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PAPER

Comparison between patient-specific deep brain stimulation simulations and commercial system SureTune3

Johannes D Johansson^{1,2} and Peter Zsigmond³¹ Department of Biomedical Engineering, Linköping University, 581 85 Linköping, Sweden² Center for Medical Image Science and Visualization (CMIV), Linköping University, 581 85 Linköping, Sweden³ Department of Neurosurgery and Department of Biomedical and Clinical Sciences, Linköping University, 581 85 Linköping, SwedenE-mail: johannes.johansson@liu.se**Keywords:** electric conductivity, finite element method (FEM), volume of tissue activated (VTA), deep brain stimulation (DBS)**Abstract**

Objective. Software to visualize estimated volume of tissue activated (VTA) in deep brain stimulation assuming a homogeneous tissue surrounding such as SureTune3 has recently become available for clinical use. The objective of this study is to compare SureTune3 with homogeneous and heterogeneous patient-specific finite element method (FEM) simulations of the VTA to elucidate how well they coincide in their estimates. **Approach.** FEM simulations of the VTA were performed in COMSOL Multiphysics and compared with VTA from SureTune3 with variation of voltage and current amplitude, pulse width, axon diameter, number of active contacts, and surrounding homogeneous grey or white matter. Patient-specific simulations with heterogeneous tissue were also performed. **Main results.** The VTAs corresponded well for voltage control in homogeneous tissue, though with the smallest VTAs being slightly larger in SureTune3 and the largest VTAs being slightly larger in the FEM simulations. In current control, FEM estimated larger VTAs in white matter and smaller VTAs in grey matter compared to SureTune3 as grey matter has higher electric conductivity than white matter and requires less voltage to reach the same current. The VTAs also corresponded well in the patient-specific cases except for one case with a cyst of highly conductive cerebrospinal fluid (CSF) near the active contacts. **Significance.** The VTA estimates without taking the surrounding tissue into account in SureTune3 are in good agreement with patient-specific FEM simulations when using voltage control in the absence of CSF-filled cyst. In current control or when CSF is present near the active contacts, the tissue characteristics are important for the VTA and needs consideration. **Clinical.** trial ethical approval: Local ethics committee at Linköping University (2012/434-31).

Abbreviations

CSF	Cerebrospinal Fluid
DBS	Deep Brain Stimulation
EF	Electric Field magnitude
EF_t	Electric Field magnitude threshold for stimulation
FEM	Finite Element Method
ST	SureTune3
VTA	Volume of Tissue Activated

1. Introduction

Deep brain stimulation (DBS) is a well-established technique for alleviation of pathological neural activity

in e.g., Parkinson's disease, essential tremor, and cervical dystonia [1–3]. DBS of the anterior nucleus of the thalamus [4] has recently been introduced for medically therapy-resistant epilepsy. DBS is also under investigation for use in severe cases with poor medical response in psychiatric conditions such as major depression, obsessive-compulsive disorder, and Tourette syndrome [5–7].

One way to estimate the primarily affected area in the brain during DBS is to use computer simulations of the volume of tissue activated (VTA). The VTA can be estimated by simulations of individual axon activation or in a simplified manner by taking a threshold value of the electric field magnitude (EF). Regardless of the model used for the VTA, the estimated activation threshold is lower for longer pulse widths [8] and

larger axon diameters with faster signal conduction [9, 10]. The pulse width dependency is described by the chronaxie which is the pulse width at which the double pulse strength is required for axon stimulation and clinical effect compared to an infinitely long electric pulse. The chronaxie is relatively straightforward to measure experimentally in patients, see e.g. [8]. The axon diameter dependency on the other hand requires indirect estimates through modelling and simulation, see e.g. [9], or invasive single fiber recordings in animal experiments [10].

