Brief Functional Descriptions of Medtronic Investigational Research Tools
For Consideration in Support of the NIH SPARC Initiative

The "Activa RC+S" *General Purpose* Research System
(for those interested in beta testing next-gen technology)

The Medtronic Implantable Research System, "Activa RC+S," will have capabilities similar to Activa RC, but limited to constant current stimulation. The system includes equivalent stimulation programming parameters (pulse width, rate, amplitude, modes) and the use of a new Research Programmer to enable distance telemetry (approximately 1m) and control both stimulation and sensing functions. The system is compatible with the same leads as the Activa RC/PC system (Model 3387, 3389, 3391, Restore family of pain leads, and the Resume-based electrode systems for investigational use); the extension is equivalent to the Model 37086 extension, in 40 and 60 cm lengths for two leads, or can support a 37082 extension for a full 4 electrode by 4 lead network configuration. Passive field potential sensing, evoked potential sensing, and inertial sensing capability are included in the Activa RC+S research system. Sensing and accelerometer operation is controlled and its data managed with a User-intuitive Research Programmer, and the telemetry speed is being enhanced compared to the Activa PC+S. Closed Loop algorithms can be explored with the addition of the Nexus Algorithm Toolkit (described below). Sensing and inertial performance is summarized as follows:

LFP/ECoG Sensing		Embedded Algorithm Characteristics	
Operating Power Dissipation (Time Domain)	5µW/channel	Algorithm Power	<5µW/channel (embedded)
Operating Power Dissipation (Spectral Mode)	500nW/channel	Algorithm Type (Embedded)	Support Vector Machines, State Machines, etc
Typical Function modes	Time domain/Fourier Transforms in DSP	Algorithm Upgrade Capability	In-vivo through telemetry and embedded bootloader
MUX, channels available PC Dual Lead Implant System Assumed	Input mux allows 16 → 4 down-selection of best channels for upload	**Memory Buffer (Monitoring Diagnostics)**	
Minimal Detectable Signal	<200nVrms	SRAM	250kb
Spot Noise Spectral Density	<150 nV/√Hz	**Stimulation Capability**	
Bandpower Center Frequency	dc to 500Hz	Stimulation Channels	8 for bilateral (4/lead) (unipolar/bipolar)
Bandwidth of Spectral Estimate	1-20Hz (FFT determined)	**Inertial Sensor**	
CMRR/PSRR	>80dB	Operating Power (3-axis Measurement)	2µW
High Pass Corners	0.05-8Hz	Inertial Algorithm Power Dissipation	25µW (posture, activity, tremors, etc)
Input Range (Stim compliance)	> +/-10V	Sensitivity	125mV/g (.01g/LSB)
Telemetry and Recharge Intervals		Dynamic Range	+/-5g (Falls, footsteps, high impact activity)
Data Rate	195kbits/s	Noise (X,Y axis)	3.5 mg$_{RMS}$ (0.1-10Hz)
Data Capacity	4 channels preprocessed	Noise (Z axis)	5 mg$_{RMS}$ (0.1-10Hz)
Data Streaming capability	4 Time Domain at 250 or 500Hz, 2 Time Domain at 1kHz	Nonlinearity and Sensing Floor	<1%, 10mg any axis
Recharge Interval (100% streaming)	>24hrs	Shock Survival	>10,000g

Full details of the implantable system will be available in the paper: D Bourget *et al* 2015 *IEEE Neural Engineering Conference Proceedings*.

Nexus Systems (-D [distributed] and –E [embedded])

The Nexus Systems are meant to serve as an investigational algorithmic development tool for first principled approaches to closed loop systems. The Nexus-D System is a data conduit (i.e., bi-directional data port) that transmits data for the current Activa PC, RC, RC+S, RestoreSensor to a host computer. It transmits real-time sensing data and allows a host computer to update the neurostimulator's stimulation parameters based on real-time analysis of the sensor data by the host computer. All decisions regarding stimulation updates are made by a host computer which is outside the boundaries of the Nexus-D System, using algorithm prototyping environments such as Matlab or C#. This functionality provides the ability for research sites to explore potential closed-loop therapy algorithms in a flexible manner to assess the feasibility of closed loop therapy adjustment. The Nexus-E system allows for firmware upgrades to the system for algorithms that are shown promising using the Nexus-D. This frees up the restrictions imposed by the computer-in-the-loop, but also brings about additional risk mitigations that the investigator should consider.

