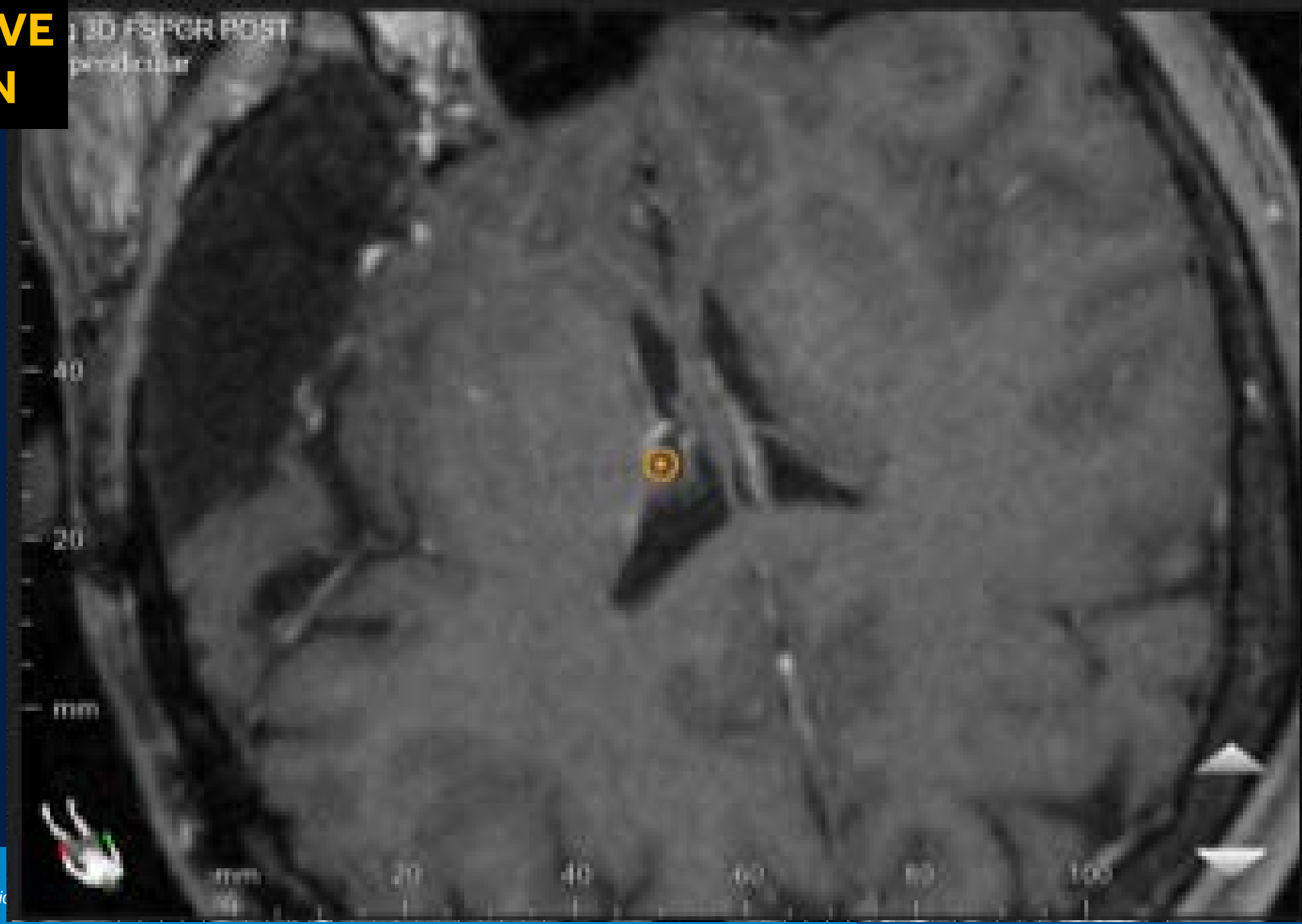


Image Courtesy of Dr. A Bari, UCLA

REPRESENTATIVE SURGICAL PLAN

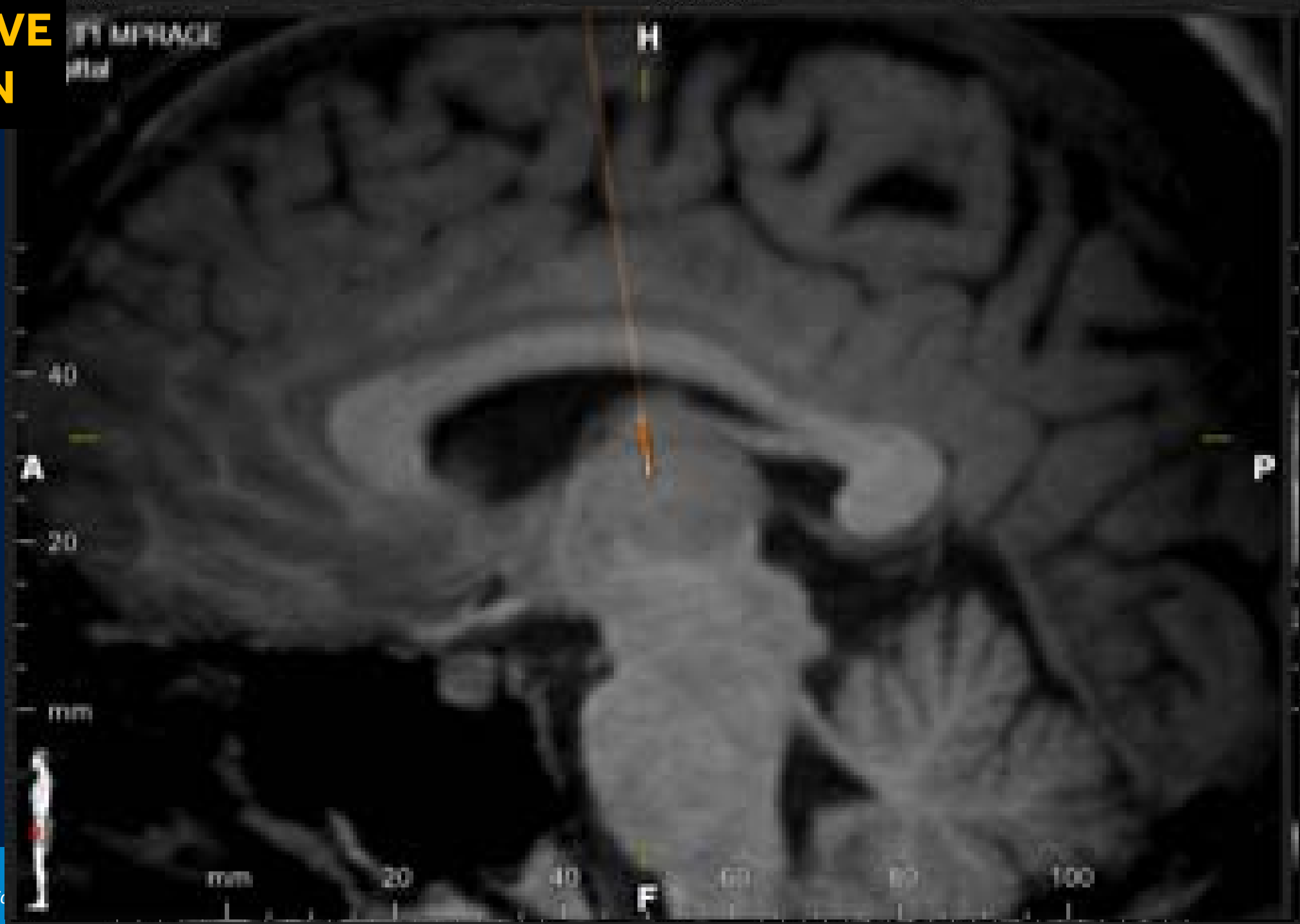
Planes centered at contact 2

RH

3389

MPRAGE