Currently available commercial systems with VTA estimation include GUIDE (Boston Scientific, USA) and SureTune3 (Medtronic, USA). GUIDE was originally developed by the McIntyre group at The Department of Biomedical Engineering at Cleveland Clinic Foundation, USA, under the name Cicerone [11]. The fundamental part of SureTune3 is originating from the Neuroengineering group at The Department of Biomedical Engineering at Linköping University, Sweden [9], and was further developed within the FP7 project IMPACT coordinated by Sapiens Steering Brain Stimulation B.V., The Netherlands, and thereafter transferred to Medtronic for further development and commercialization. SureTune3 is based on the simulation of different axon diameters [9] and visualizes estimated VTAs for 2, 2.5 and 3 μm outer axon diameters including the myelin sheet. Both GUIDE and SureTune3 are built upon pre-calculated results from finite element method (FEM) simulations assuming a homogeneous brain and do not take the different electric conductivities of different tissue types into account for voltage control. For current control, where tissue conductivity still affects the results even in a homogeneous surrounding, SureTune3 assumes an intermediate conductivity between grey and white brain matter.

The use of EF thresholds, EF_t , to estimate the VTA has previously been validated by comparing the spatial extent of the EF_t in FEM simulations of homogeneous tissue [9, 12] with the onset of noticeable side effects from known structures in clinical studies [13, 14] and with axon model stimulations [9, 15]. These FEM simulations assume a single homogeneous conductivity in the tissue around the DBS electrodes and

do not take the patient-specific electric conductivity into account.

The patient-specific electric conductivity from MRI classification into grey matter, white matter, blood, and cerebrospinal fluid (CSF) [16, 17] is taken into account in our FEM simulations of the electric field from DBS. Pulse width and axon diameter-dependent EF_t isolevels from FEM simulations are a convenient way to visualize the brain volume affected by the DBS and have for example been used in studies on DBS for Tourette Syndrome [18], the impact of cerebrospinal fluid (CSF)-filled Virchow-Robin spaces [19, 20] and different electrode lead designs [21]. A gratis open access compiled version of the software package for patient-specific DBS simulations used in this study has recently been released. It consists of a tissue classification application named ELMA and an application for EF simulations named DBSim [17]. The software is available for download at [22] and can be used by anyone to set up similar models and simulations as presented in this paper.

The aim of this study is to compare the tissue-independent VTAs from the commercial system SureTune3 with patient-specific FEM simulations where the tissue's electrical conductivity is considered in order to elucidate when a tissue-independent model is sufficient and when it is not.

2. Material and methods

In order to compare the two methods, simulations were performed with both SureTune3 and our FEM models using the same homogenous brain models, the same lead configurations, and stimulation parameters. In addition, simulations were performed with a heterogenous brain model (patient-specific) using the same parameter settings of the leads and stimulation. An overview of the varied parameters is given in figure 1.

2.1. FEM models of DBS in the brain

Models of the Medtronic 3389 lead were set up in COMSOL Multiphysics 5.4 (COMSOL, Sweden) with

a surrounding tissue domain of $80 \times 80 \times 100 \text{ mm}^3$. The electric field magnitude, EF , was calculated from the equation for steady currents,

$$\nabla \cdot (-\sigma \nabla V(\mathbf{r})) = 0 (\text{A/m}^3) \quad (1)$$

$$EF(\mathbf{r}) = |-\nabla V(\mathbf{r})| (\text{V/m}) \quad (2)$$

where σ is the electric conductivity of the tissue (S m^{-1}), V the electric potential (V) varying over space $\mathbf{r}$ (m). The outer boundary of the tissue domain was set to ground, i.e., $V = 0 \text{ V}$, corresponding to using the large implantable pulse generator case far away on the patient's chest as return electrode. In voltage control, the active contacts were assigned the corresponding electric potential. In current control, the active contacts were assigned the corresponding current divided by the number of active contacts. The inactive contacts were assigned to floating potential, modelling electrically inactive but highly conducting surfaces where the electric potential will be the same over the entire surface. Plastic surfaces of the lead were set as electric isolation. For more details of the FEM models, see e.g. [12, 23].