D/Nexus-E System for stimulation and sensing performance specifications.

Further description of the architecture and capability of Nexus are available in the paper: Afshar P., et. al. *Frontiers in Neural Circuits 2012; 6: 121*.

("Synapse") Firmware Upgrades for Novel Stimulation Pattern Generation

This capability provides an investigational neurostimulation system that seeks to meet a key need for translational neuroengineering: the exploration of how the nervous system responds to different patterns of actuation. Many common patterns of neurostimulation were derived empirically, and there remains a need to better understand the transfer functions of the nervous system. By allowing a more flexible and complete investigation of potential stimulator patterns, we hope this research system may yield insight into more effective patterns of neurostimulation in the future.

The components of this system include a User Interface executing on a Windows PC and a customized telemetry head for interfacing to a chronically implantable stimulator. Stimulators that are currently supported include the Activa RC+S, PC, SC, and RC as well as the Restore-family of devices. The implantable stimulator consists of a commercially available implantable device, such as an Activa PC, running temporary research firmware. For assurance of research compliance, there is an access code generator to restrict the use of the system to approved investigational studies. The system can be used with a range of implantable devices which allows for exploration of several neural circuits in the brain, spinal cord, etc. The key functional feature of this research system is to expand the technological capabilities for stimulation patterns beyond what is commercially available.

These capabilities include:
- Expanded parameter ranges and resolutions for amplitude, frequency and pulse width
- Biphasic and burst stimulation patterns
- Stochastic stimulation patterns (both random and constrained within set frequency boundaries)
- Sunset timer to self-remove capabilities upon completion of investigation

The architecture of the system segments the pattern generation in firmware from the stimulation actuation in hardware. The pattern generator can be driven by flexible neural codes that are achieved via a firmware upgrade through a wireless telemetry download. The download of these patterns and capabilities into the research system can be used to drive complex sequences. Patterns that can be generated include stochastic patterns, bounded spread spectrum, bursts, and look up tables. Once research is completed, the investigational firmware can be reverted back to market released firmware without undergoing another download.

A representative use case was recently reported at the IEEE Neural Engineering Meeting by the Courtine group at EPFL: *"Towards Corticospinal Neuroprosthesys to Restore Locomotion after Neuromotor Disorders or Injuries;"* this work provides an example of the systems capabilities.

RestoreSensor

The Medtronic Implantable System, RestoreSensor, is a commercially-available INS with an embedded accelerometer capable of adjusting stimulation in response to changes in position. The product includes stimulation capabilities, the use of the 8840 Clinician Programmer and software and Patient Programmers, and is compatible with Activa PC leads and extensions. For situations in which posture responsive stimulation is desired, the embedded algorithm used to determine patient position may be employed.

Accelerometer capability is included in the RestoreSensor INS. Sensing is controlled and its data managed with a user-intuitive Research Programmer. The Research Programmer will not adjust or control therapy. Likewise, the 8840 Clinician Programmer and the Patient Programmer will not adjust or control sensing. Sensing performance is summarized as follows:

Inertial Sensor	
Operating Power (3-axis Measurement)	$2\mu W$
Inertial Algorithm Power Dissipation	$25\mu W$
Sensitivity	125mV/g (.01g/LSB)
Dynamic Range	+/-5g (Falls, footsteps, high impact activity)
Noise (X,Y axis)	3.5 mg$_{RMS}$ (0.1-10Hz)
Noise (Z axis)	5 mg$_{RMS}$ (0.1-10Hz)
Nonlinearity	<1%
Shock Survival	>10,000g
Telemetry	
Physical Layer	Established 175kHz (ISM)
Data Capacity	4 DOF/preprocessed
Training Mode	2 DOF/ raw high data rate
Stimulation Capability	
Stimulation Channels	16 for bilateral (8/lead) (bipolar)
Stimulation Parametrics	Predicate Approved (RestoreSensor)
Embedded Algorithm Characteristics	
Algorithm Power	$5\mu W$/channel (typical)
Algorithm Type (Embedded)	Support Vector Machine (Linear kernel, 4DOF)
Algorithm Upgrade Capability	In-vivo through telemetry and embedded bootloader