Image Courtesy of Dr. A Bari, UCLA



REPRESENTATIVE SURGICAL PLAN

Planes centered at contact 3

RH

3389

T1 w/c

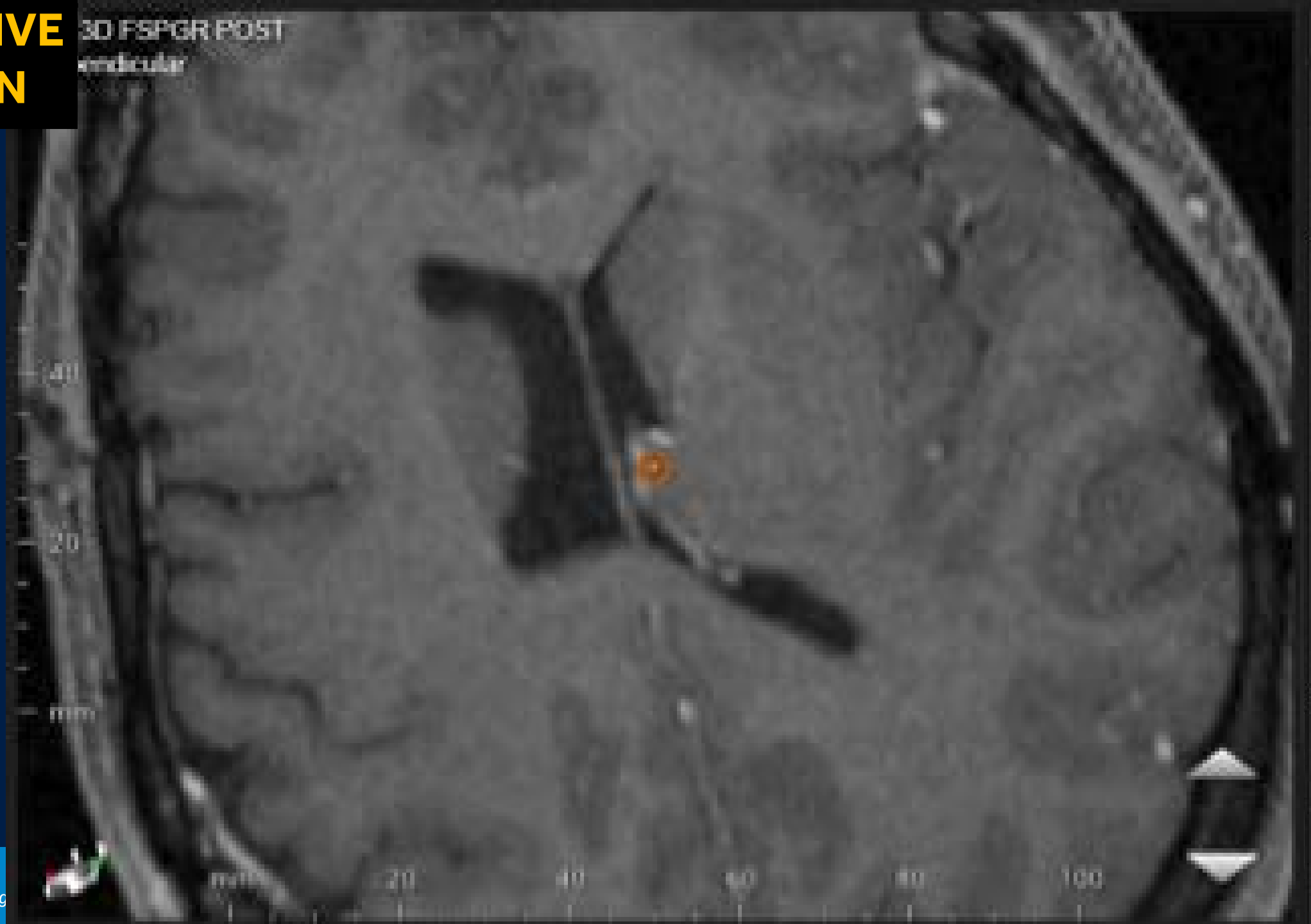
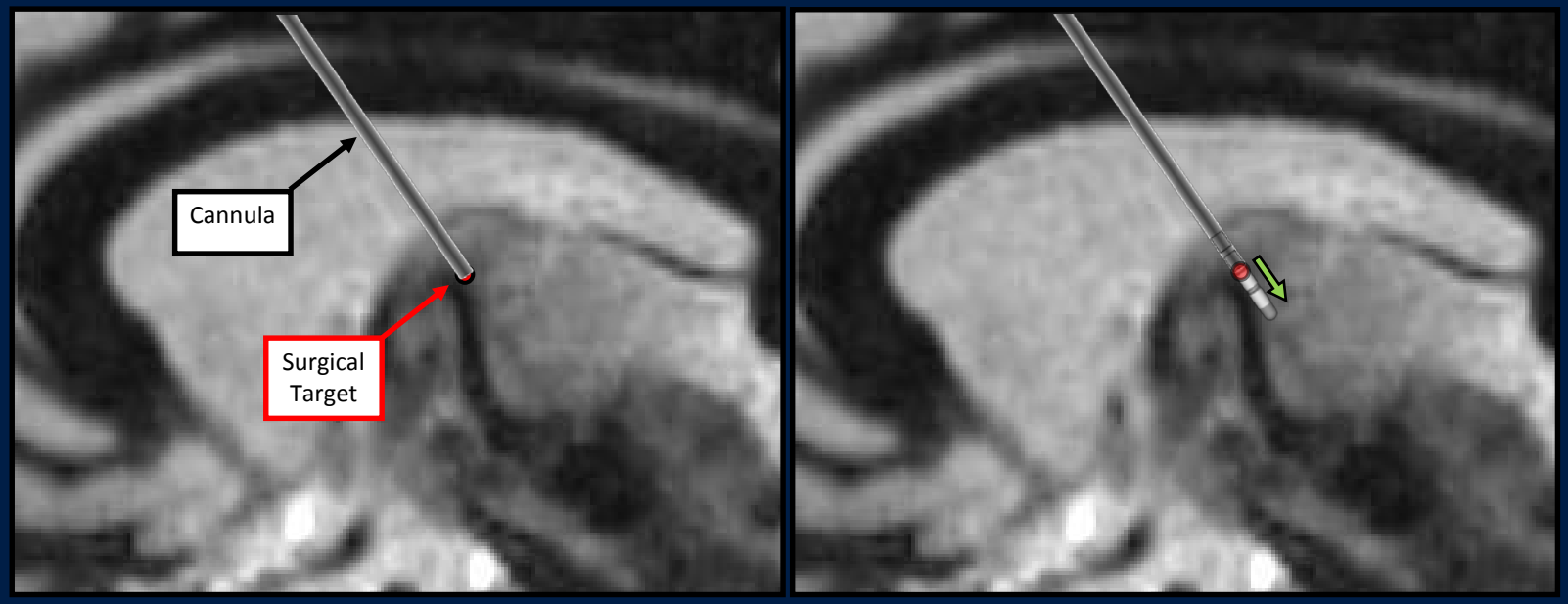


