ANT DBS for Refractory Epilepsy

Fundamentals

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MEDTRONIC IS COMMITTED TO THE BRAIN MODULATION BUSINESS

We alleviate pain, restore health and extend life by delivering a Medtronic brain modulation solution to every eligible patient.

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Off Label Disclosure Slide

Thank you for participating in this educational event!

This program, sponsored by Medtronic, is intended to *educate* and *train* customers regarding the **approved** or **cleared** uses of Medtronic products. As such, unapproved products or indications may not be presented or discussed during the program.

You may contact Medtronic's Office of Medical Affairs at 800.876.3133 ext. 6044 or rs.msdoma@medtronic.com for any specific clinical questions you may have.

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MEDTRONIC DBS THERAPY—
IMPROVING LIVES THEN, NOW, TOMORROW.

1980s

1987
Medtronic DBS Therapy is implanted for the first time in Grenoble, France.

1st implant

1990s

1995
10,000th person worldwide implanted with Medtronic DBS Therapy.

CE Mark approval in Europe for treating essential tremor and tremor associated with Parkinson's disease.

1997
Medtronic DBS Therapy receives Food and Drug Administration (FDA) approval to treat essential tremor and tremor associated with Parkinson's disease.

1998
Medtronic DBS Therapy approved in Europe for Parkinson's disease.

PD and ET Tremor

2000s

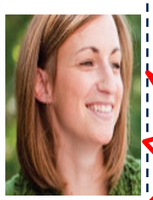
2002
Medtronic receives FDA approval of DBS Therapy for the treatment of Advanced Parkinson's Disease.

Advanced PD

2003
Medtronic DBS Therapy receives approval in Europe and Humanitarian Device Exemption (HDE)* approval in the U.S. for managing the symptoms of primary dystonia.

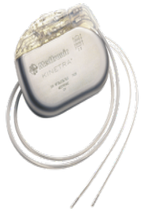
Dystonia

2007
50,000th person worldwide implanted with Medtronic DBS Therapy.



2009
Medtronic DBS Therapy receives approval in Europe and an HDE* approval in the U.S. for the treatment of Obsessive-Compulsive Disorder.

OCD



2010s

2010
European approval of Medtronic DBS Therapy to treat medically refractory epilepsy patients with partial-onset seizures.†

2012
Medtronic DBS Therapy receives approval in Australia and Canada for the treatment of medically refractory epilepsy patients with partial-onset seizures.†

2015
CE Mark in Europe and FDA approval of full-body MR Conditional MRI scans under specific conditions. FDA Approval of Expanded PD Labeling

2015
EU and US Launch of Full Body MRI Labeling

2016
US Launch of Expanded PD Labeling

2016
140,000th person worldwide implanted with Medtronic DBS Therapy.

US Launch of Expanded PD Labeling

2017
160,000th person worldwide implanted with Medtronic DBS Therapy

2018
Medtronic DBS Therapy receives Food and Drug Administration (FDA) approval to treat as an **adjunctive treatment for reducing the frequency of partial-onset seizures in those who are refractory to ≥3 antiepileptic medications.**

*Humanitarian device exemption (HDE) in the United States; the effectiveness of this device for the treatment of dystonia and obsessive-compulsive disorder (OCD) has not been demonstrated.

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THERAPY OVERVIEW

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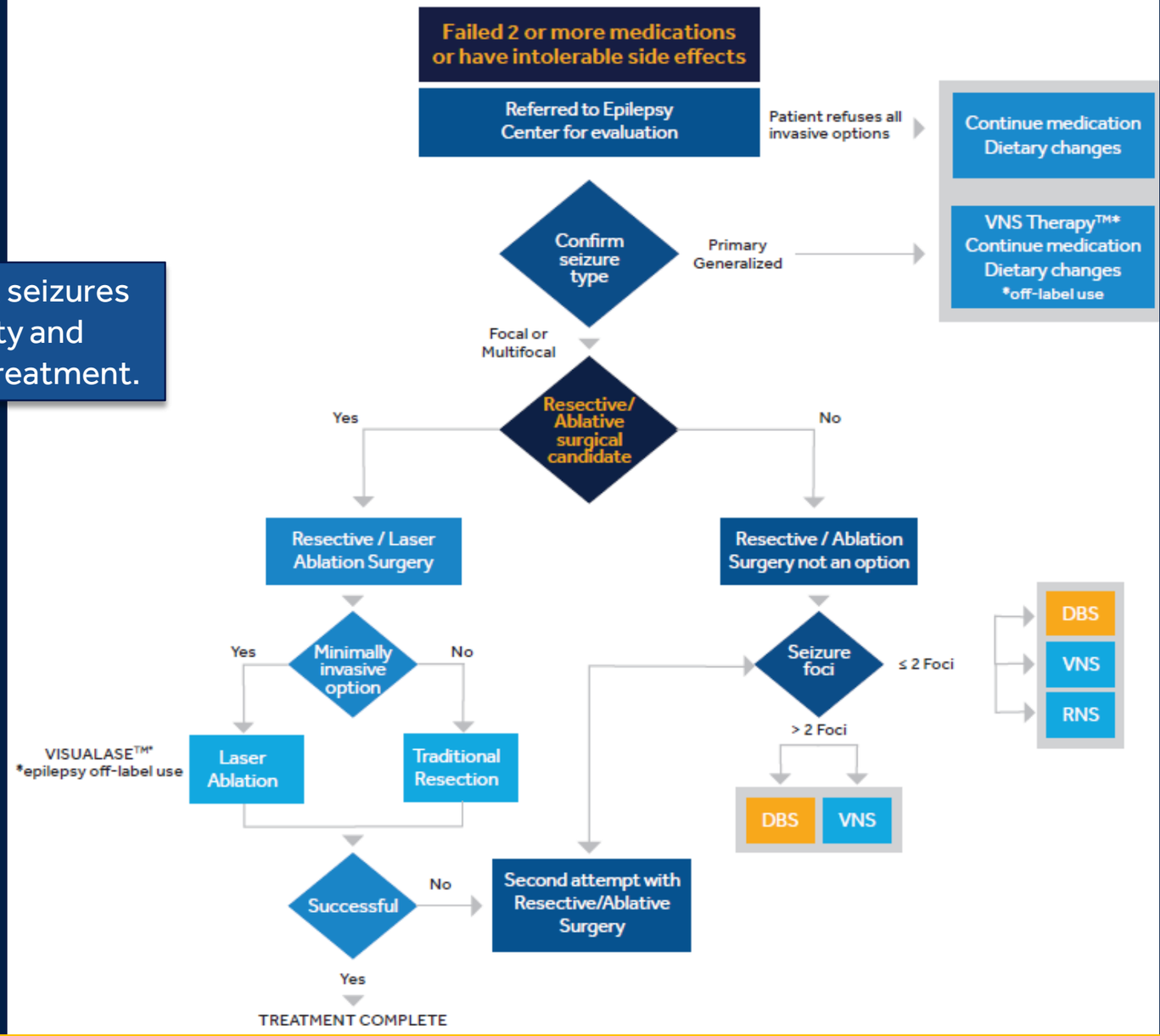
MEDTRONIC DBS FOR EPILEPSY-
INDICATION

- ***Bilateral anterior thalamic nucleus*** *stimulation using the Medtronic DBS System for Epilepsy is indicated as* ***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 in patients who average 6 or more seizures per month over the three most recent months (with no more than 30 days between seizures), and has not been evaluated in patients with less frequent seizures.*

Treatment Pathway

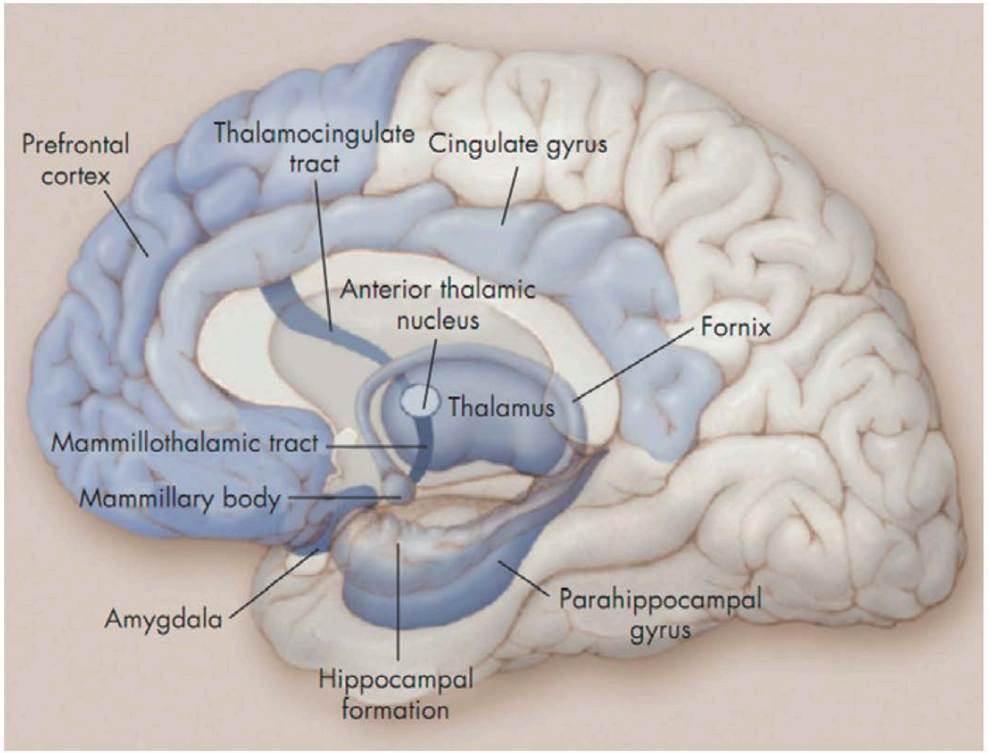
In approximately 30–40% of patients, seizures recur in varying degrees of intensity and frequency despite antiepileptic drug treatment.

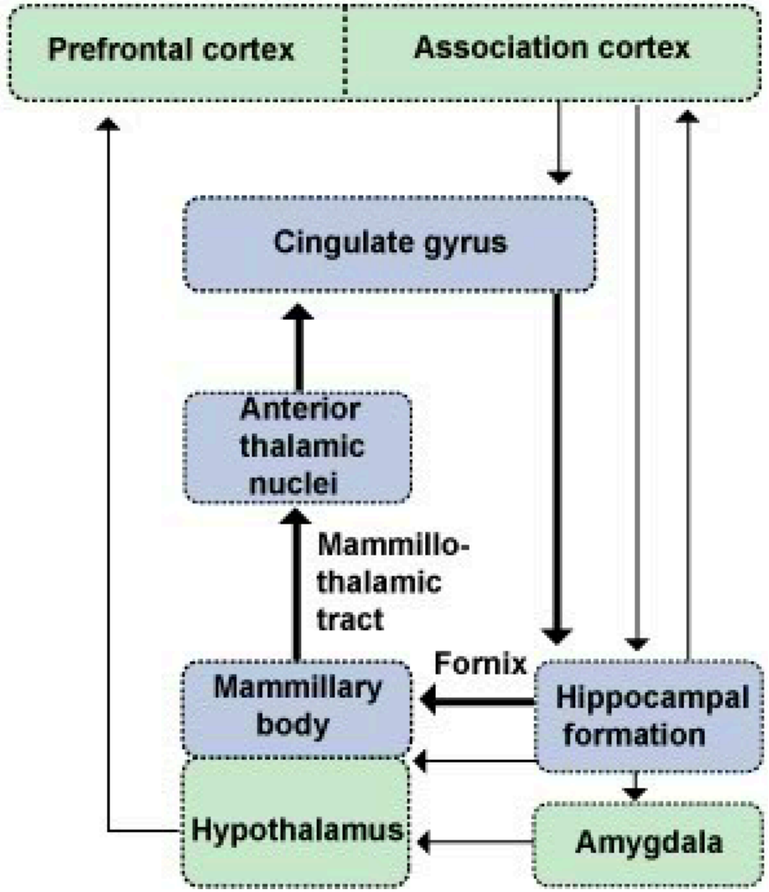


Medtronic DBS indication - "Refer to product labeling regarding the instructions for use, indications, contraindications, warnings, precautions, and potential complications/adverse events."