2.2. Homogeneous simulations

The parameters of the model were varied in all 81 possible combinations with 1, 2 or 3 active contacts, a voltage of 1, 3 or 5 V in voltage control mode, a current of 1, 3 or 5 mA in current control mode, a pulse width of 60, 120 or 240 μs , an axon diameter of 2 or 3 μm and a tissue conductivity of 0.123 S m^{-1} (grey matter) or 0.075 S m^{-1} (white matter) [24–26] when using current control mode. The contacts were activated from the lowest DBS contact (contact 0) for one active contact and upwards with contact 1 and finally 2 added (figure 1). For homogeneous tissue in voltage control mode, the conductivity value used does not affect the electric field and tissue type was thus not varied in this case.

Calculations of the VTA were performed in SureTune3 for the same settings as in the FEM models. The underlying FEM and axon stimulation simulations, whose results SureTune3 is based on, are described in detail in [9]. The design matrix for the varied parameters is presented in appendix A (tables A1–A3) together with the results.

2.3. Patient-specific simulations

Patient-specific simulations of 11 patients from Linköping University Hospital with a total of 18 leads operated for PD, ET or dystonia were also performed with the same method as above except that the electric conductivity $\sigma(\mathbf{r})$ was varied as a scalar function of space $\mathbf{r}$ and the patient-specific DBS settings were used. The simulations were approved by the local ethics committee at Linköping University (2012/434-31) and all patients gave informed written consent. This patient data has previously also been used for a study on impact of lead displacement. The electric

Table 1. Dependence of pulse width and outer axon diameter on electric field threshold, EF_t .

Pulse width (μs)	Outer axon diameter (μm)	EF_t (V/mm)
60	2	0.46
120	2	0.32
240	2	0.25
60	3	0.24
120	3	0.16
240	3	0.13

conductivity was assigned as a function of space based on the patients' preoperative T2-weighted MRI, assuming isotropic tissue. Tissue classification and conductivity assignment was performed using the software ELMA [16, 17] with blood being assumed to have a conductivity of 0.7 S m^{-1} and CSF assumed to have a conductivity of 2.0 S m^{-1} [24, 25]. Three of the leads had bipolar settings. In these cases, the outer tissue boundaries were set to electric insulation and the positive anode contacts to 0 V. The EF was scaled by a factor of 0.6 in all the tissue volume with an electric potential magnitude lower than the average electric potential magnitude in the entire tissue volume. This was done in order to account for that anodic (positive) stimulation is less effective than cathodic (negative) stimulation and requires about 70% higher stimulation current [27]. As no non-linear effects of the electric field are considered in the models, scaling the EF to an effectively lower value will have the same impact as scaling the threshold value EF_t . The individual patient parameters are presented in appendix B (table B1).

2.4. Data analysis

The VTAs from the FEM simulations were calculated as the tissue within an electric field threshold, EF_t , estimated from simulations by Åström *et al* [9], with a chronaxie of 100 μs to extrapolate EF_t for the pulse width of 240 μs [12] according to table 1.

The VTA volumes were then compared with volumes calculated in SureTune3 for the same settings. The relation between the simulated volumes was calculated with linear regression between VTA volumes from SureTune3 (ST), VTA_{ST} , and the VTA volumes from the FEM simulations, VTA_{FEM} . The regressions were calculated with the *regress* function in Matlab 2015a (Mathworks, US).

The VTA volumes were also exported from the FEM simulations and SureTune3 in voxels of $0.25 \times 0.25 \times 0.25 \text{ mm}^3$ for calculation of the Dice coefficient [28–31]. The Dice coefficient, D , was calculated as twice the common volume, i.e., the intersection $\cap$, between the two VTAs divided by the sum of the volumes.

$$D = \frac{2|VTA_{FEM} \cap VTA_{ST}|}{|VTA_{FEM}| + |VTA_{ST}|} \quad (3)$$

Examples of bipolar stimulation are given in figure 10.