Image Courtesy of Dr. A Bari, UCLA

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.

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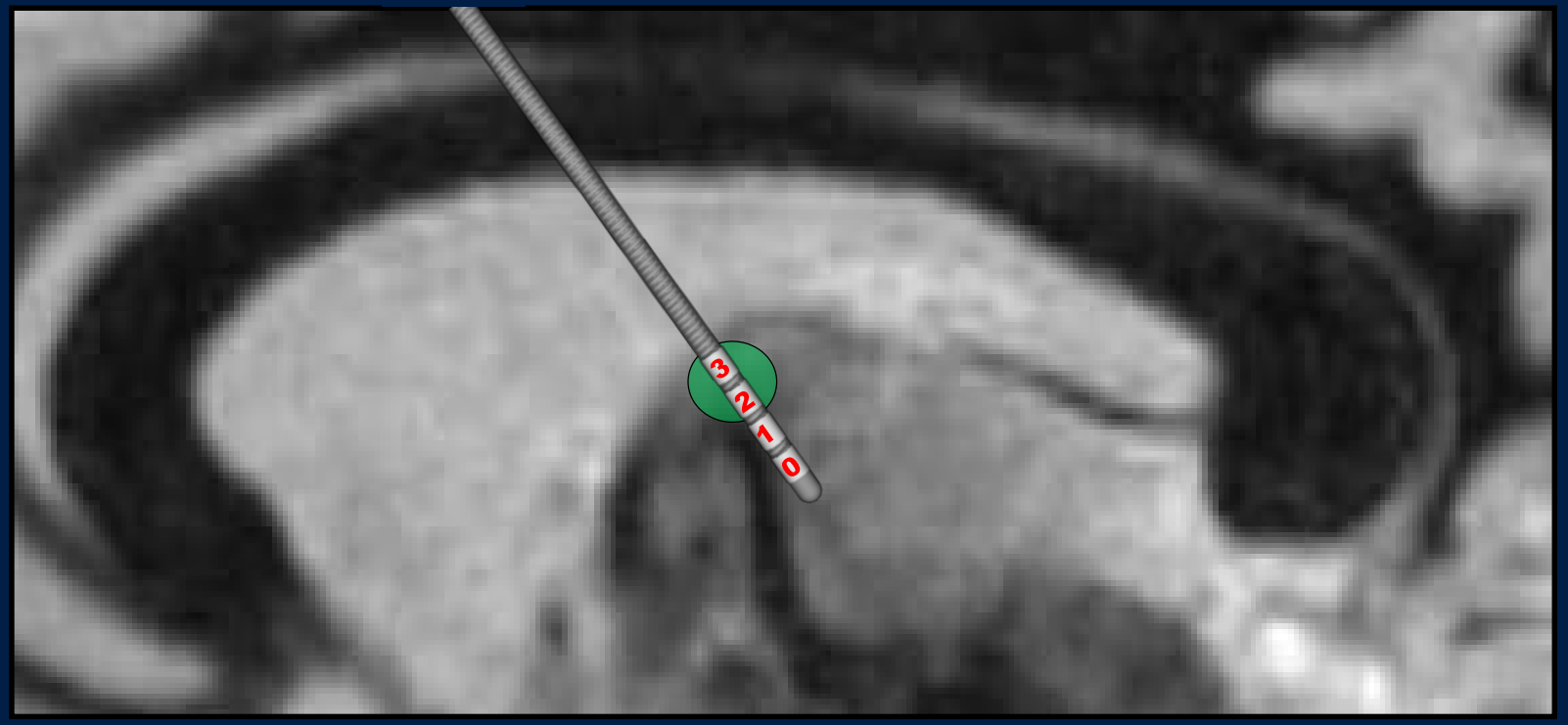
SURGICAL CONSIDERATIONS – CONTACT PLACEMENT