ANT DBS: RATIONALE, TARGET

Irving Cooper reasoned that due to its location with the Circuit of Papez the ANT could serve as key location to disrupt limbic seizures

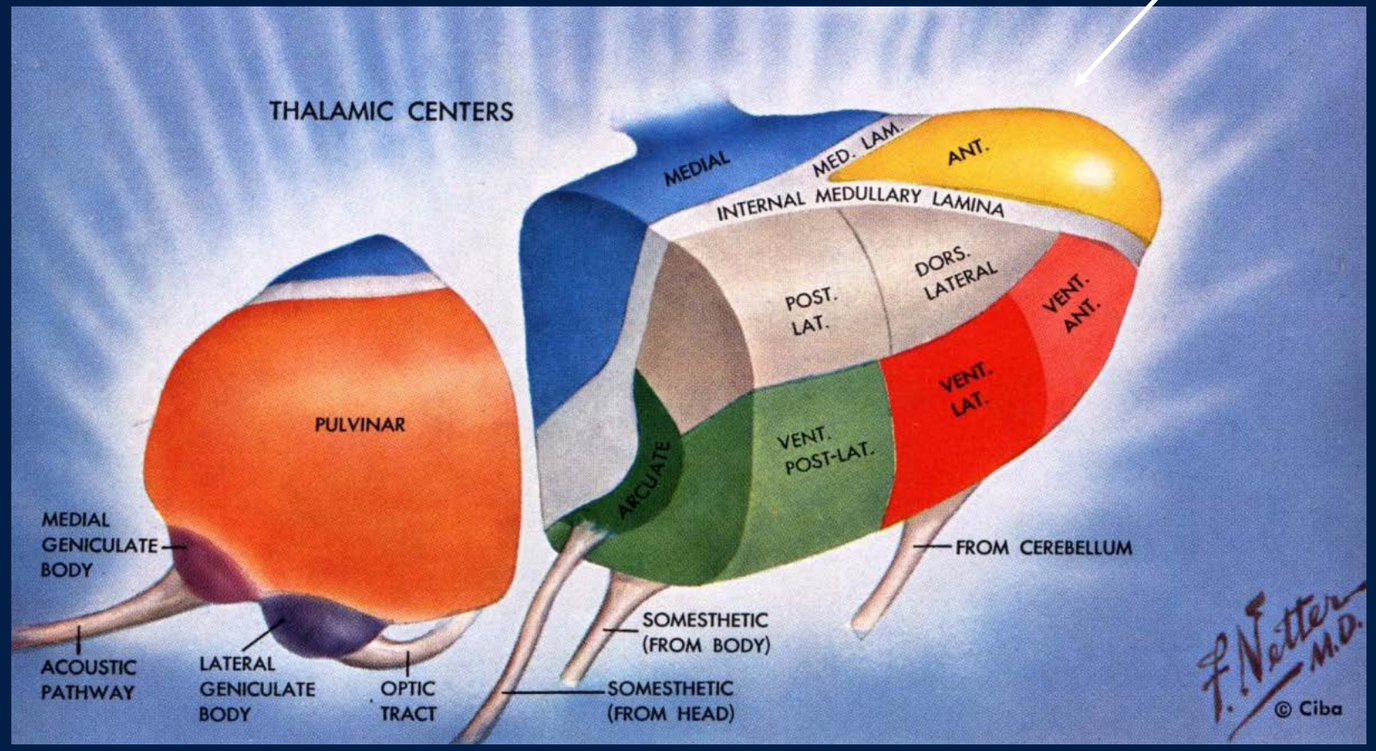




Wu & Sharan, Neuromodulation, 2013

THE ANTERIOR THALAMUS

Anterior Thalamic Nuclei



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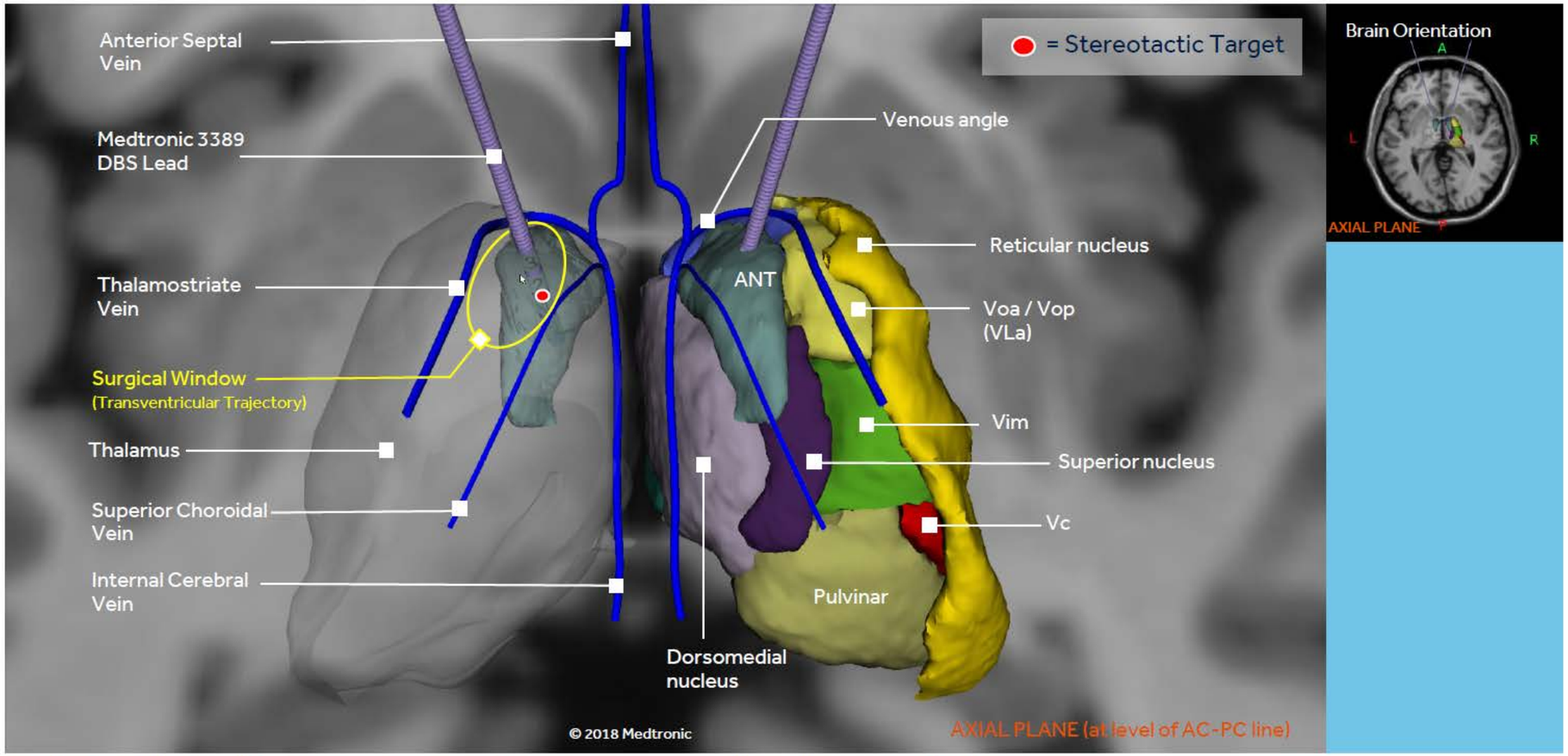
ANT: EFFECTIVELY-PLACED LEADS (DORSAL VIEW)



- Medtronic DBS Lead Model 3389 shown in both hemispheres. Only ANT is shown within left thalamus.
- Transventricular trajectory approach depicted
- Desired area for stimulation in this illustration is at contact(s) 2 and/or 3

Anatomy	Preferred Location for DBS Lead	Observed Effect if Stimulated
ANT	Surgical target at termination point of mammillothalamic tract. Lead implanted such that contacts 2 & 3 are within ANT (or contacts 1 & 2 if contact 3 is intentionally placed within the ventricle	Reduction in seizure frequency following adequate duration of stimulation

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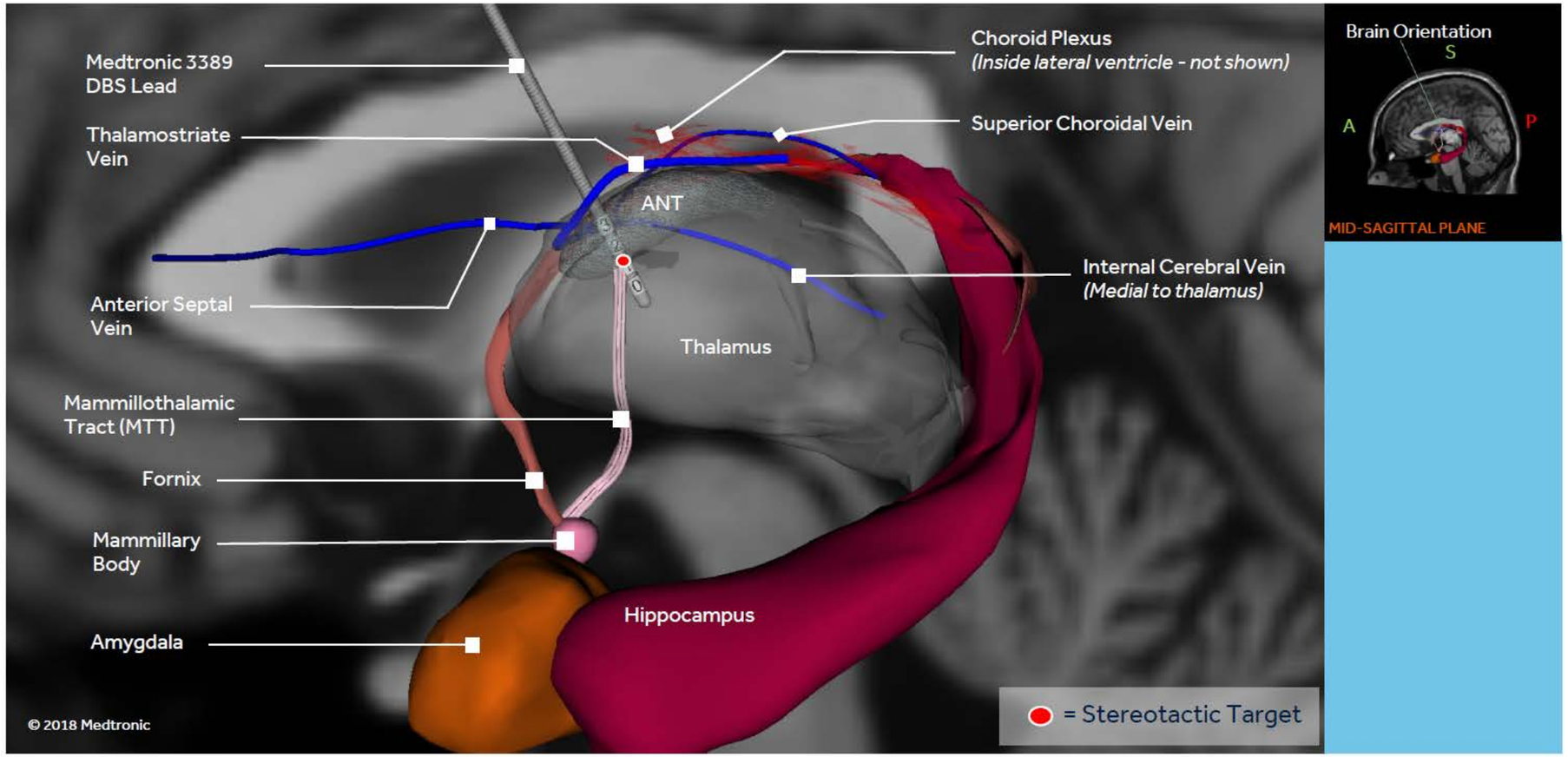
ANT: EFFECTIVELY-PLACED LEAD (LATERAL VIEW)



- Medtronic DBS Lead Model 3389 shown in left hemisphere. Only ANT is shown within the left thalamus to aid lead visualization.
- Transventricular trajectory approach shown.
- Desired area for stimulation in this illustration is at contact(s) 2 and/or 3

Anatomy	Preferred Location for DBS Lead	Observed Effect if Stimulated
ANT	Surgical target at termination point of mammillothalamic tract. Lead implanted such that contacts 2 & 3 are within ANT (or contacts 1 & 2 if contact 3 is intentionally placed within the ventricle	Reduction in seizure frequency following adequate duration of stimulation

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SANTÉ STUDY:

Long-term safety and effectiveness outcomes

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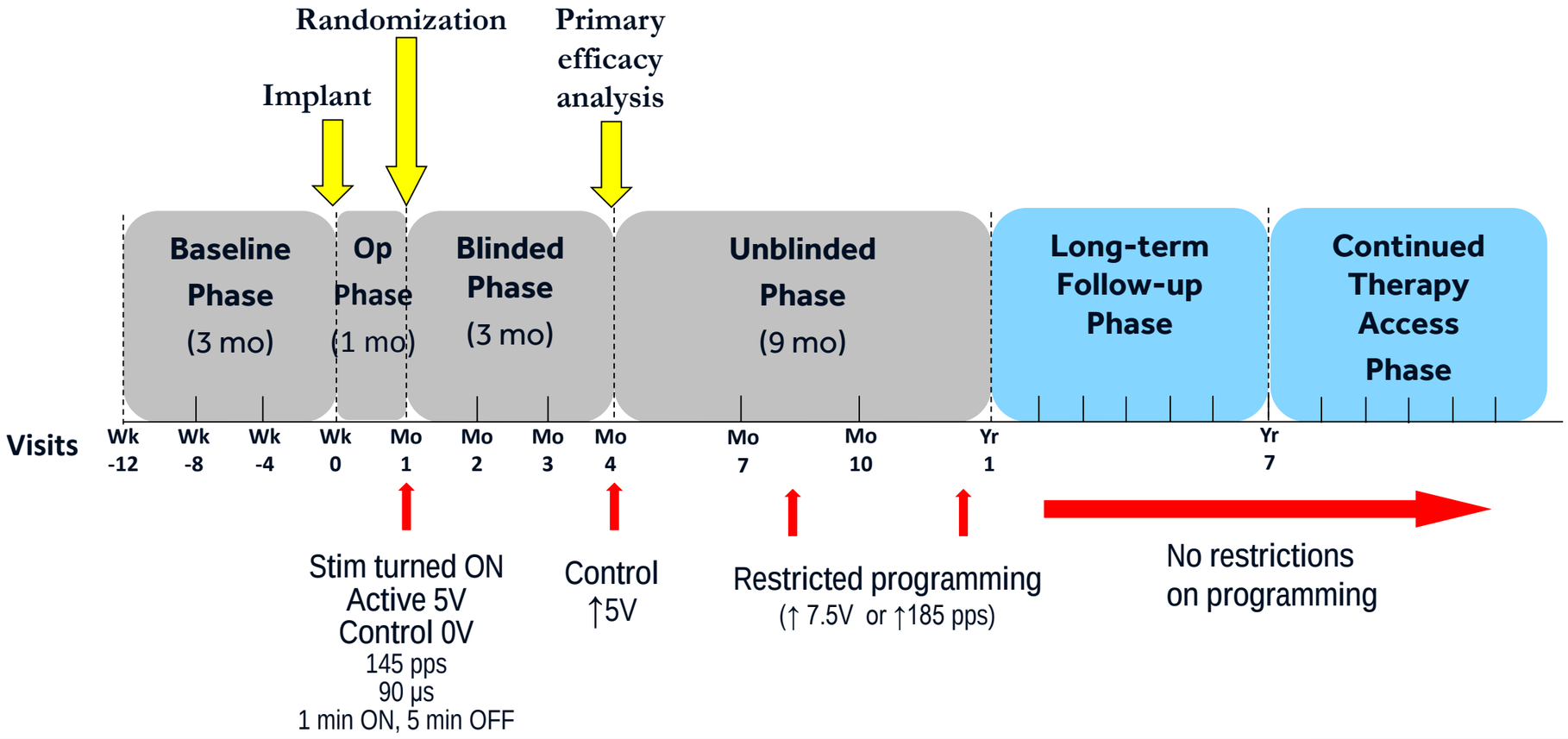
SANTÉ CLINICAL TRIAL

SANTÉ: Stimulation of the Anterior Nucleus of the Thalamus for Epilepsy

Medtronic-sponsored, multicenter, prospective randomized controlled pivotal clinical trial conducted at 17 centers in the United States with initial implant in 2004.