Characteristics of the posture response capability are available in the paper: Denison T., Litt B. *Neuromodulation 2014*;17(suppl 1):48-57

Sacral Neuromodulation

Medtronic Sacral Neuromodulation, delivered by the InterStim® System, offers long-term control of bladder control and bowel control symptoms through modulation of the nerves that help control the pelvic floor and lower urinary tract.The implantable neurostimulation system uses a neurostimulator and lead to send electrical pulses to an area near the sacral nerve to help normalize neural activity from the bladder or bowel to the brain. The stimulation parameters are controlled by external, handheld clinician and patient programmers.

http://professional.medtronic.com/pt/uro/snm/prod/index.htm#.VvcZqE32Y5s

Enterra Neurostimulator for Gastric Electrical Stimulation

The Enterra® gastric neurostimulator is a multiprogrammable device designed to deliver therapy through gastric electrical stimulation when connected to a lead system. It uses mild electrical pulses to stimulate the antrum portion of the stomach muscle wall, which may reduce the symptoms of nausea and the number of vomiting episodes related to gastroparesis.[1]

References

1. Abell T, McCallum R, Hocking M, et al. Gastric electrical stimulation for medically refractory

http://professional.medtronic.com/pt/gastro/ges/prod/enterra-gastric-neurostimulator/index.htm#.VvcaUU32Y5s

LINQ

Medtronic Reveal LINQ Model LNQ11 Insertable Cardiac Monitor – The Reveal LINQ ICM is a small, leadless device that can be implanted under the skin. The device uses 2 electrodes on the body of the device to monitor subcutaneous electrical activity continuously. The device memory can store up to 27 min of ECG recordings from automatically detected arrhythmias and up to 30 min of ECG recordings from patient-activated episodes. The system provides 3 options for segmenting the patient-activated episode storage: up to four 7.5 min recordings, up to three 10 min recordings, or up to two 15 min recordings. Arrhythmia detection parameters are set to pending automatically, based on patient information entered on the programmer during pre-implant device setup: the patient's Date of Birth and the clinician's Reason for Monitoring the patient. Arrhythmia detection parameters can also be programmed manually by the clinician.

This device is commercially available and is indicated to monitor patients with clinical syndromes or situations at increased risk of cardiac arrhythmias and patients who experience transient symptoms that may suggest a cardiac arrhythmia.

Parameter	Programmable values	Shipped value	Nominal/Reset value
Reason for Monitoring a	Syncope; Palpitations; Seizures; Ventricular Tachycardia; Suspected AF; AF Ablation; AF Management; Stroke; Other	—	Other
Device Date/Time…b	(Enter current date and time)	Current time (manufacturing time zone)	Not applicable / 1 Jan 1994
Wireless Transmission Time…c	00:00 ; 01:00; 02:00 … 11:00; 12:00; 13:00 … 23:00	00:00 (midnight)	00:00 (midnight)
Wireless Data Priority	Brady, Tachy, Pause; Brady, Pause, Tachy; Tachy, Brady, Pause; Tachy, Pause, Brady; Pause, Tachy, Brady; Pause, Brady, Tachy	Pause, Tachy, Brady	Pause, Tachy, Brady
Device Data Collection d	On	Off	On

a Reason for Monitoring is used to set arrhythmia detection parameters to pending automatically.
bThe times and dates stored in episode records and other data are determined by the Device Date/Time clock.
c Wireless Transmission Time programming is based on the Device Date/Time clock.
dTurning on Device Data Collection enables sensing and data collection (all episode types). After being turned on, Device Data Collection cannot be turned off.