- 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.

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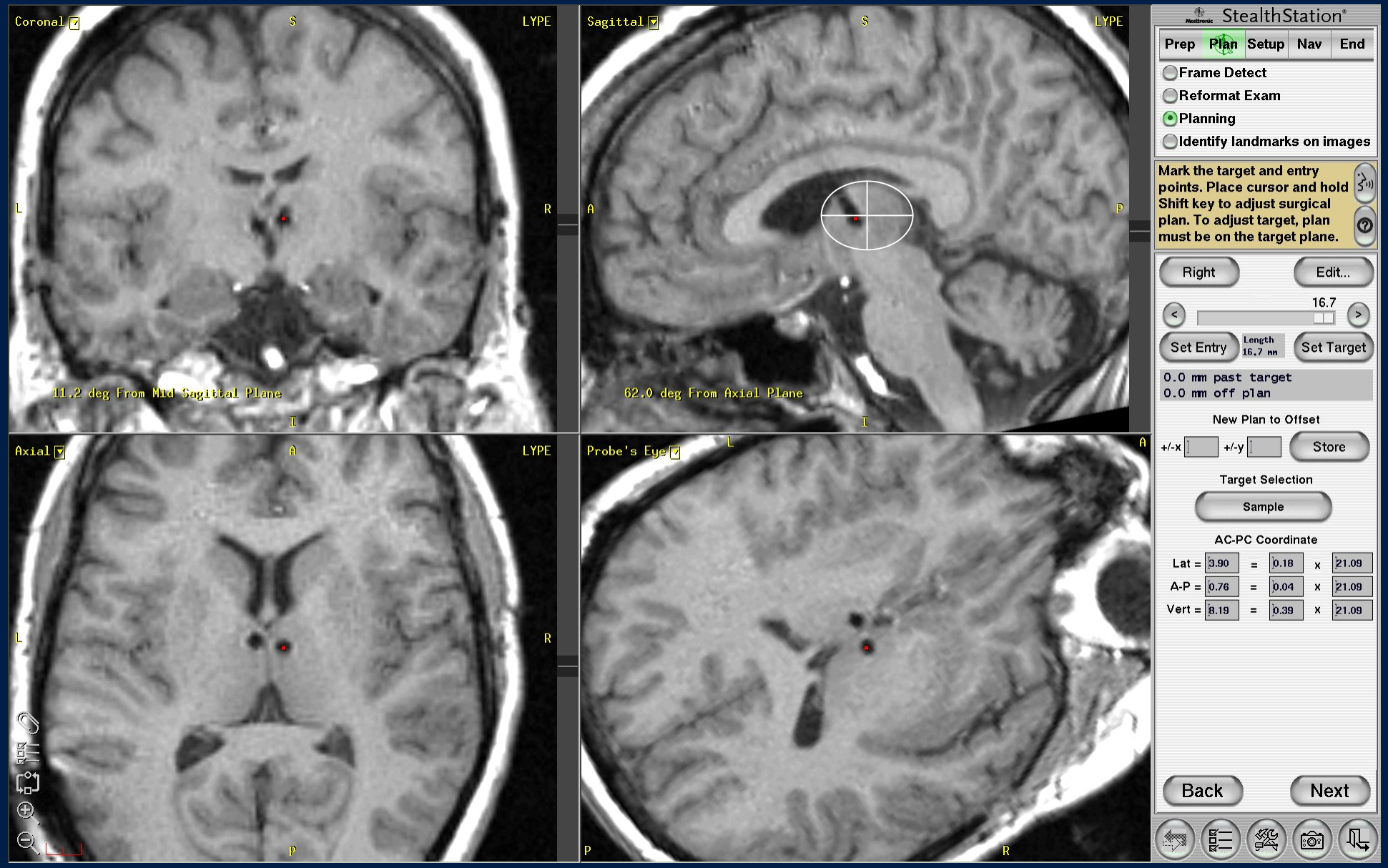
LEAD PLACEMENT EXAMPLES