STUDY POPULATION

Eligibility Criteria (abbreviated)

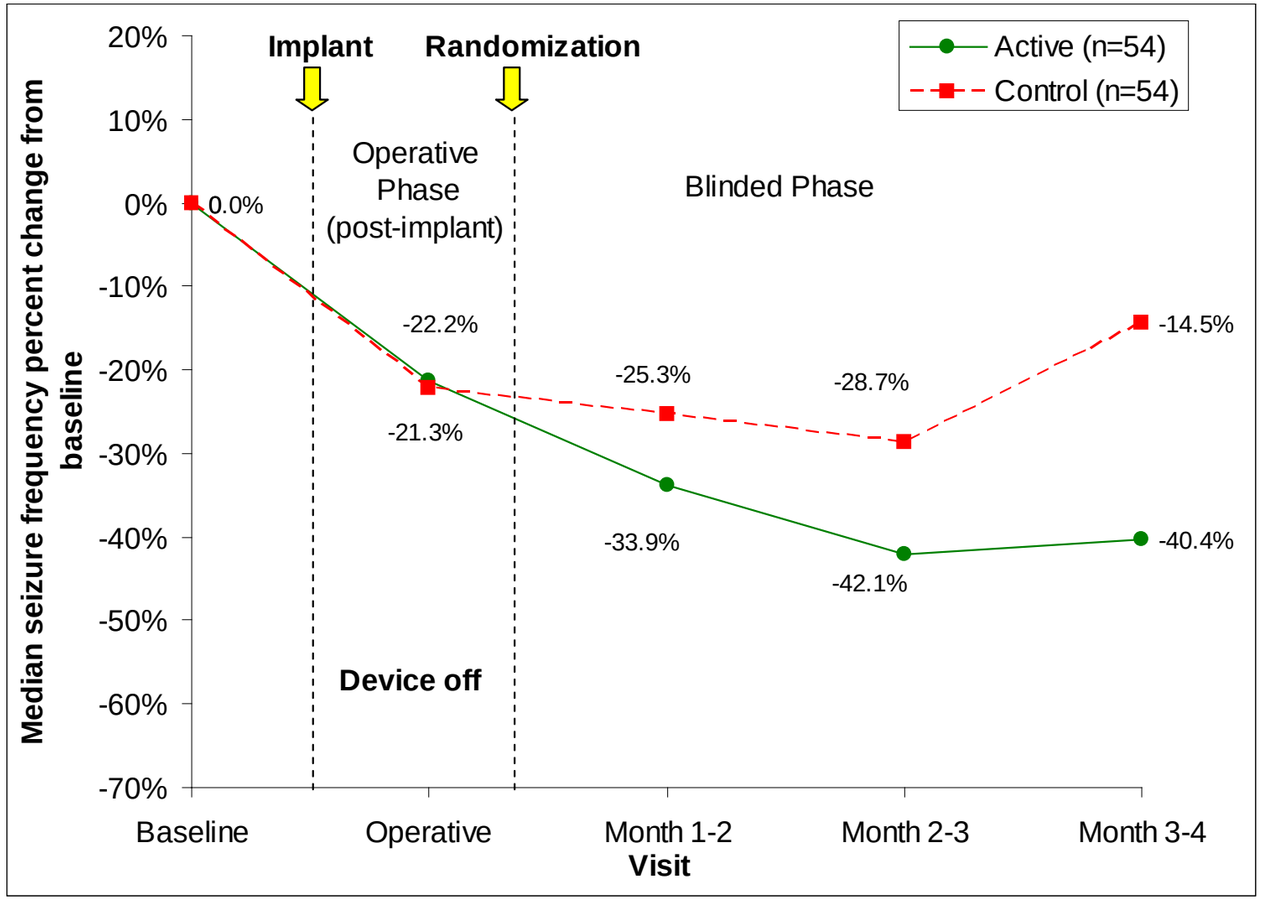
- Age 18-65, inclusive
- 6 or more partial seizures with or without secondary generalization per month
- Refractory to at least 3 antiepileptic drugs (AEDs), currently taking 1-4 AEDs

Demographics (n=110 implanted)

Age (mean)	36.1 years
Female (%)	50%
Years with epilepsy (mean)	22.3 years
Baseline seizure counts per month (median)	19.5
Number of epilepsy meds (%):	
1	11%
2	49%
3	37%
4	3%
Previous VNS (%)	45%
Previous epilepsy surgery (%)	25%

TOTAL SEIZURE FREQUENCY
BLINDED PHASE RESULTS

- Both groups had a similar drop in the Operative Phase
- The **active** group **continues to improve** while the control group trends towards baseline



Negative values indicate a seizure frequency reduction compared with baseline.
Note: Operative Phase diary data were not available for 2 subjects (active n=1, control n=1)

Fisher R, Salanova V, Witt T, et al. Electrical stimulation of the anterior nucleus of thalamus for treatment refractory epilepsy. Epilepsia. 2010;51(5):899-908.

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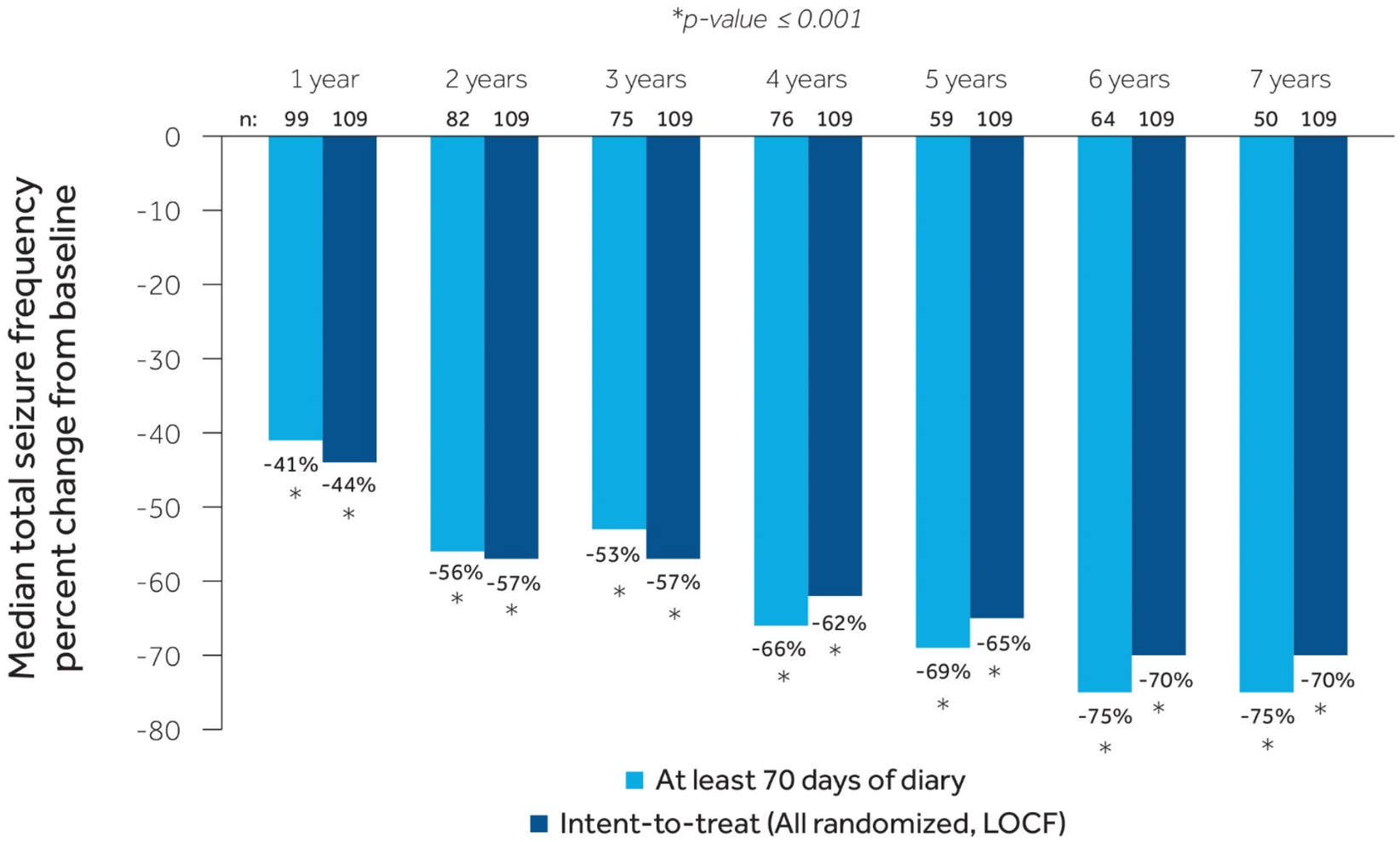
TOTAL SEIZURE FREQUENCY
LONG TERM RESULTS

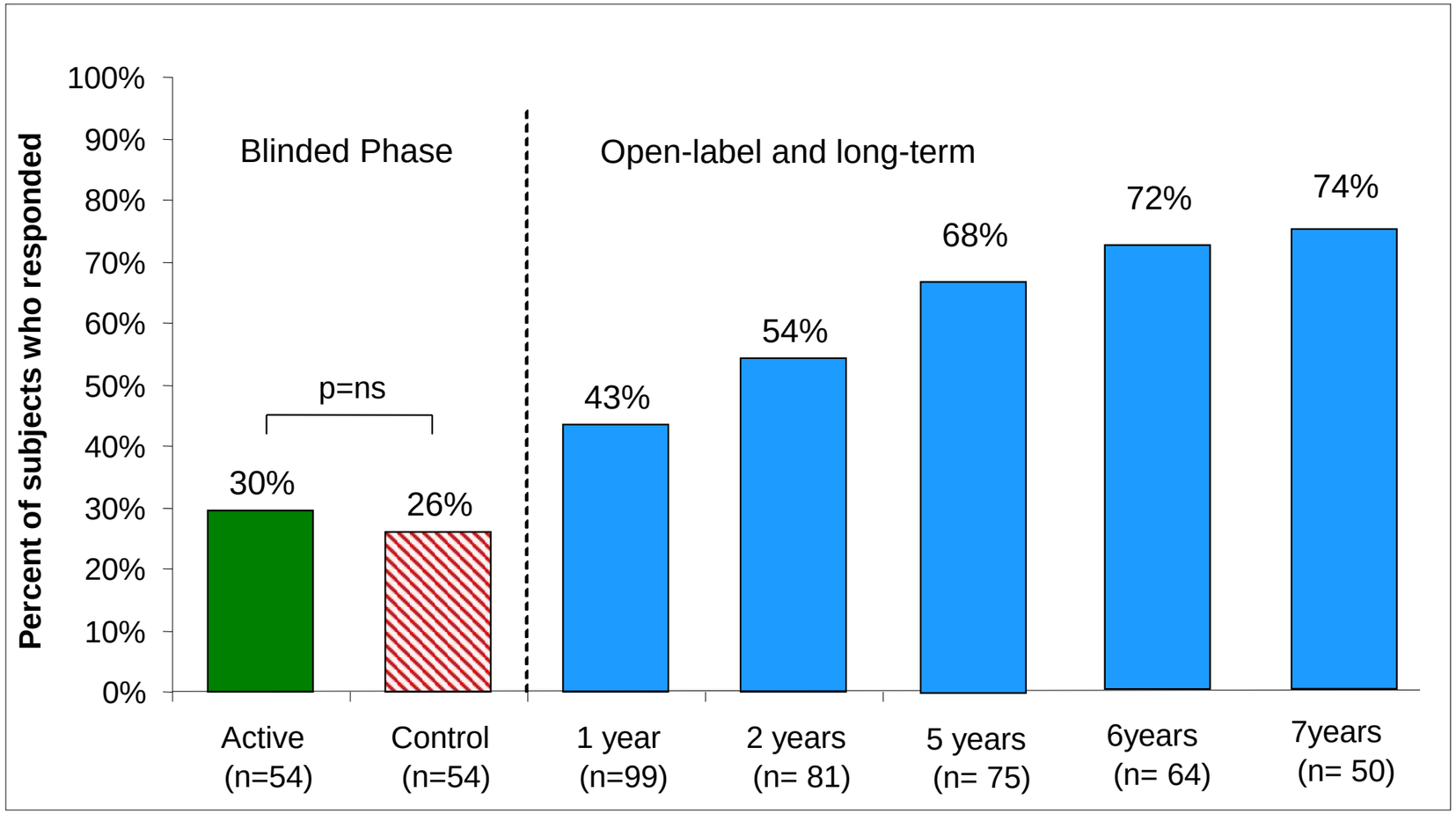


DATA IMPUTATION

- The last observation carried forward (LOCF) analyses included all randomized subjects (N=109) and was used to assess the potential impact of missing data on the effectiveness results.
- Missing values were imputed using subjects' most recent seizure frequency data prior to discontinuation.