3. Results

3.1. Homogeneous simulations

Examples of VTA contours for SureTune3 and FEM simulations are given in figure 2. Resulting VTA volumes from the homogeneous simulations are presented in the appendix A (tables A1–A3). The relation between the simulated volumes were $VTA_{FEM} = 1.3 \cdot VTA_{ST} - 26 \text{ mm}^3$ for voltage control, i.e., the smallest VTAs were larger in SureTune3 and the largest VTAs were larger in FEM. More specifically, all VTAs smaller than 60 mm^3 in SureTune3 were larger in SureTune3 and all VTAs larger than 800 mm^3 in SureTune3 were larger in the FEM simulations (figure 3). The relations for current control were $VTA_{FEM} = 0.77 \cdot VTA_{FEM} - 9.7 \text{ mm}^3$ in grey matter and $VTA_{FEM} = 1.6 \cdot VTA_{ST} - 14 \text{ mm}^3$ in white matter (figure 3). The impact from number of contacts, voltage, current, pulse width, and axon diameter are presented with median values in appendix C-table C1 and with distributions and Dice coefficients in figures 4–7.

The VTA volumes increased with number of contacts for voltage control but not for current control (figure 4). The VTA volumes increased with increasing stimulation strength for both voltage and current control (figure 5). The VTA volumes also increased with increasing pulse width, though not as much as with increasing voltage or current (figure 6). Finally, the VTA volumes were larger for larger axons (figure 7).

3.2. Patient-specific simulations

The relation between the simulated volumes in the patient-specific cases are presented in figure 8. The relation was $VTA_{FEM} = 1.3 \cdot VTA_{ST} - 9.1 \text{ mm}^3$ for 2 μ m axons and $VTA_{FEM} = 1.2 \cdot VTA_{ST} - 23 \text{ mm}^3$ for 3 μ m axons. One simulation was conspicuously outside the regression line and this corresponded to a patient with a 10 mm^3 CSF-filled cyst near the active contacts (figure 9).

4. Discussion

In this study, tissue-independent VTAs from the commercial software SureTune3 have been compared with tissue-specific FEM simulations. The objective of the study was to evaluate when patient-specific electric conductivity is of importance for the estimated VTA and when a homogeneous model without specific tissue considered, as in SureTune3, is sufficient.

4.1. Homogeneous simulations

For voltage control in homogeneous tissue, the estimated volumes are similar for the two systems with larger estimates in FEM for large volumes and larger estimates in SureTune3 for small volumes (figure 3(a)). This difference is due to that estimated activation thresholds EF_t are lower for lower voltage settings in the axon models SureTune3 and the FEM simulation EF_t s are based on [9]. Using a fixed EF_t for all voltages, as is done in the FEM simulations in this study, thus gives a smaller volume for the lowest voltages. It could have been expected that the axon model would have been the more accurate method here, but the constant EF_t for all voltages actually fits better to experimental estimates of VTA spread [9, 14]. For voltage control in homogeneous tissue, the underlying FEM model is otherwise the same for SureTune3 and the FEM simulations in this study [9]. The Dice coefficients are further lower for the comparisons of the smallest VTAs (figure 3). A reason for this is that SureTune3 considers the electrode lead itself as being part of the VTA whereas the FEM simulations leave a hole in the calculated VTA. The lead part corresponds to a very small volume of approximately 4 mm^3 and will not have much impact in larger VTAs. We believe leaving a hole in the VTA is more realistic as the lead has displaced the tissue there.

For current control however, the VTA volume becomes tissue-dependent. This is taken into account

in the FEM simulations but not in SureTune3. Grey matter has higher electric conductivity and thus lower resistance than white, and this means a lower voltage is required to obtain the same current as in white matter. This results in smaller VTA volumes in the FEM simulations compared to SureTune3 when using current control in grey matter (figure 3(b)) and larger volumes in the FEM simulations compared to SureTune3 when using current control in white matter (figure 3(c)). The larger differences in VTA volumes also reduces the Dice coefficients of the current control simulations compared to the voltage control (figures 3(d)–(f)).