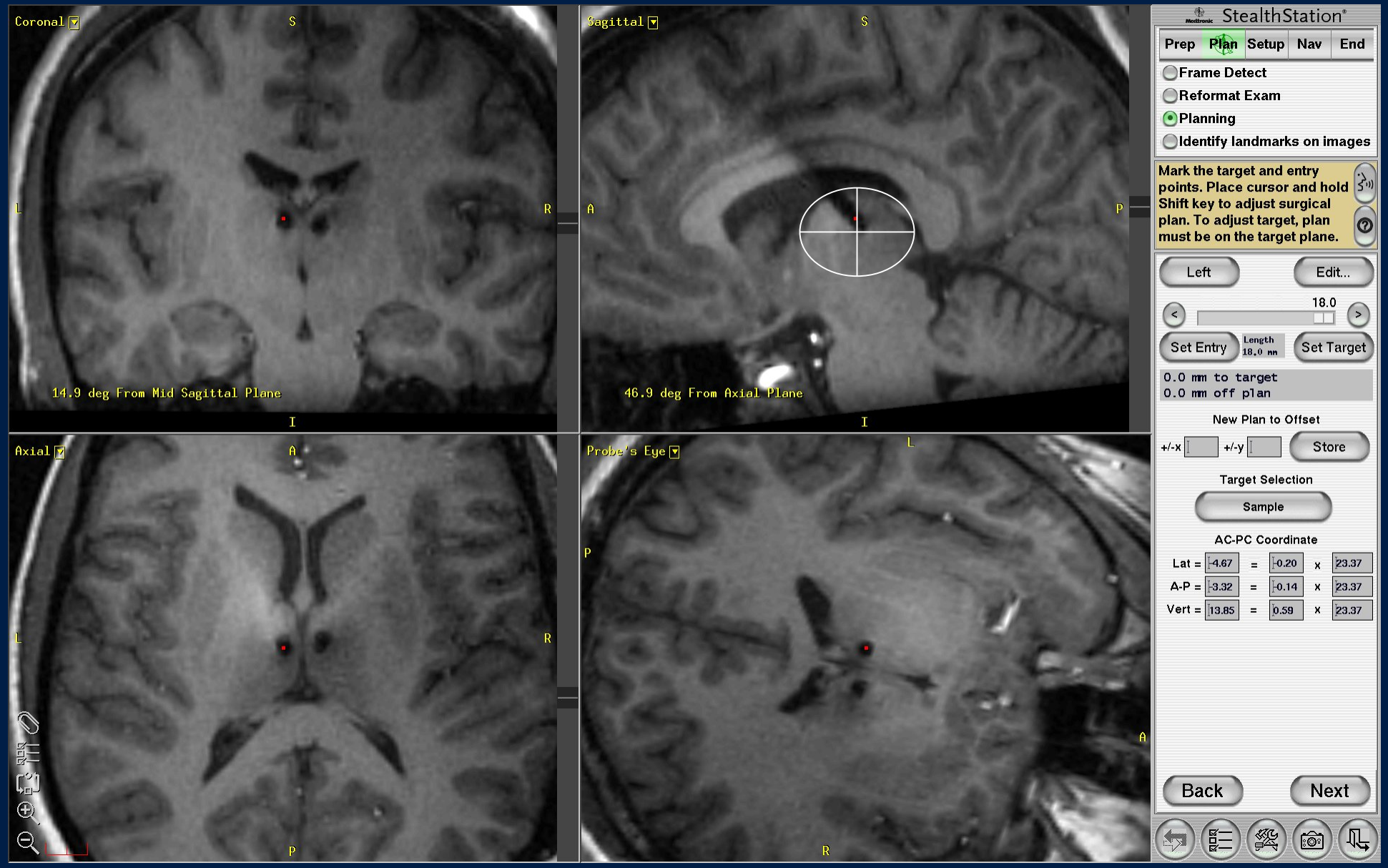
(POST-OP MRI*, SANTE STUDY)

* See *Guidelines for Medtronic deep brain stimulation systems* for more information

GOOD PLACEMENT



SLIGHT POSTERIOR



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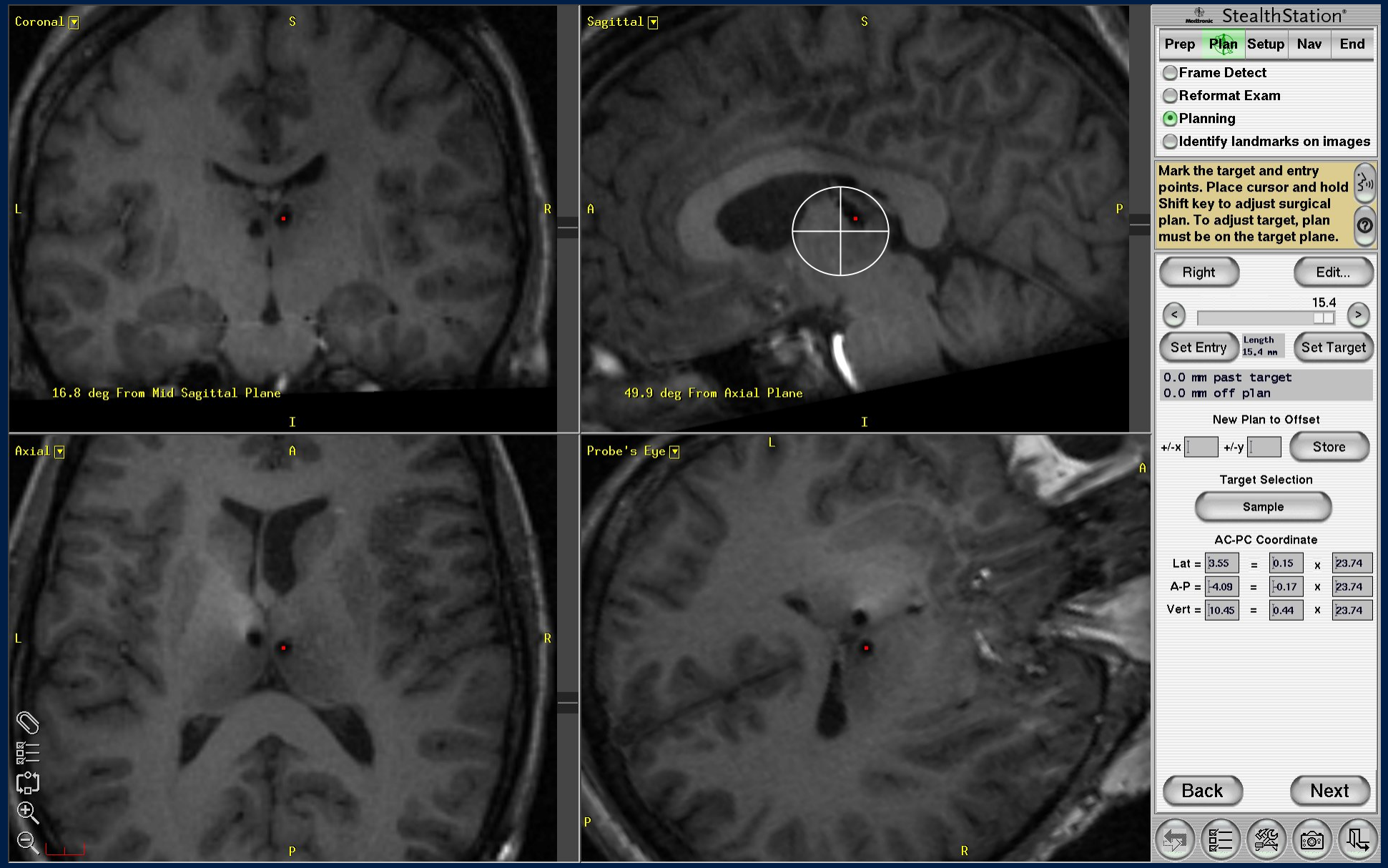
POSTERIOR