Medtronic DBS Therapy for Epilepsy Clinical Summary 2018

RESPONDER RATE[1]



[1] Percent of subjects with ≥50% reduction in total seizures

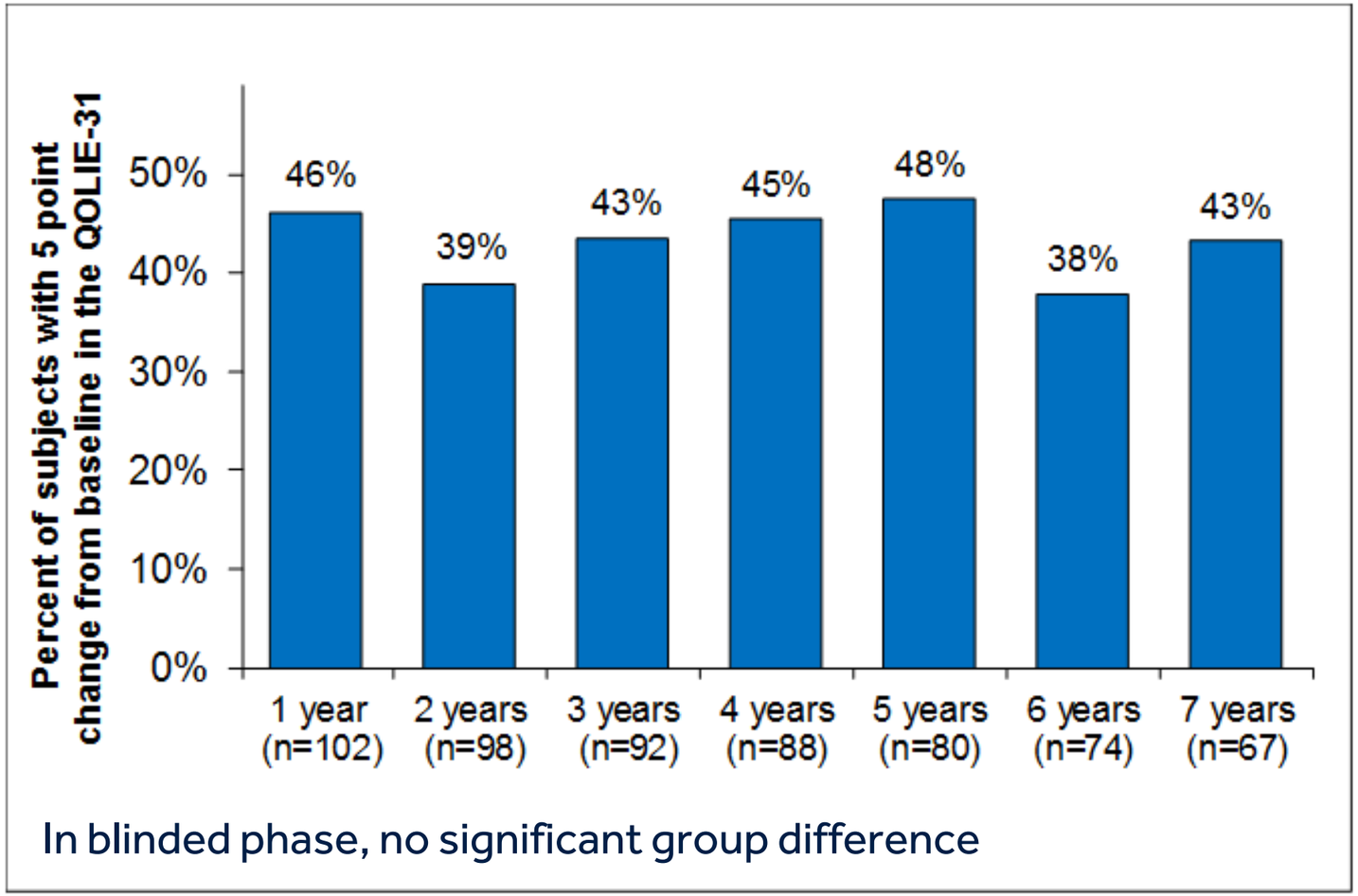
Salanova V, Witt T, Worth R et al. Long-term efficacy and safety of thalamic stimulation for drug resistant partial epilepsy. Neurology. 2015;84(10):1017-1025.

Medtronic DBS Therapy for Epilepsy Clinical Summary 2018

QUALITY OF LIFE

QOLIE 31 – RESPONDER RATE[1]

84% PATIENT SATISFACTION RATE
AFTER 7 YEARS
(54 out of 64 patients)



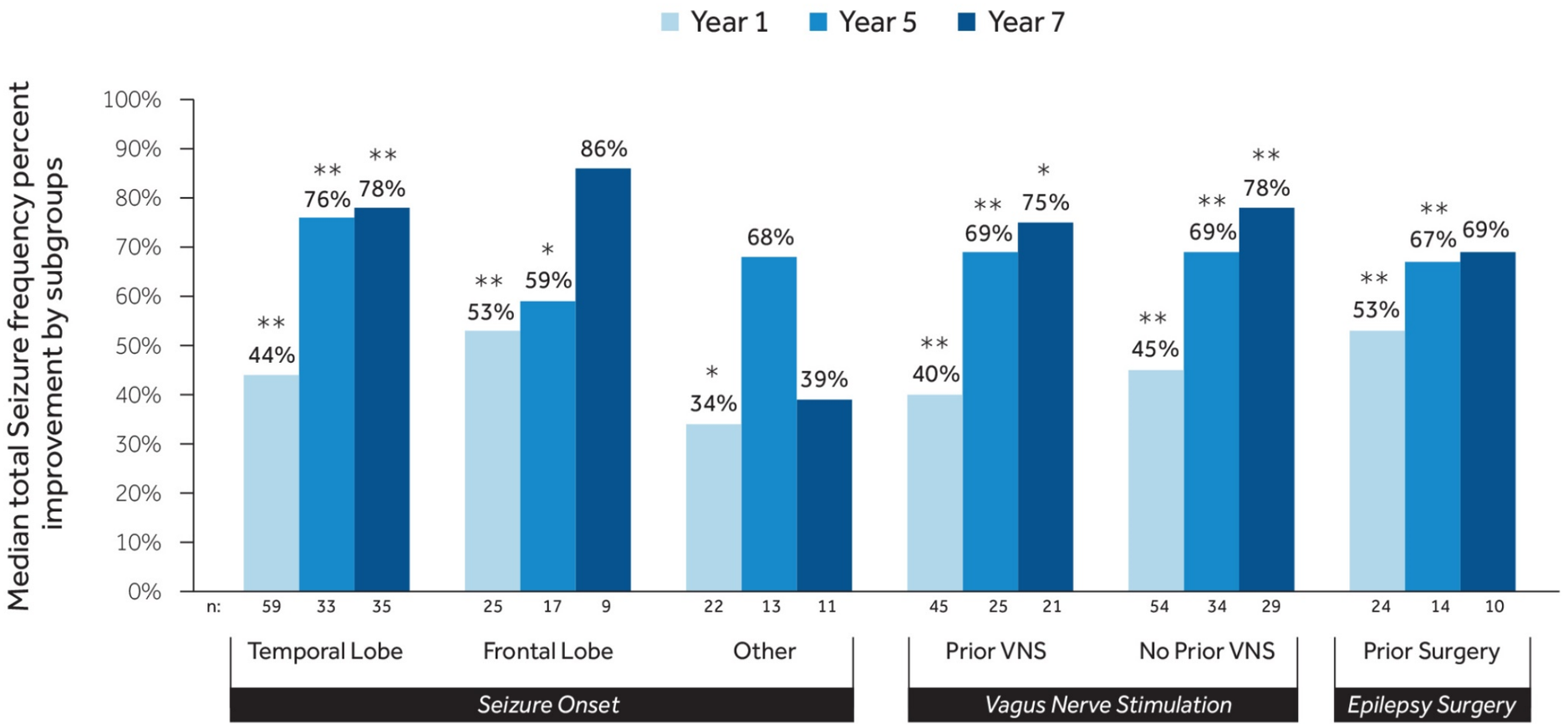
In blinded phase, no significant group difference

[1] A 5-point change in QOLIE-31 score has been estimated to be clinically meaningful.