Considerations for fMRI Investigational Technology Support

Background: The mechanism of action for neuromodulation therapies remains unclear[1,2]. Rapidly developing functional magnetic resonance imaging (fMRI) techniques enable functional connectivity networks to be characterized in human brain and are likely to help be critical tools for elucidating mechanisms and for optimizing stimulation parameter settings. Several technical challenges have prevented the widespread application of fMRI in human patients receiving neuromodulation therapies. First, existing product labeling restricts scanning to low-field (1.5T) scanners that are poorly suited to blood oxygen level dependent (BOLD) based fMRI techniques. 3T is the standard field strength for clinical fMRI since it is a signal-to-noise limited technique and functional sensitivity increases super-linearly with increasing static field (B_0)[3]. Second, characterizing the task-based BOLD response in patients requires precise synchronization of periods of stimulation 'ON' and stimulation 'OFF' with MRI scanning. This is challenging with limited tools available in the physician programmer, consequently, the few reports of task-based fMRI studies on DBS patients report using externalized leads connected to a switched pulse generator located outside of the scanner[4,5]. Most importantly, detecting the BOLD signal from an echo planar image (EPI) time series requires extensive post-processing to correct for image artifact due to subject motion and magnetic field variation.[6,7]

To address this research need, Medtronic will consider providing technical support to researchers that seek to elucidate the mechanisms of neuromodulation therapies or improve effectiveness by combining off-label 3T fMRI functional network analysis with Medtronic neuromodulation systems employing Vectris leads (http://professional.medtronic.com/pt/neuro/scs/prod/vectris-mri-leads/#.Vv522vkrJD8); this work is subject to approval of the investigator-initiated proposal by the Medtronic Clinical Research Review Board. Pending approvals, Medtronic will provide *ad hoc* patient safety analysis for specific off-label 3T fMRI protocols identified in investigator-initiated proposals to support the Clinical Research Review Board evaluation and master file submission. To help support research protocols, Medtronic will also explore hardware tools that will allow synchronizing periods of stimulation 'on' and stimulation 'off' with the fMRI acquisition and to develop 3T fMRI image artifact characterization and mitigation methods for both task-based fMRI and resting state (rs-fMRI) for approved investigational research of implanted patients. The intent of these activities is to assure patient safety for specific, approved, off-label 3T fMRI studies, with a goal to facilitate generation of high quality and reliable functional network data that may guide future therapy delivery initiatives such as identifying novel stimulation patterns and developing algorithms for parameter set optimization.

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[1] Dostrovsky JO, Lozano AM, Mechanism of deep brain stimulation. Mov Disord 2002;17 (suppl 3):S63-S68.

[2] McIntyre CC, Savasta M, Kerkerian-Le Geoff L, Vitek JL. Uncovering the mechanism(s) of action of deep brain stimulation: activation, inhibition, or both. Clin Neurophysiol 2004; 115(6):1239-1248.

[3] Van der Zwaag W, Francis S, Head S, Peters A, et. al. fMRI at 1.5, 3 and 7T: characterizing BOLD signal changes. NeuroImage 2009;47:1425-1434.

[4] Arantes PR, Cardoso EF, Barreiros MA, Teixeria MJ, et al. Performing functional magnetic resonance imaging in patient with Parkinson's disease treated with deep brain stimulation. Mov Disord 2006;21:1154-1162.

[5] Jech R, Urgosik D, Tintera J, Nebuzelsky A, et al. Functional magnetic resonance I aging during deep brain stimulation : a pilot study in four patients with Parkinson's disease. Mov Disord 2001;16 (4):1126-1132.

[6] Power JD, Schlaggar BL, Petersen. Recent progress and outstanding issues in motion correction in resting state fMRI. NeuroImage 2015;105:536-551.

[7] Kasper L, Bollmann S, Vannesjo JS, Gross S, et. al. Monitoring, analysis, and correction of magnetic field fluctuations in echo planar imaging time series. Magn Reson Med 2014 (ahead of print).