Coronal
S
L
R
I
16.8 deg From Mid Sagittal Plane
Sagittal
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49.9 deg From Axial Plane
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Probe's Eye
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R
StealthStation
Prep
Plan
Setup
Nav
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Frame Detect
Reformat Exam
Planning
Identify landmarks on images
Mark the target and entry points. Place cursor and hold Shift key to adjust surgical plan. To adjust target, plan must be on the target plane.
Right
Edit...
15.4
Set Entry
Length
15.4 mm
Set Target
0.0 mm past target
0.0 mm off plan
New Plan to Offset
+/-x
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Target Selection
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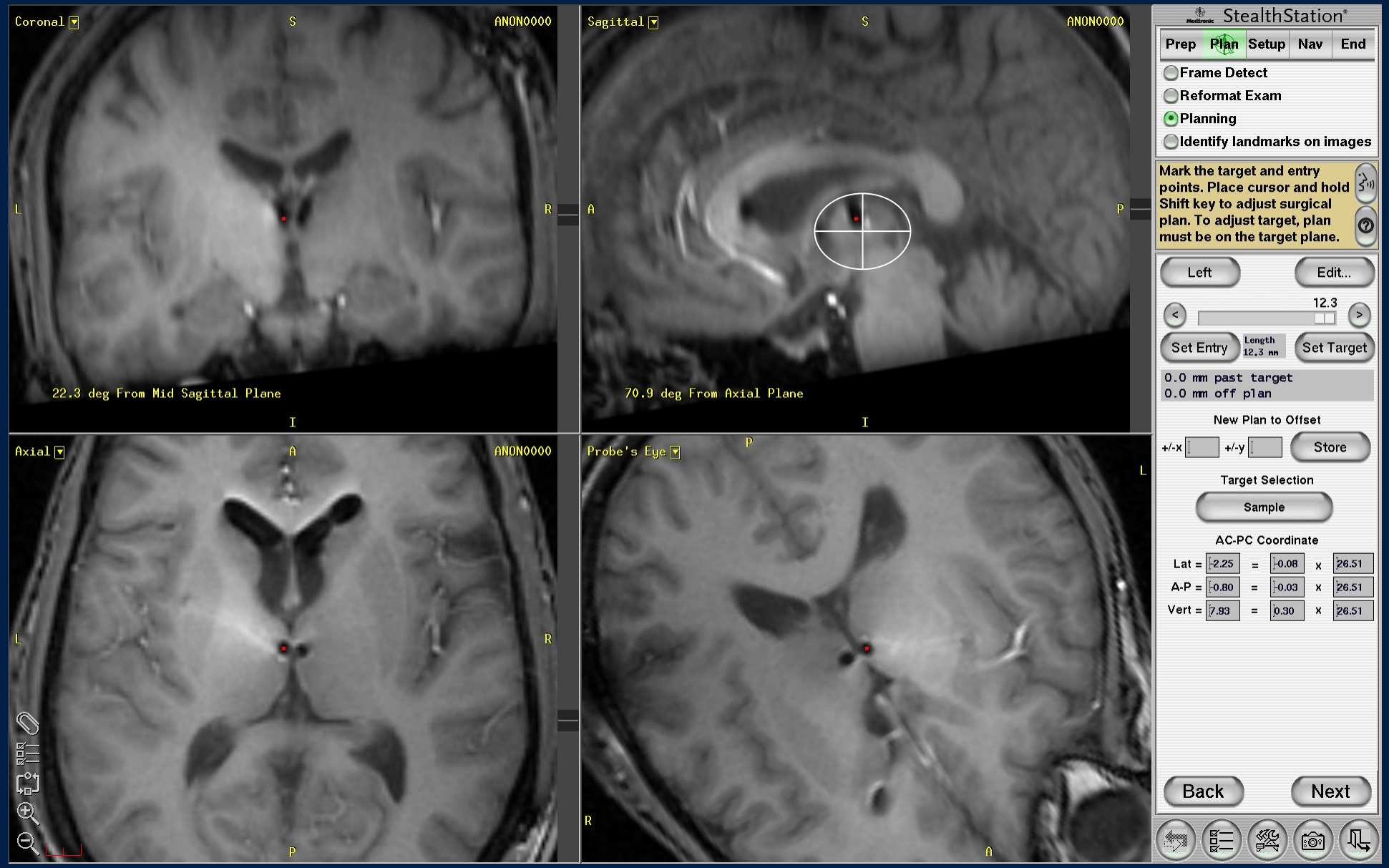
AC-PC Coordinate
Lat = 3.55 = 0.15 x 23.74
A-P = -4.09 = -0.17 x 23.74
Vert = 10.45 = 0.44 x 23.74
Back
Next