Medtronic DBS Therapy for Epilepsy Clinical Summary 2018

SEIZURE FREQUENCY SUBGROUPS

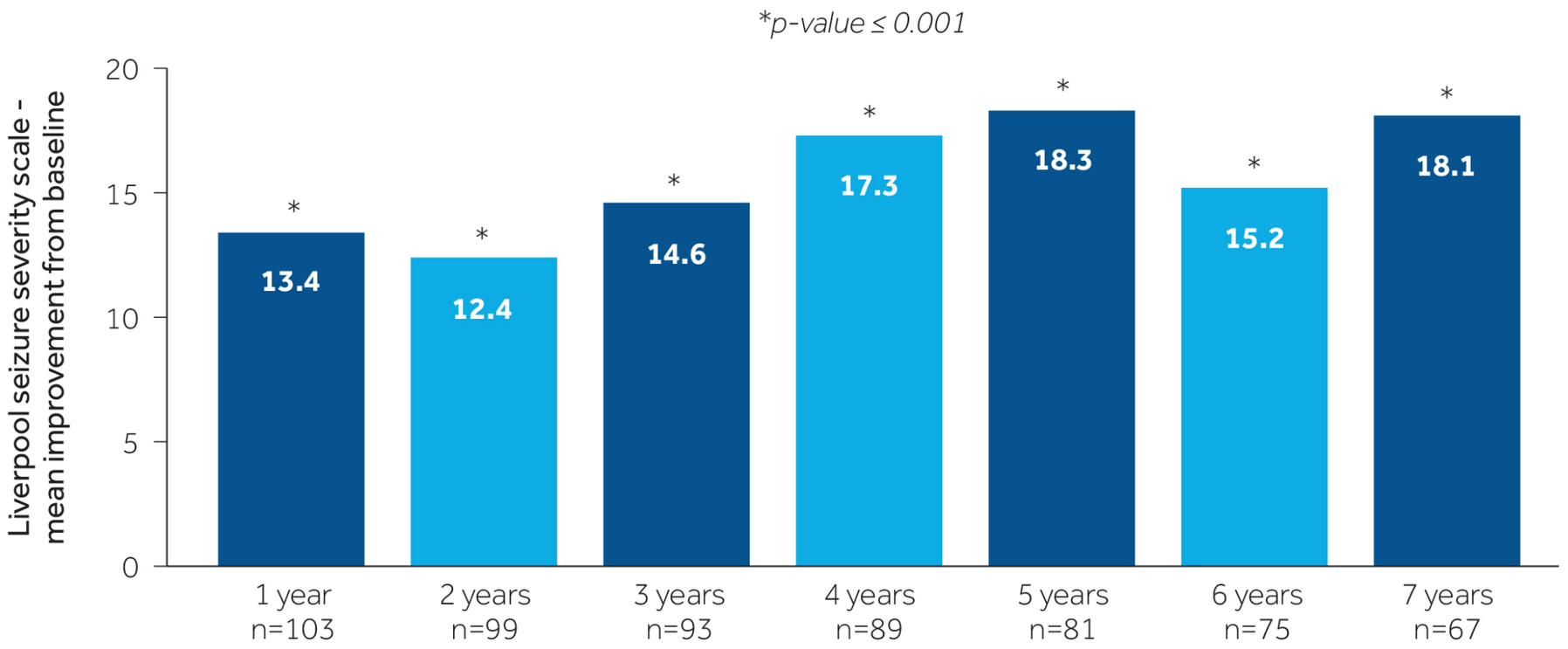
SEIZURE ONSET, PRIOR VNS/PRIOR SURGERY



*p-value ≤ 0.05 **p-value ≤ 0.001

Medtronic DBS Therapy for Epilepsy Clinical Summary 2018

LIVERPOOL SEIZURE SEVERITY SCALE



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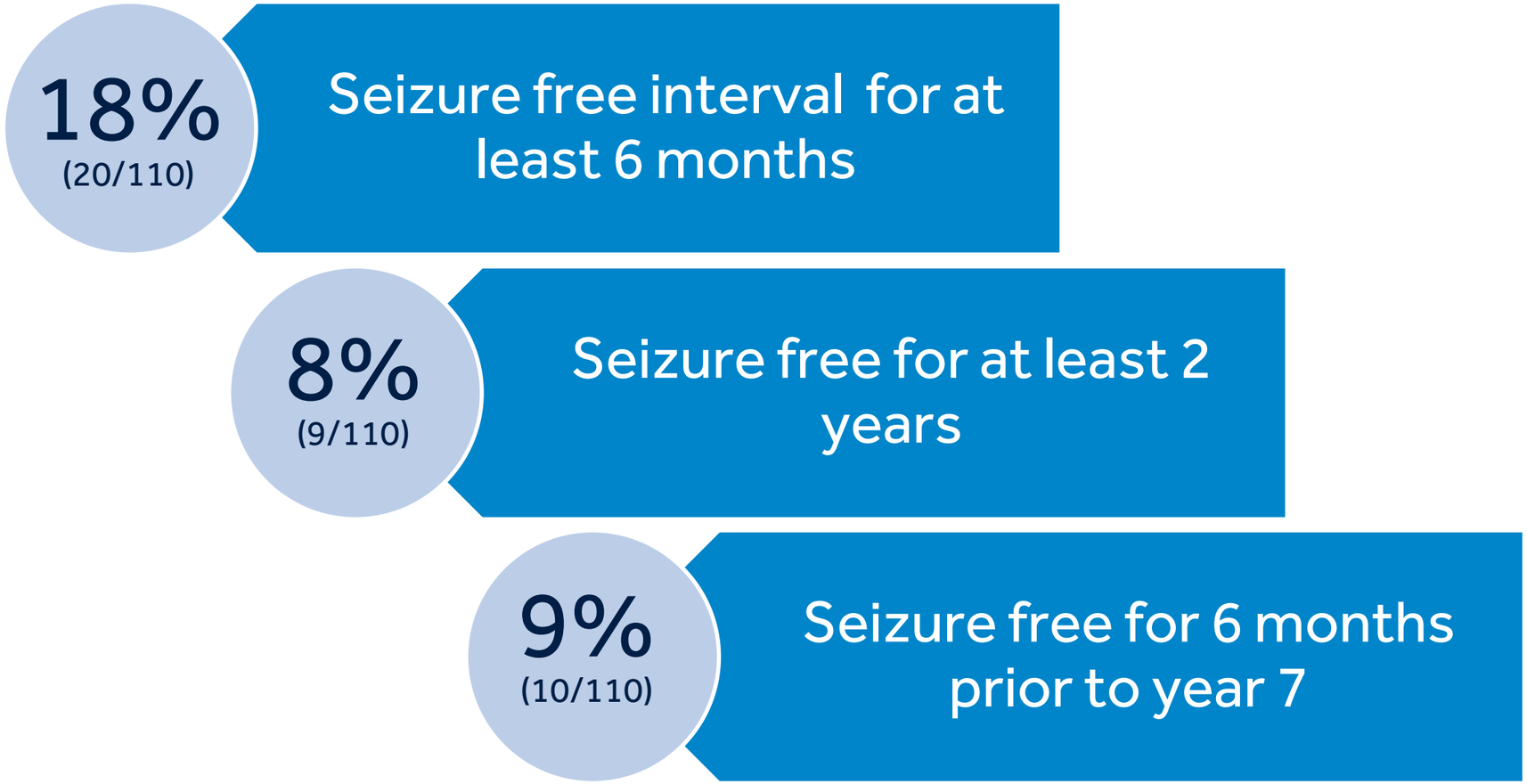
SELF-REPORTED MOST SEVERE SEIZURES[1]

Time period	n	Median	25th percentile	75th percentile	Wilcoxon p-value[a]
Year 1	74	-39.2%	-90.3%	-8.3%	<0.001
Year 2	62	-58.4%	-87.6%	-10.8%	<0.001
Year 3	55	-61.9%	-92.1%	-18.5%	<0.001
Year 4	55	-47.5%	-86.1%	-13.5%	<0.001
Year 5	42	-75.4%	-100.0%	-42.4%	<0.001
Year 6	44	-63.7%	-91.5%	-14.7%	0.005
Year 7	30	-71.1%	-100.0%	-25.5%	<0.001

[1] Subjects were asked at baseline to identify which of their seizure types they considered to be the most severe.

Medtronic DBS Therapy for Epilepsy Clinical Summary 2018

SEIZURE FREEDOM



Medtronic DBS Therapy for Epilepsy Clinical Summary 2018

SAFETY SUMMARY

- No unanticipated adverse device effects
- Depression and memory impairment self-reported more frequently in Active group patients
- No significant cognitive declines or worsening of depression scores were observed through the blinded phase or in open-label at 7-years.
- Seizures may occur upon initiation of stimulation
- No symptomatic intracranial hemorrhages
- SUDEP rate similar or lower than reported in a similar population
- Procedural and hardware-related risks consistent with other DBS therapies

Medtronic DBS Therapy for Epilepsy Clinical Summary 2018
Fisher R, Salanova V, Witt T, et al. Electrical stimulation of the anterior nucleus of thalamus for treatment refractory epilepsy. Epilepsia. 2010;51(5):899-908.
Salanova V, Witt T, Worth R et al. Long-term efficacy and safety of thalamic stimulation for drug resistant partial epilepsy. Neurology. 2015;84(10):1017-1025.

DBS
PRODUCT OVERVIEW

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IMPLANTABLE SYSTEM COMPONENTS

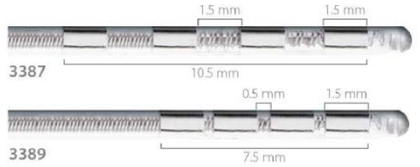
Three Components*

1. Implantable Neurostimulator (INS): Power
2. Extension: connects the INS to the lead
3. Lead: Implanted in the brain, electrodes in contact with target tissue

*Some systems may include a pocket adaptor

MEDTRONIC DBS SYSTEM FOR EPILEPSY

- **Activa PC Model 37601 Neurostimulator**
- **Model 3387/3389 DBS Lead**
  - Electrodes in the Activa PC Neurostimulator are numbered 0-7 on the (frequently left side) and 8-15 on the (frequently the right side)
  - Provides connection to electrode 0-3 or 8-11 depending on the neurostimulator socket being used
  - Tablet programmer software defaults to the correct lead configuration
  - The DBS Leads have four electrodes



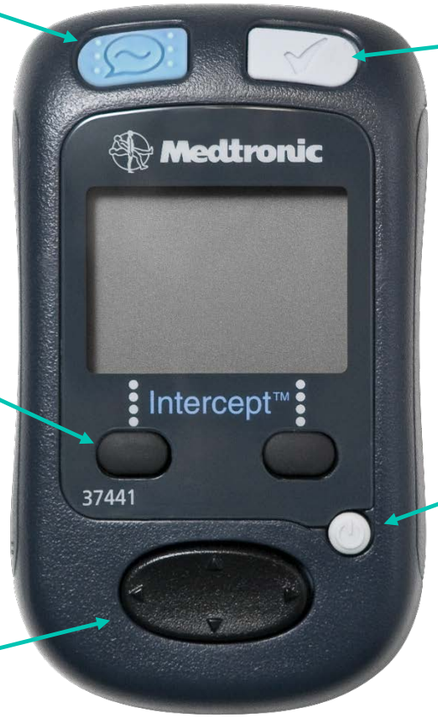
- **Model 37086 Extension**
  - Proximal (INS connection) end has eight contacts
  - 4 active, 4 inactive
  - Distal (Extension connection) end has four contacts
  - Available in lengths
    - 40 cm
    - **60 cm**
    - 95 cm
  - Stretch coil extension allows for up to15% extensibility

INTERCEPT™ PATIENT PROGRAMMER

Seizure Key
Used to log occurrence of a seizure or aura and restart stimulation cycle

Selection Keys
Used to turn therapy on and off
Clears the Seizure Confirmation screen

Navigator Key
Used to navigate to next available screen
Clears Information screens



Check Key
Used to synchronize the neurostimulator and patient programmer

Power/Backlight On/Off Key
Used to turn the patient programmer and backlight on or off

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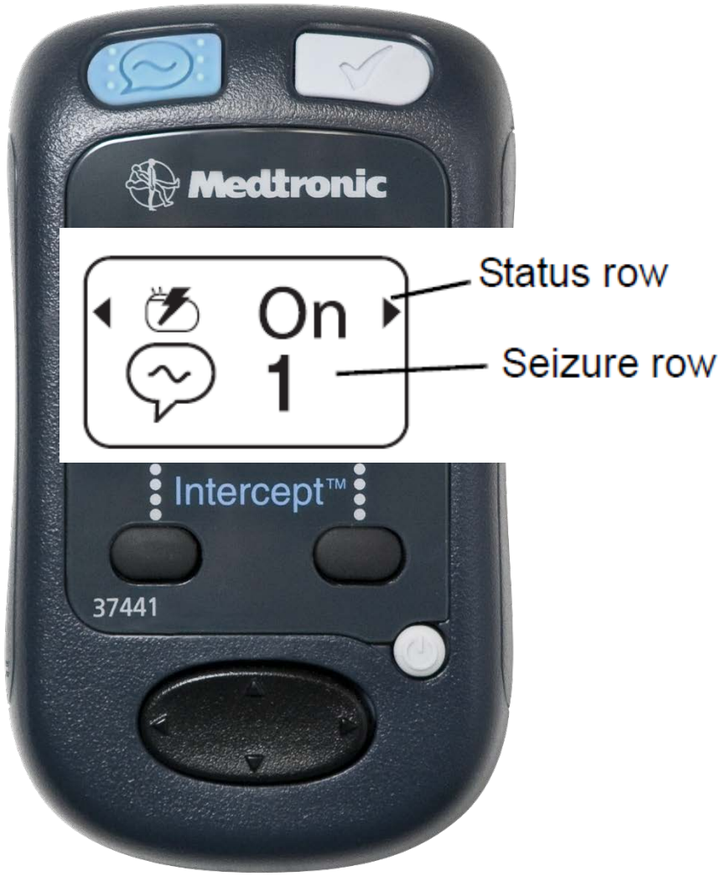
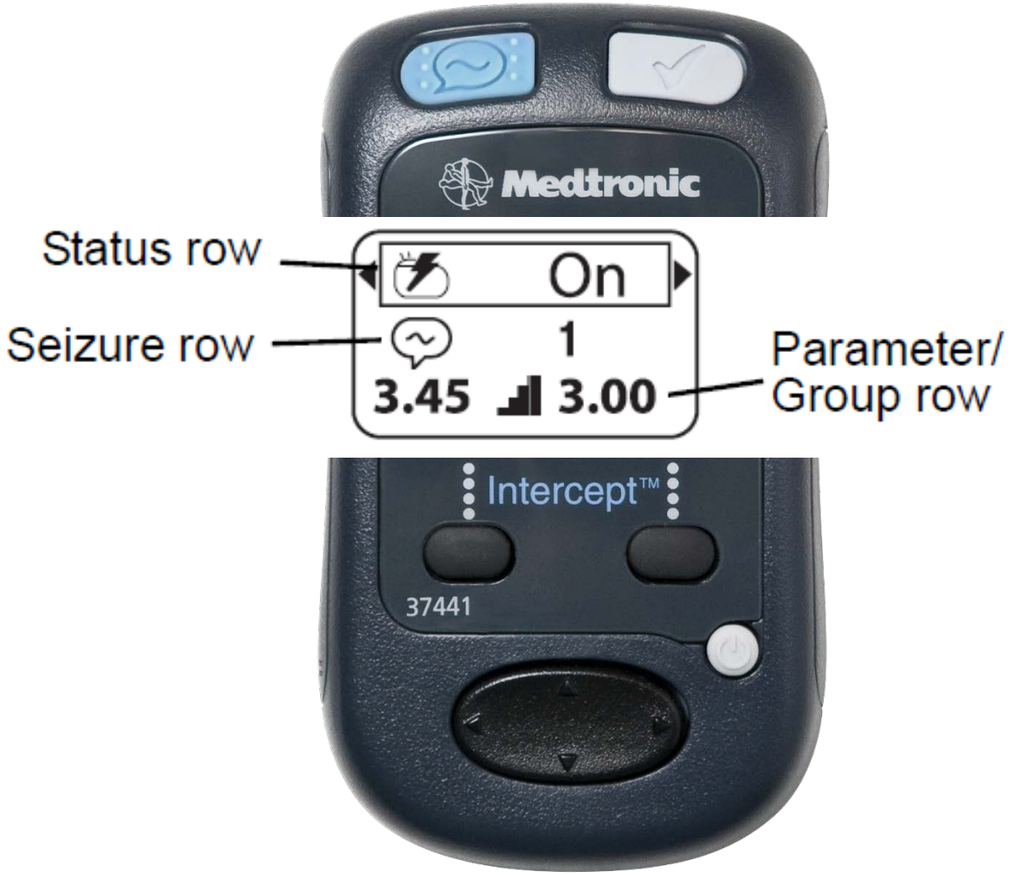
MODE THERAPY SCREEN

- **Simple Mode Therapy Screen shows:**
  - Therapy ON/OFF status
  - Seizure Count



- **Advanced Mode Therapy Screen shows:**
  - Therapy ON/OFF status
  - Seizure Count
  - Parameter settings and active group



DBS THERAPY FOR EPILEPSY
INITIAL PROGRAMMING ACTIVITIES

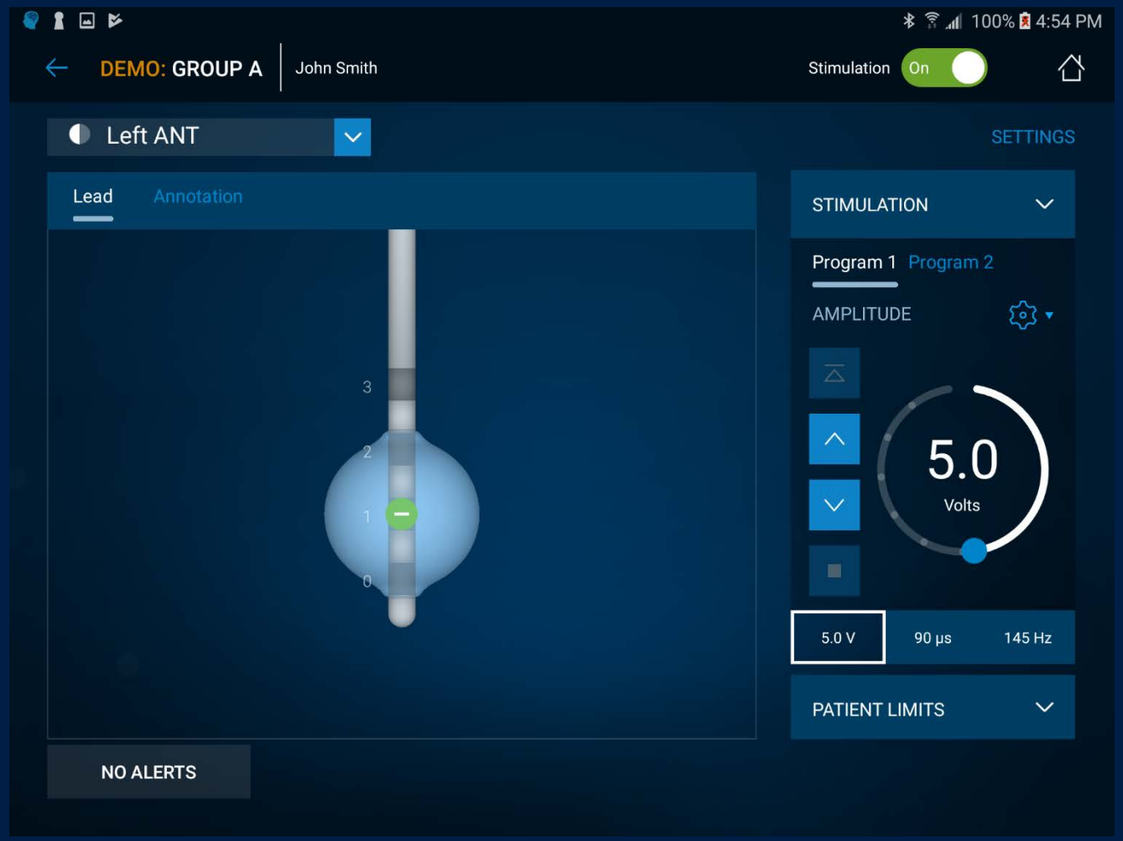
- Configure leads (completed in SET-UP)
- Verify system integrity (check electrode impedances)
- Program initial stimulation parameters
- Program the neurostimulator for patient control
- Provide patient and caregiver with instructions on use of patient programmer and tracking of seizures (count, type, severity)
- Emphasize adherence to AED regimen
- Verify tolerability of stimulation