One thing that is not clear in Medtronic's pulse generator manuals is that the current is split between the active contacts in current control mode. This may give a counterintuitive result for increasing the number of active contacts as in traditional voltage control mode it will increase the VTA volume as the voltage on the individual contacts remain unchanged. In contrast, the total VTA volume will remain relatively unchanged in current control mode as the individual voltage for the contacts are reduced in order to maintain the same total current (figure 4). For this reason, it is important to state the number of active contacts when comparing current and voltage control in clinical studies or when studying voltage control in general for proper comparison of the total energy used. On the other hand, the Vercise™ system from Boston Scientific uses multiple current sources for the contacts. In this case, current control functions more like traditional voltage control. Each contact has a separate

current source and adding extra contacts will not reduce the current on the others as in the case of a single current source assumed in this study.

Larger axons have lower EF_t and thus give larger VTA volumes, as can be seen in figure 7. A common EF_t to use for 60 μs pulses is 0.2 V mm^{-1} as this corresponds to the initiation of effects in experimental clinical studies [13, 14]. This corresponds to a slightly larger axon diameter of 3.4 μm [9] than used in this study where the thresholds for the axon diameters of 2 and 3 μm implemented in SureTune3 were used instead. It should be noted that all these diameters are among the larger axon diameters in the human brain and that typical axon diameters are much smaller. For example, the median inner axon diameter excluding myelin is around 0.5 μm in humans in a number of different white matter tracts [32, 33] and similar inner diameter distributions can be seen in the STN and GPi of rhesus monkeys, with somewhat smaller diameters in the GPi [34]. In humans, the most common outer diameter including myelin has been found to be 1.1 μm in the medullary pyramid tract [33] and 0.8–1.1 μm in the corpus callosum [35]⁴. It is thus expected that noticeable axon activation starts to occur around 0.2 V mm^{-1} but that higher EF will have a stronger effect as a larger fraction of the axons within the VTA should become activated by the DBS

⁴ It is not stated in the paper whether the inner or outer axon diameter was measured but the authors state that it was the outer diameter including the myelin sheath (personal communication with Prof. Bente Pakkenberg).

Figure 8. Comparison of patient-specific simulations. (a), (b) The relation between VTAs from SureTune3 (ST) and the FEM simulations is similar as in homogeneous tissue (figure 3a) except for one case where a CSF-filled cyst was present (figure 9). (c), (d) Dice coefficients between the VTAs were lower for the cyst case and for the bipolar stimulations.

Figure 9. VTA for 2 (red) and 3 μm (green) axons in patient-specific simulations in the FEM simulation with a 10 mm^3 CSF-filled cyst. The higher electric conductivity of the CSF distorts the electric field and thus the simulated VTA.

according to the axon models [15]. The commonly used outer axon diameter of 5.7 μm [36] originates from models of peripheral nerves in cats [37–39]. It

can be noted that the underlying single cable axon model for SureTune3 and the EF_t in this study estimates easier stimulation than the double cable

NEURON model used in e.g. [36], with the EF_t required for stimulation of $3.4 \mu\text{m}$ axons in the former being approximately equal to the EF_t required for stimulation of $5.7 \mu\text{m}$ axons in the latter [9, 39]. Experimental comparisons with isolated axons of known diameters with the models would be needed to determine which model is the most realistic, but given the extreme rarity of $5.7 \mu\text{m}$ axons, we lean towards believing more in the single cable model.

An interesting thing about the bipolar stimulation in both SureTune3 and the FEM simulations is that choosing two negative contacts and one positive gives a relatively even radial VTA extension along the height of the DBS lead (figure 10). This is in contrast to a more pear-like shape that would be the case for bipolar stimulation with one negative and one positive contact. The larger area on the negative side is in this case reducing the electric field magnitude and compensating for the stronger efficiency of cathodic stimulation compared to anodic. SureTune3 makes a VTA estimation with two completely separated regions around the negative and positive contacts (figure 10(a)). This is in contrast with the EF simulation from the FEM models (figure 10(b)) or simulations with individual axons [9, 21, 40, 41] where the VTA remains contiguous. Apart from that, the volume and shape are similar in SureTune3 and the FEM simulations.