MEDIAL


Coronal
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70.9 deg From Axial Plane
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Probe's Eye
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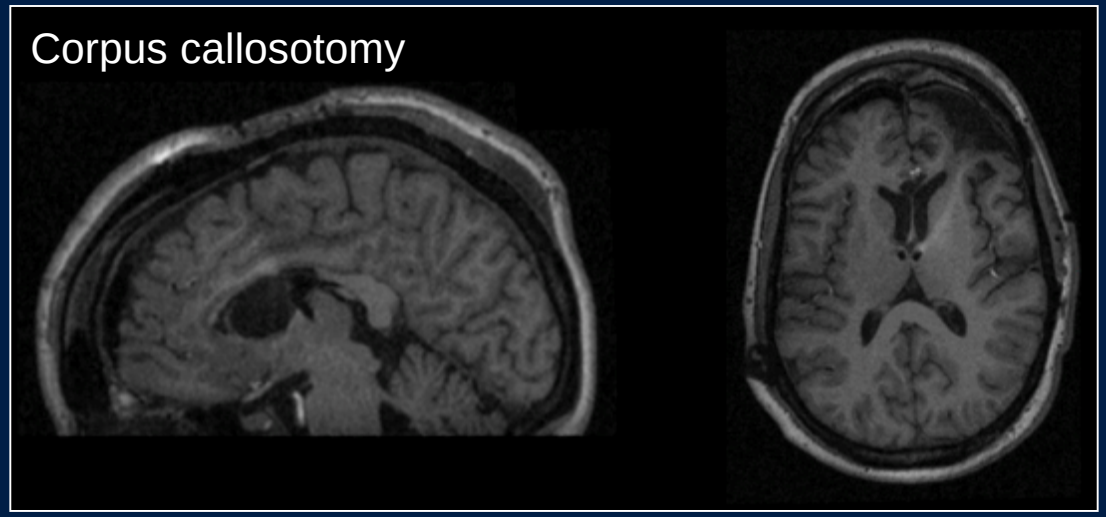
StealthStation
Prep
Plan
Setup
Nav
End
Frame Detect
Reformat Exam
Planning
Identify landmarks on images
Mark the target and entry points. Place cursor and hold Shift key to adjust surgical plan. To adjust target, plan must be on the target plane.
Left
Edit...
12.3
Set Entry
Length
12.3 mm
Set Target
0.0 mm past target
0.0 mm off plan
New Plan to Offset
+/-x
+/-y
Store
Target Selection
Sample
AC-PC Coordinate
Lat = -2.25 = -0.08 x 26.51
A-P = -0.80 = -0.03 x 26.51
Vert = 7.93 = 0.30 x 26.51
Back
Next

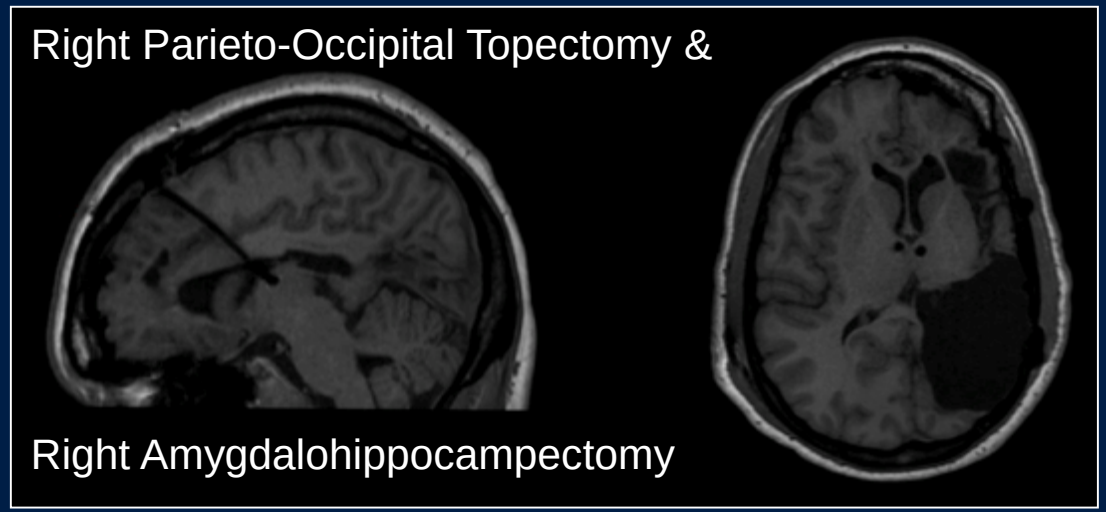
SUCCESSFUL LEAD IMPLANTATIONS WITH DISORDERED ANATOMY