SANTE STIMULATION PARAMETERS: EPILEPSY

Parameter	Typical Starting Value
Amplitude	5 V
Pulse Width	90 μs
Rate	145 Hz
Electrode Configuration	Unipolar Mode: Single electrode or two adjacent electrodes negative, case positive (all patients in the SANTE clinical trial were in unipolar mode)
Cycle of Therapy	Cycling mode ON: 1 minute on, 5 minutes off
SoftStart™Stop	programmed to 8 seconds

Tablet Clinician Programmer

Launched June 2018



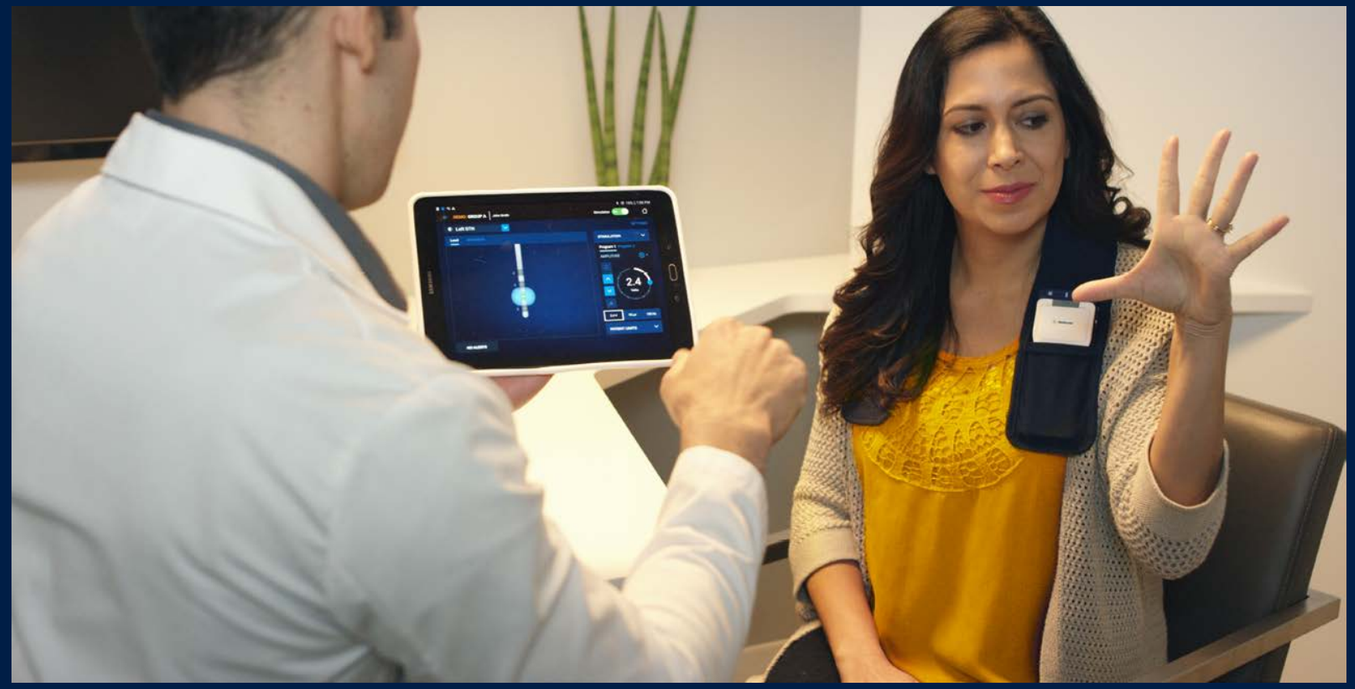
Modern, usable interface.

Focus on control of stimulation and documentation of outcomes.

Intuitive patient management.

CLINICIAN PROGRAMMER & ACCESSORIES

COMMUNICATOR AND DRAPE



* Optional protective case and drape may be ordered from Medtronic

* *Activa App is NOT compatible with Soletra/Kinetra Neurostimulators

SYSTEM COMPONENTS

1.) TABLET *(with Activa App)

- Compatible with ALL Activa™ Family devices**

2.) COMMUNICATOR

- Encrypted Bluetooth connection from the programmer to the communicator
- Proprietary, proximal telemetry from the communicator to the implanted device

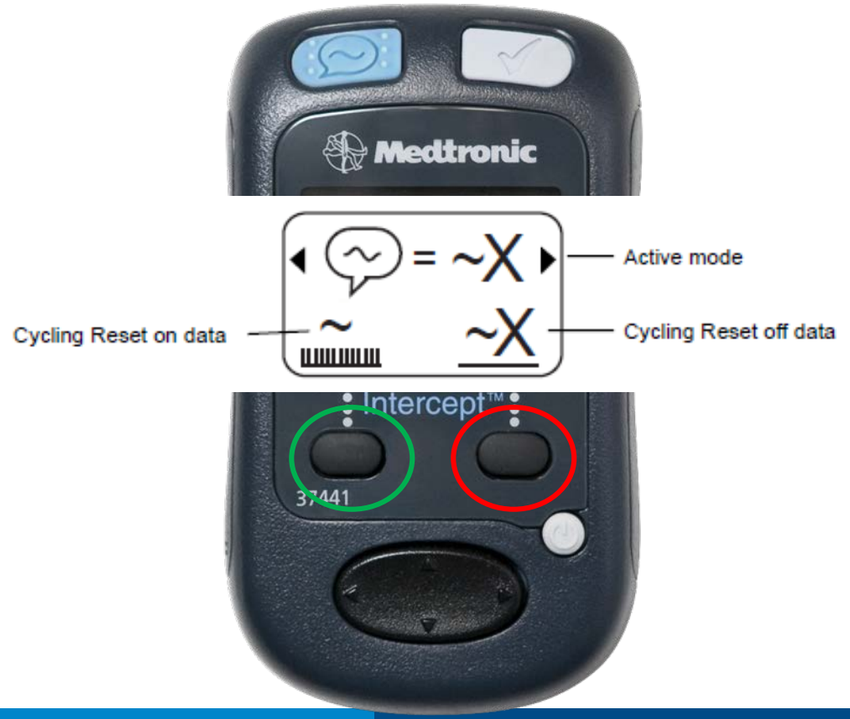
3.) DRAPE*

- Freedom of movement

SETTING SEIZURE MODE

- Turn patient programmer ON (do not interrogate)
- Press and hold Selection Keys until Lead Connections Screen Appears
- Navigate to Seizure Mode Screen
- Set to on or off
- This is meant to be utilized by HCP programmers only and NOT the patient

Note: Default setting for Seizure mode is off



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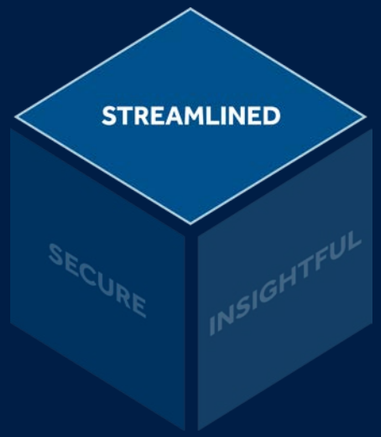
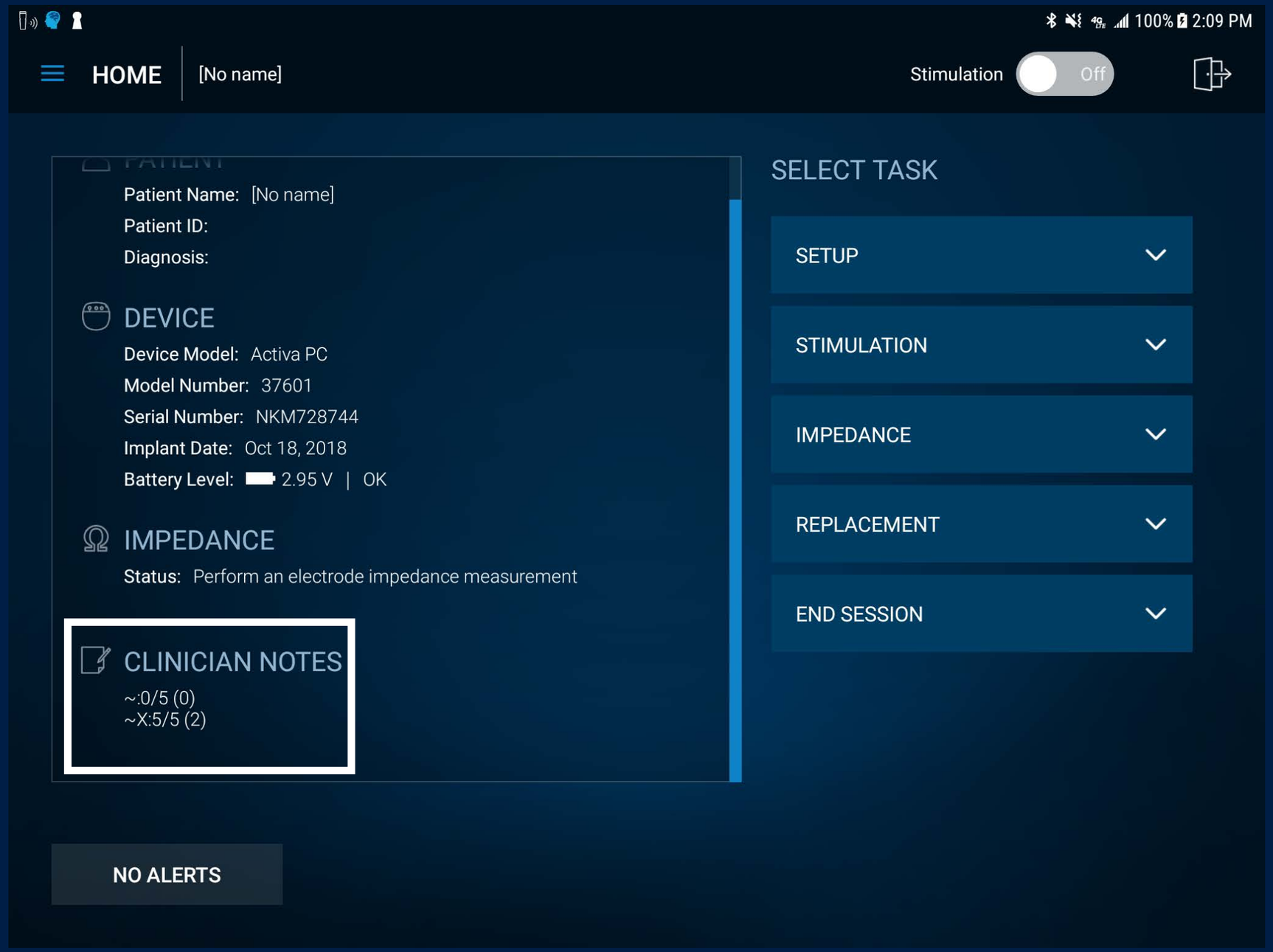
STREAMLINED