4.2. Limitations

The axons in the simulations that form the basis for both SureTune3 and the FEM electric field thresholds EF_t are all assumed to be oriented in straight lines tangential to the active contact surface. It could be of interest to study other axon orientations such as e.g., axons beginning near the active contact and extending away in a radial direction or axons that bends. For example, Duffley *et al* [40] tested the assumption of axons with all possible orientations (called AF-3D) in a specific geometric point in addition to tangential orientation (called AF-Max). However, we believe the tangential orientation is the most representative one,

as an axon in a straight line always will be tangential to the contact surface when it is closest to it and thus experiencing the strongest electric field. The Duffley study also predicts a stronger stimulating effect on the anodic side when using all possible orientations and a weaker stimulating effect when using the tangential orientations. As the latter case agrees with experimental data confirming that anodic stimulation is weaker and require a stronger current [27], the Duffley study supports that the assumption of tangentially oriented axons is a reasonable one.

A parameter that is not taken into account in either the FEM models of this study or SureTune3 is the pulse frequency. In practice, increasing the pulse frequency from the standard 130 Hz does not strengthen the clinical effect much but lowering it can greatly reduce the efficiency or even reverse it [8]. The clinical effect of DBS could be caused by synaptic depletion [42, 43], which is not modelled in this study in either the FEM simulations or SureTune3. Impact of pulse frequency on synaptic response should be possible to include in the FEM models by a nonlinear scaling function for EF_t in a similar way as the scaling factor for the anodic side in bipolar stimulation. It would be of great interest to perform more experimental studies where the pulse frequency is varied to investigate such scaling function in detail and whether different functions are needed for different synapses.

Another parameter that is not included in SureTune3 or the FEM models in this study is perielectrode conductivity changes after implantation. Implantation of a foreign object in the body will result in a small inflammation and edema formation around it with increased electric conductivity. The edema will recede in time and be replaced with gliosis in the tissue with reduced electric conductivity. These changes have been found to result in measured impedance reduction during the first week after implantation followed by an impedance increase after one month [44]. Perielectrode conductivity changes can be included in

FEM models and have been used to estimate an enlarged VTA in the acute edema phase compared to the chronic gliosis phase [12, 31, 41, 45, 46].

5. Conclusion

In conclusion, the studied parameters in this study give similar results for SureTune3 and the FEM simulations for voltage control in tissue without CSF. For current control, the tissue conductivity affects the voltage required and thus the VTA. The presence of CSF in e.g., Virchow-Robin spaces affects the VTA also in voltage control. These tissue conductivity-dependent effects are not taken into account in SureTune3 but are included in patient-specific FEM simulations. Some caution should thus be exercised with the interpretation of the results from SureTune3 for current control or in the presence of CSF near the active electrode contact.

Acknowledgments

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Data availability statement

The data that support the findings of this study are available upon reasonable request from the authors.

Appendix A. Design matrices and results

Table A1. Voltage control in homogeneous tissue.

Homogeneous Voltage control			SureTune3	FEM		
Voltage (V)	Pulse width (μ s)	Number of active contacts	2 μ m axon VTA (mm ³)	3 μ m axon VTA (mm ³)	2 μ m axon VTA (mm ³)	3 μ m axon VTA (mm ³)
1	60	1	11.0	25.9	6.5	19.5
3	60	1	42.5	109.5	36.1	110.2
5	60	1	70.7	203.3	81.6	242.5
1	120	1	18.8	55.6	11.9	34.3
3	120	1	70.7	203.3	64.8	196.3
5	120	1	131.7	393.7	148.8	431.5
1	240	1	30.5	88.6	17.8	50.5
3	240	1	119.9	345.5	100.6	288.4
5	240	1	220.4	635.5	222.1	635.8
1	60	2	17.9	41.1	8.7	35.2
3	60	2	58.6	172.9	68.5	209.5
5	60	2	111.9	335.9	156	459.5
1	120	2	31.9	81.4	19.6	65.2
3	120	2	111.9	335.9	124.8	371.2
5	120	2	203.2	622.1	282.6	818.6
1	240	2	46.7	134.4	31.7	97.4
3	240	2	187.3	556	191.3	548.9
5	240	2	335.9	1032.6	420.7	1204.3
1	60	3	22.0	63.3	9.6	46.4
3	60	3	85.7	256.9	96.1	307.2
5	60	3	163.3	462.2	226.6	685.2
1	120	3	44.7	124.3	23.6	46.4
3	120	3	163.3	462.2	180.5	307.2
5	120	3	295.5	877.6	417.8	685.2
1	240	3	70.0	206.6	41.4	139.4
3	240	3	256.9	795.7	279.7	816.0
5	240	3	489.3	1381.6	625	1774.3