Corpus callosotomy

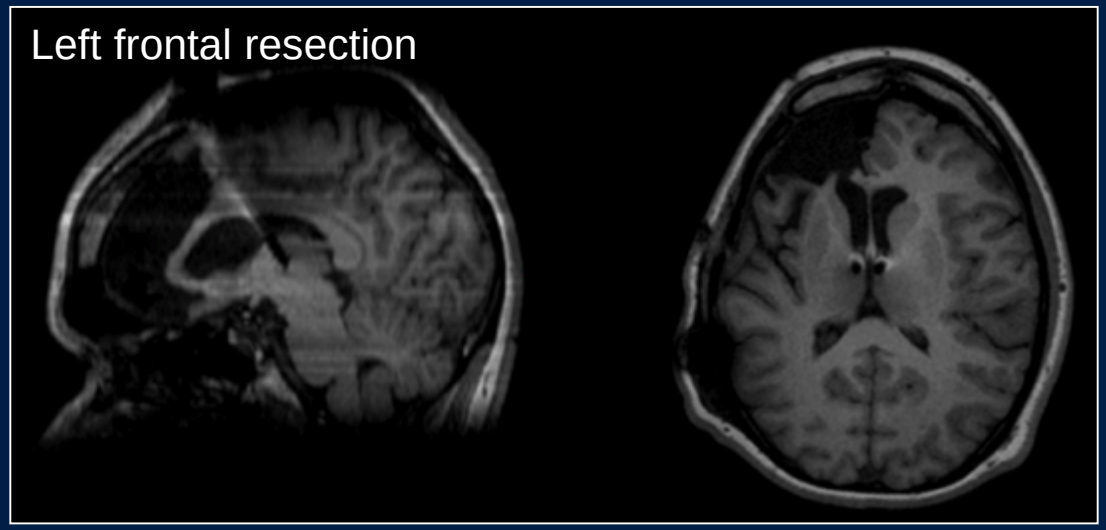


Right Parieto-Occipital Topectomy &

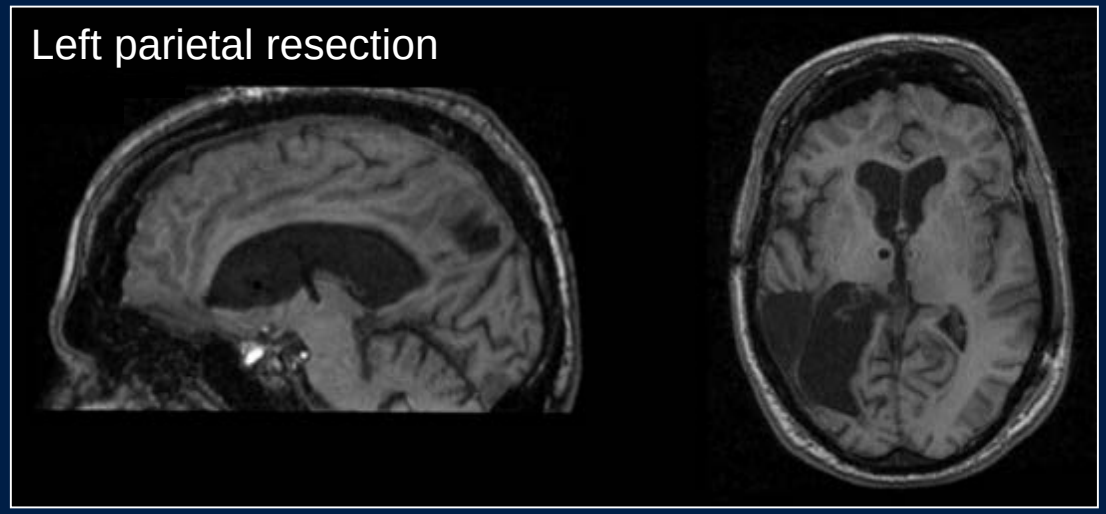
Right Amygdalohippocampectomy



Left frontal resection

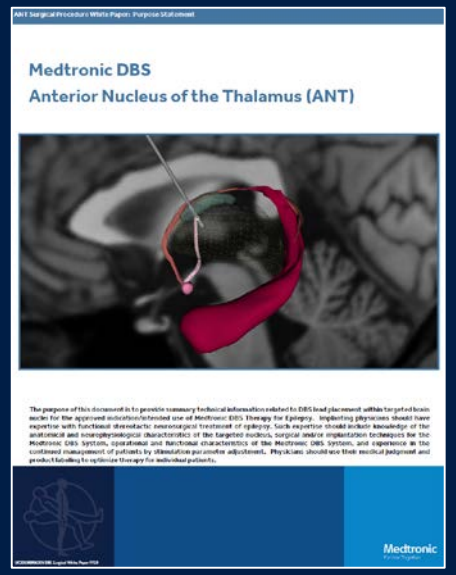


Left parietal resection

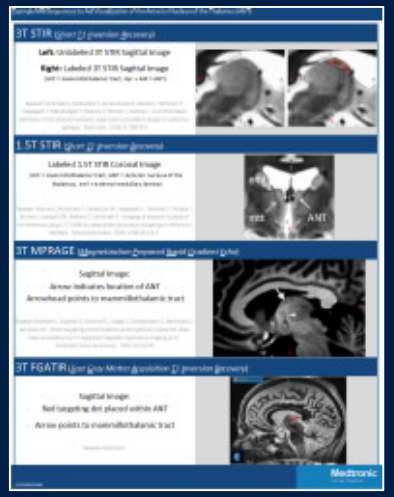


Images Courtesy of Dr. R Gross, Emory University Hospital

PHYSICIAN RESOURCES:



ANT Surgical White Paper

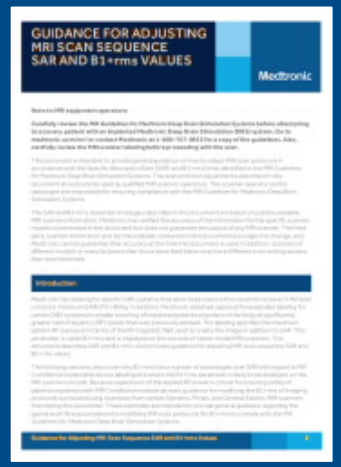


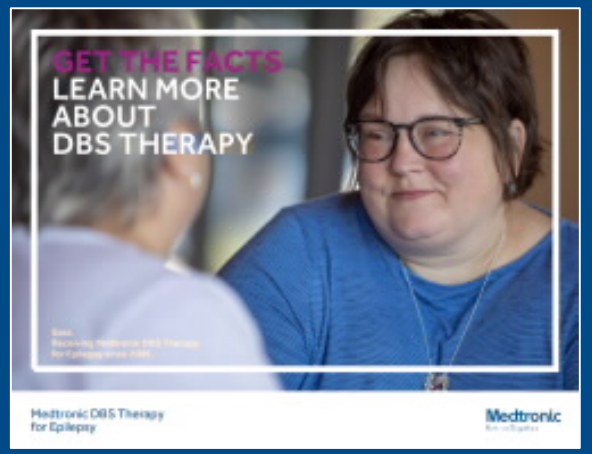
Example ANT MRI Sequences

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)

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.

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