MODERN TECHNOLOGY UNLEASHED





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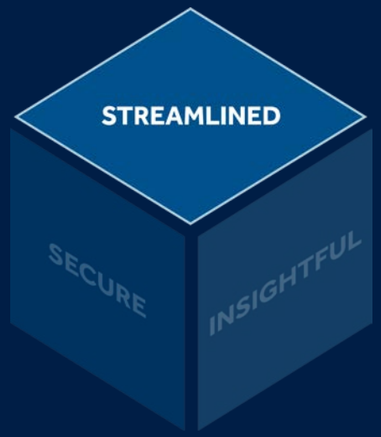
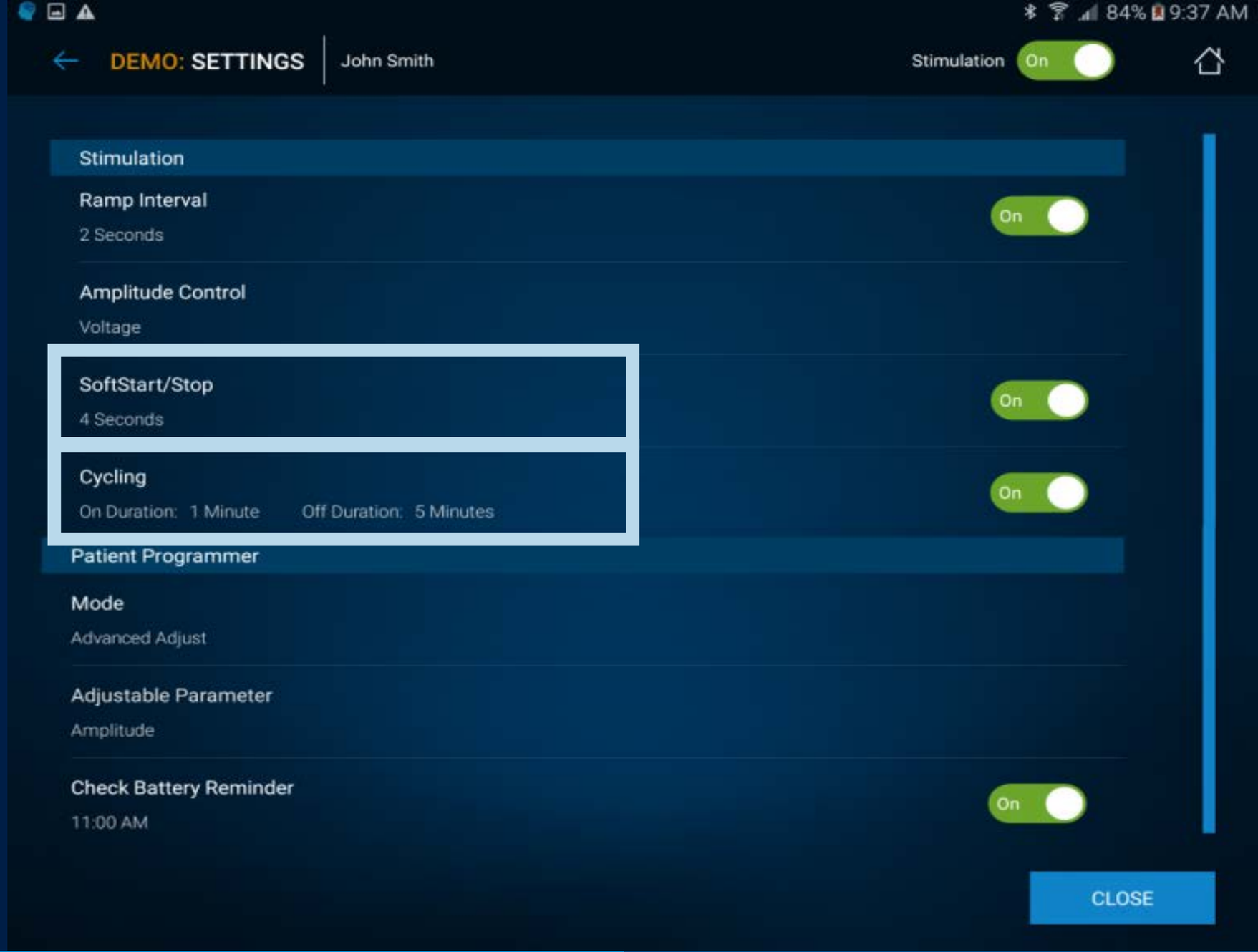
STREAMLINED

APP BASED
CONVENIENCE





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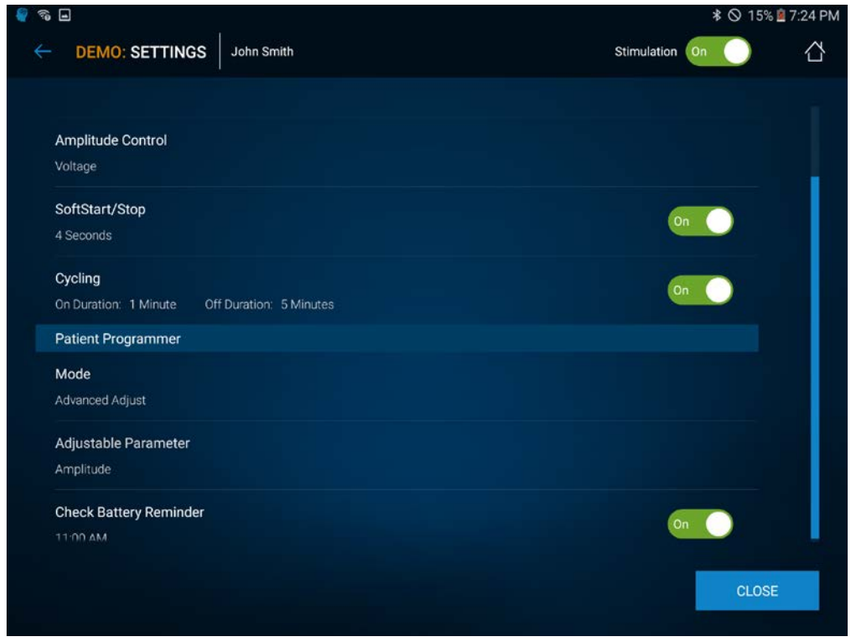
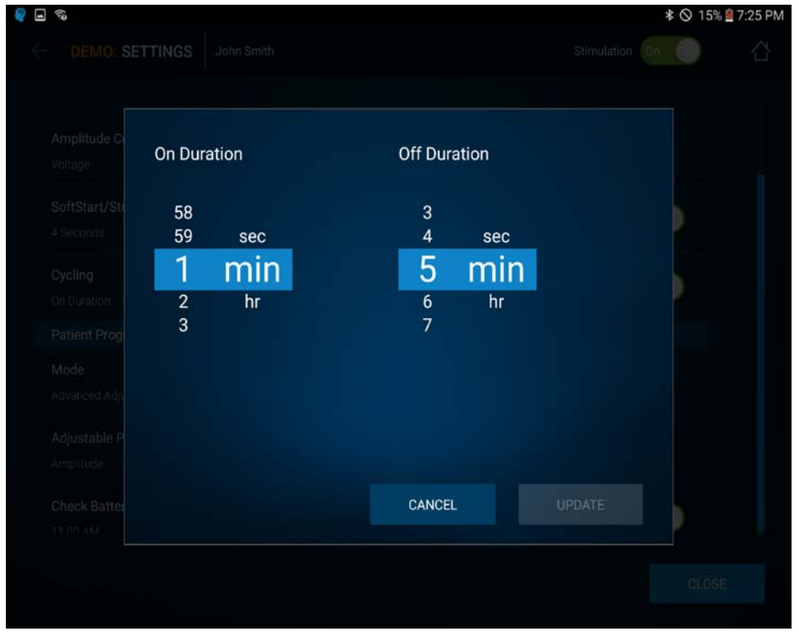
STIMULATION CYCLE OPTIONS
SETTING UP ON/OFF DURATION

- Minimum off or on time: 0.1sec
- Maximum off or on time: 24 hours
- SANTE Starting Parameters-Intervals:

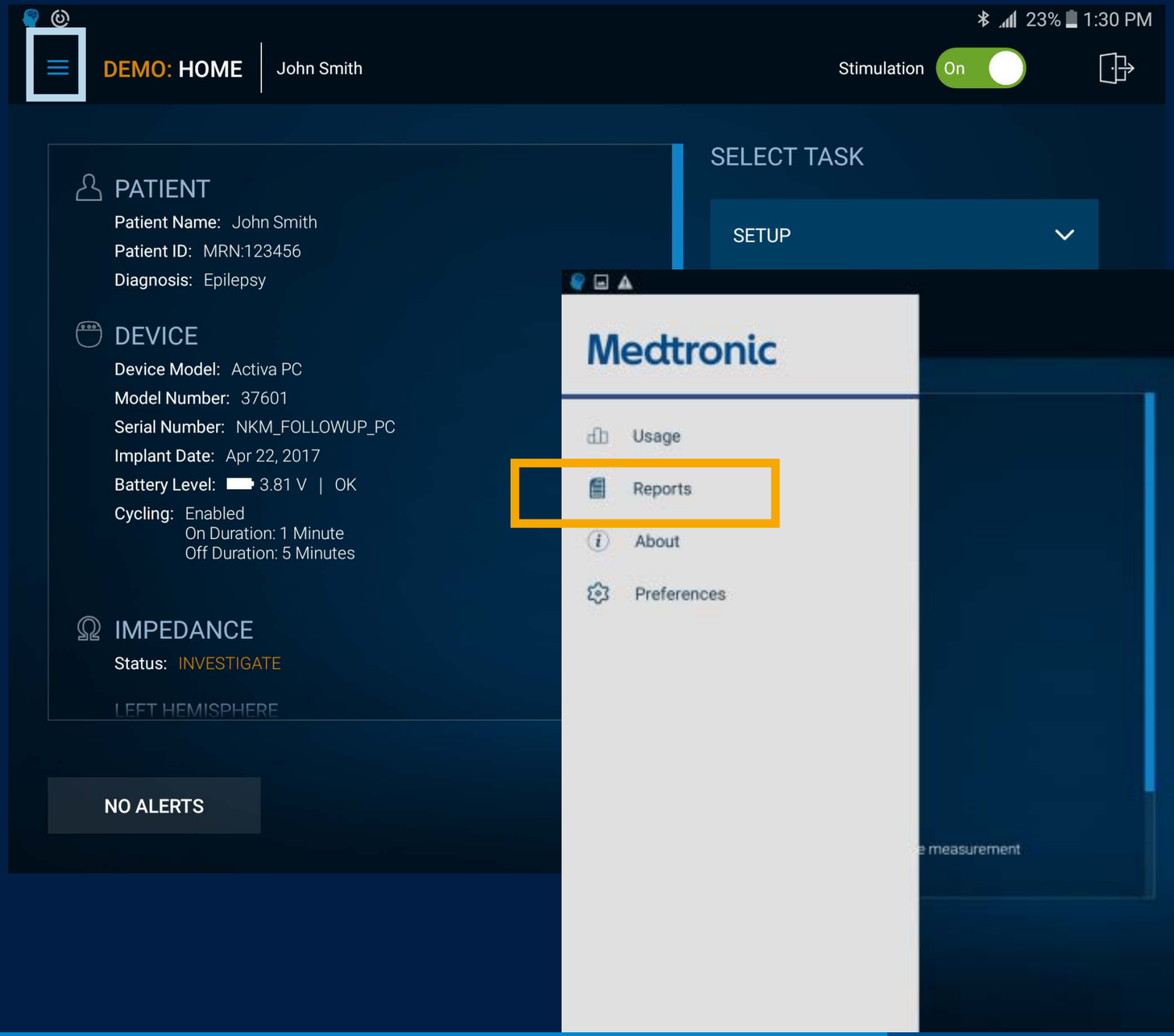
1 min on 5 Minutes off





* Enabling cycling at certain parameter settings may decrease the device longevity of non-rechargeable devices.

MENU OPTIONS



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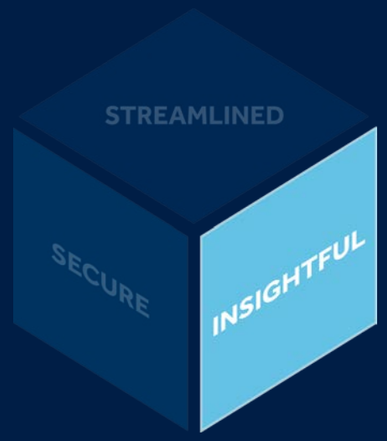
INSIGHTFUL
INFORMATION YOU NEED - REPORTS

Various report types



Session Report
[No name]
Activa PC NKM728744

Medtronic
Session Date:
Oct 24, 2018 1:35 PM

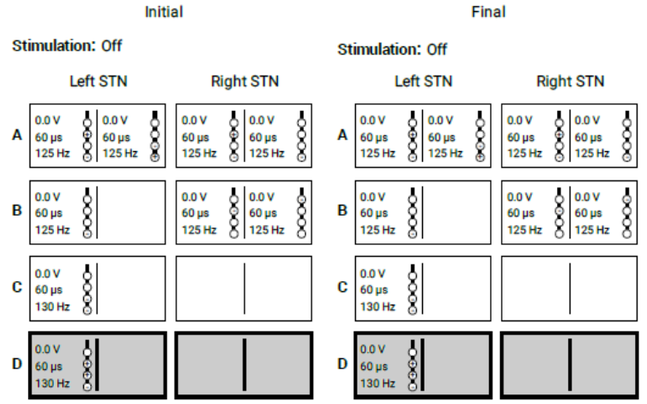
[No name]

Diagnosis:
Patient ID:

DEVICE

NEUROSTIMULATOR	Serial Number	Implanted
Activa PC	NKM728744	Oct 18, 2018
Model Number	**Firmware Version**	
37601	2.20	
Neurostimulator Location	**Battery Level**	
Chest Left	2.95 V | OK	

STIMULATION SETTINGS



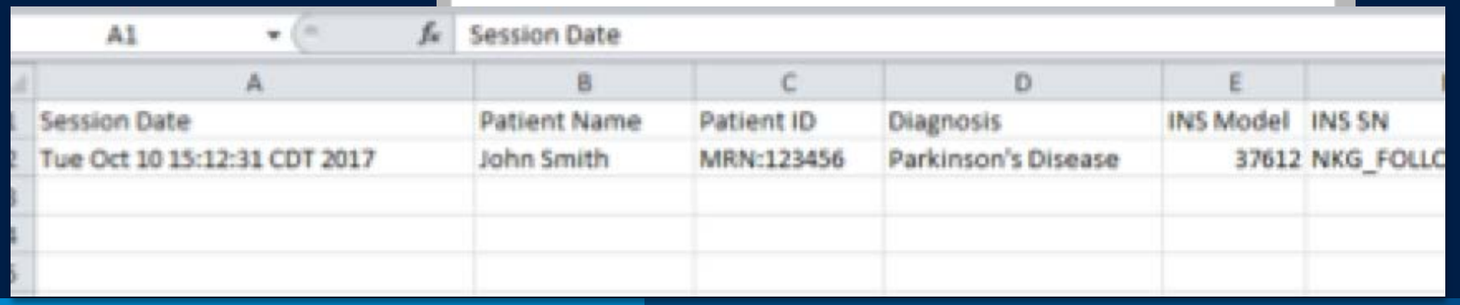
Oct 24, 2018 1:37 PM from Programmer RF2H300D6AE Page 1

Session Report
[No name]
Activa PC NKM728744

Medtronic
Session Date:
Oct 24, 2018 1:35 PM

Clinician Notes

~:0/5 (0)
~X:5/5 (2)



A1 Session Date

	A	B	C	D	E	
1	Session Date	Patient Name	Patient ID	Diagnosis	INS Model	INS SN
2	Tue Oct 10 15:12:31 CDT 2017	John Smith	MRN:123456	Parkinson's Disease	37612	NKG_FOLLC

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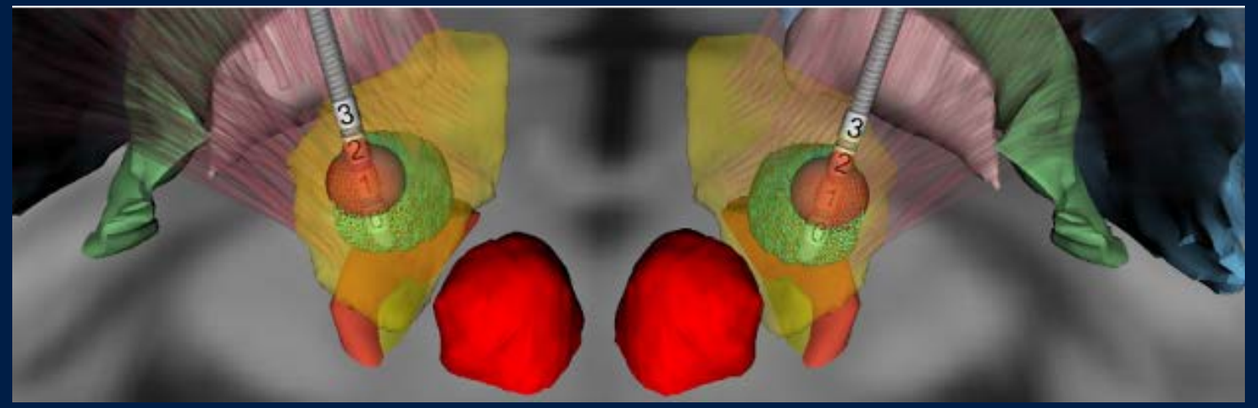
GOAL OF DBS PROGRAMMING

Deliver the therapy to the brain target of interest while minimizing stimulation of surrounding structures

- Using the lead electrode closest to the desired target provides maximal benefit and minimizes stimulation-induced adverse effects
- Setting appropriate stimulation parameters ensures that the desired brain target, but not adjacent structures, receives the stimulation



DBS PROGRAMMING ALGORITHM SAMPLE

INITIAL PROGRAMMING

Post-implant patient

Postpone initial programming 2-4 weeks to allow edema to subside

Maintain medication regimen

Establish Baseline Conditions

1. Assess surgical incisions
2. Assess patient seizure diary
3. Confirm leads
4. Review documentation of lead placement

Measure Impedance

Check and record impedance and current drain for each electrode

Initial Settings

1. Initial suggested settings are:
   a. Pulse width = 90µsec
   b. Rate = 145 Hz (maintain rate as invariable parameter)
   c. Amplitude = 5V
2. Record effects

Subsequent Programming Visits

1. Remind patient to use patient programmer seizure key.
2. Remind patients to bring seizure diary to subsequent visits to assess therapy effectiveness

SANTE PROGRAMMING
IMAGING , INITIAL SETTING, FOLLOW UP

Initial

- Obtained post-operative image to confirm lead location within the ANT
- From post-op imaging, identified electrode within the ANT and programed as the negative electrode (negative electrode exerts the therapeutic effect)
  - Most SANTE study patients with optimal lead placement are using electrodes 1/9 or 2/10 (with the most proximal electrode being located in the ventricle)
- Programed **rate (145 Hz**) and **pulse width (90 μs)**

Follow up

- Programming changes were restricted through the Unblinded phase of the study (Months 4-13) and AEDs remained stable.
- During the Unblinded phase (mo 4-13) , either voltage increases to **7.5 V** or rate increases to **185 Hz** were allowed, but not both.
- During the Long-term follow-up phase (beyond Month 13), there were no restrictions on programming or AED changes.
- In the Long-term follow-up phase parameters were changed at the discretion of the investigator.

SANTE LONG TERM PROGRAMMING/MEDICATION MANAGEMENT

CONCLUSIONS

- Patient selection is important for success and key learnings continues.
- Looking at the population as a whole, the protocol-specified programming **changes of increased voltage or increased frequency did not appear to reduce seizure frequency change from baseline.**
- Individual changes in programming did result in a benefit for some subjects, but these same changes routinely showed no benefit for other subjects.(i.e. cycling)
- DBS is indicated as an adjunctive treatment in combination with antiepileptic medications
- Epilepsy and comorbid conditions require ongoing medication management and titration

Care should be exercised when interpreting the effects of parameter changes. Parameter changes were not varied experimentally (ie, no randomization), and investigators/subjects self-selected for these changes. While some changes may have been made to try to improve efficacy, others may have been made to reduce side effects. For some subjects, multiple parameters were modified. It is therefore not possible to even directionally attribute any particular changes in parameters to changes in efficacy.

HOW IS DBS THERAPY FOR EPILEPSY DIFFERENT FROM OTHER DBS INDICATIONS?

Topic	DBS therapy for Epilepsy	DBS therapy for PD
Brain target	ANT	STN, GPi
Age of typical DBS candidate	30s-40s	60s +
Unilateral or bilateral stim per indication	Bilateral	Bilateral
Cycling	Yes	No
Awake vs Asleep	May be done asleep (Gen. Anaesth.)	Awake TEST STIM SUCESSFUL
Medication Use impact	No demonstrated change in AED use with DBS	Demonstrated reduction in med use with DBS
Other Neurostimulation devices	LivaNova (VNS), NeuroPace (RNS)	ABT, BSX (both DBS)
Other treatment path / positioning	Considered when resective surgery is NOT an option	lesion / permanent surgery (e.g. pallidotomy)

MRI

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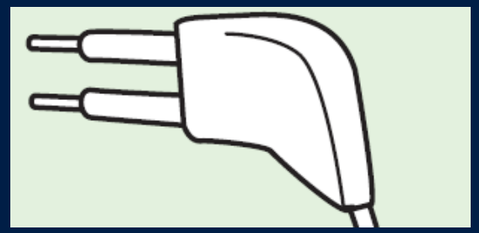
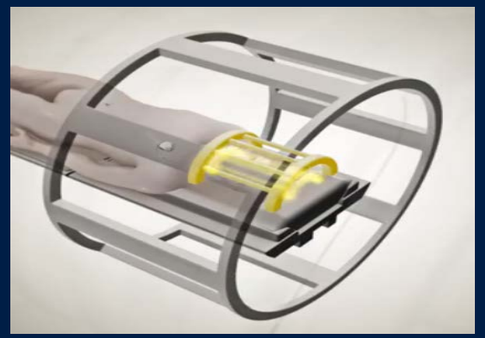
Further, Together

HEAD-ONLY MR PROTOCOL

- 1.5 T Horizontal Closed Bore
- RF Transmit/Receive Head coil (ONLY)
- ≤ 0.1 W/kg displayed avg Head SAR
- ≤ 200 T/m/s (Gradient Slew Rate)
- Approx. 64 MHz (RF Freq)
- Normal Operating Mode

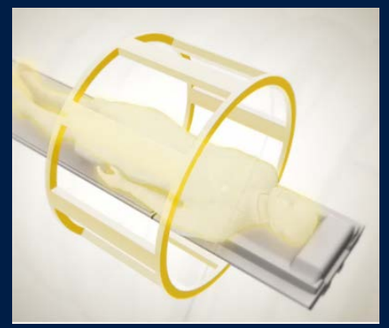


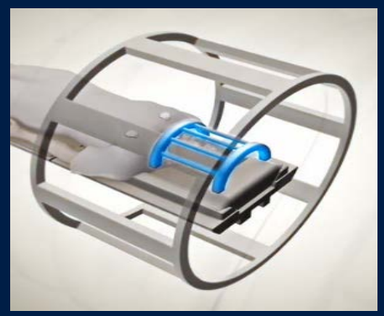


FULL BODY MR PROTOCOL

- 1.5T horizontal Closed Bore
- RF Built-in Body Coil or Head Transmit/Receive Coil, Quadrature Only, Any receive-only coil
- **≤ 2.0 µT B1+rms**
- If B1+rms is not available, a maximum RF power of 0.1 W/kg (0.05 W/lb) whole body and head SAR.
- Normal Operating Mode
- Maximum spatial gradient </= 19 T/m
- Approx. 64 MHz (RF Freq)
- Active scan time < 30 min within a 90 min window.

*Using a SAR setting may result in a more restrictive MRI scan





INS SETTINGS (HEAD-ONLY AND FULL-BODY SCAN)

PC with **NO** pocket Adaptor

Full Body Eligible

PC **WITH a pocket Adaptor**

Head Scan ONLY

Bipolar/Unipolar Defined

Table 2. Recommended neurostimulator settings (for all programs) for MRI

System type	Settings
37612, 37603, 37601 (no pocket adaptor implanted)	Unipolar configuration[a] — Turn therapy off. Bipolar configuration[b] — Keep therapy on or turn therapy off.
37612, 37603, 37601 (with pocket adaptor implanted)	Turn therapy off.
37602 **KINETRA**	Turn therapy off.
7428 **SOLETRA**	Turn therapy off. Disable magnetic (reed) switch. Disable day cycling.
7426	Turn therapy off. Set to bipolar configuration. Set amplitude to 0 volts.

[a] At least one electrode is negative and the case is positive, the other electrodes can be either negative or off.

[b] At least one electrode is positive, one electrode is negative, and the case is off.

BRIEF STATEMENT: MEDTRONIC DBS THERAPY FOR PARKINSON'S DISEASE, TREMOR, DYSTONIA AND EPILEPSY

Indications:

Medtronic DBS Therapy for Parkinson's Disease: Bilateral stimulation of the internal globus pallidus (GPi) or the subthalamic nucleus (STN) using Medtronic DBS Therapy for Parkinson's Disease is indicated for adjunctive therapy in reducing some of the symptoms in individuals with levodopa-responsive Parkinson's disease of at least 4 years' duration that are not adequately controlled with medication, including motor complications of recent onset (from 4 months to 3 years) or motor complications of longer-standing duration.

Medtronic DBS Therapy for Tremor: Unilateral thalamic stimulation of the ventral intermediate nucleus (VIM) using Medtronic DBS Therapy for Tremor is indicated for the suppression of tremor in the upper extremity. The system is intended for use in patients who are diagnosed with essential tremor or parkinsonian tremor not adequately controlled by medications and where the tremor constitutes a significant functional disability.

Medtronic DBS Therapy for Dystonia: Unilateral or bilateral stimulation of the internal globus pallidus (GPi) or the subthalamic nucleus (STN) using Medtronic DBS Therapy for Dystonia is indicated as an aid in the management of chronic, intractable (drug refractory) primary dystonia, including generalized and/or segmental dystonia, hemidystonia, and cervical dystonia (torticollis), in patients seven years of age or above.

Medtronic DBS Therapy for Epilepsy: 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 and, for Parkinson's disease and Essential Tremor, patients for whom test stimulation is unsuccessful. 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 they have 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 and, for Parkinson's disease and essential tremor, a potential risk to drive tremor using low frequency settings. Extreme care should be used with lead implantation in patients with an increased 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. Abrupt cessation of stimulation should be avoided as it may cause a return of disease symptoms, in some cases with intensity greater than was experienced prior to system implant ("rebound" effect). Onset of status dystonicus, which may be life-threatening, may occur in dystonia patients during ongoing or loss of DBS therapy. For Epilepsy, cessation, reduction, or initiation of stimulation may potentially lead to an increase in seizure frequency, severity, and new types of seizures. For Epilepsy, symptoms may return with an intensity greater than was experienced prior to system implant, including the potential for status epilepticus. Patients using a rechargeable neurostimulator for Parkinson's disease or Essential Tremor should check for skin irritation or redness near the neurostimulator during or after recharging, and contact their physician if symptoms persist. 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 Movement Disorders and Epilepsy, although no direct cause-and-effect relationship has been established. For Epilepsy, 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 systems 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.

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BRIEF STATEMENT: MEDTRONIC DBS THERAPY FOR PARKINSON'S DISEASE, TREMOR, DYSTONIA AND EPILEPSY

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.

Safety and effectiveness has not been established for patients with previous surgical ablation procedures, dementia, coagulopathies, or moderate to severe depression, or patients who are pregnant. Parkinson's disease and essential tremor: safety and effectiveness has not been established for patients under 18 years or patients with neurological disease other than idiopathic Parkinson's disease or Essential Tremor. Essential tremor: safety and effectiveness has not been established for bilateral stimulation or for patients over 80 years of age. Dystonia: age of implant is suggested to be that at which brain growth is approximately 90% complete or above. Epilepsy: 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.

Humanitarian Device (Dystonia): Authorized by Federal Law as an aid in the management of chronic, intractable (drug refractory) primary dystonia, including generalized and/or segmental dystonia, hemidystonia, and cervical dystonia (torticollis), in patients seven years of age or above. The effectiveness of the devices for treating these conditions has not been demonstrated.

USA Rx only Rev 08/18

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THANK YOU

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