Table A2. Current control in grey matter.

Homogeneous grey matter			SureTune3		FEM	
Current control			2 μm axon	3 μm axon	2 μm axon	3 μm axon
Current (mA)	Pulse width (μs)	Number of active contacts	VTA (mm^3)	VTA (mm^3)	VTA (mm^3)	VTA (mm^3)
1	60	1	12.0	29.6	5.4	16.5
3	60	1	46.4	122.1	30.6	92.9
5	60	1	78.8	236.1	67.6	205.9
1	120	1	21.1	62.3	10.1	29.1
3	120	1	80.7	234	54.8	166.8
5	120	1	143.4	442.4	126.1	364.6
1	240	1	35.0	99.6	15.1	42.9
3	240	1	133.7	387.2	84.3	244.9
5	240	1	237.4	704.1	188.4	538.7
1	60	2	13.3	29.4	1.7	12.5
3	60	2	40.3	124.8	28.3	89.5
5	60	2	75.2	229	66.8	204.4
1	120	2	23.7	55	6.1	26.7
3	120	2	74.4	229.2	53.829	163.6
5	120	2	141.4	426.3	121.7	362.1
1	240	2	33.7	91.7	11.0	41.6
3	240	2	124.8	373.1	81.6	244.1
5	240	2	229	688.6	186.3	534.7
1	60	3	11.6	31.6	0.4	7.7
3	60	3	46.5	127.1	20.7	83.4
5	60	3	80.7	240.9	60.3	195.1
1	120	3	22.5	61.4	2.4	19.0
3	120	3	80.4	243.7	46.9	155.1
5	120	3	151	437.9	115.4	359.4
1	240	3	36.1	95.3	6.5	34.5
3	240	3	133.6	401.3	75.6	237.0
5	240	3	240.9	748.1	177.3	535.8

Table A3. Current control in white matter.

Homogeneous white matter			SureTune3		FEM	
Current control			2 μm axon	3 μm axon	2 μm axon	3 μm axon
Current (mA)	Pulse width (μs)	Number of active contacts	VTA (mm^3)	VTA (mm^3)	VTA (mm^3)	VTA (mm^3)
1	60	1	12	29.6	12.1	35.1
3	60	1	46.4	122.1	65.8	201.1
5	60	1	78.8	236.1	151.3	442.6
1	120	1	21.1	62.3	21.6	62.6
3	120	1	80.7	234	122.9	355.6
5	120	1	143.4	442.4	269.2	775.5
1	240	1	35	99.6	32.2	96.1
3	240	1	133.7	387.2	184.0	527.6
5	240	1	237.4	704.1	404.1	1143.9
1	60	2	13.3	29.4	8.1	33.3
3	60	2	40.3	124.8	65.1	199.0
5	60	2	75.2	229	147.6	437.8
1	120	2	23.7	55	18.4	61.8
3	120	2	74.4	229.2	118.6	353.4
5	120	2	141.4	426.3	268.6	779.4
1	240	2	33.7	91.7	30.1	92.8
3	240	2	124.8	373.1	181.6	521.9
5	240	2	229	688.6	401.4	1147.6
1	60	3	11.6	31.6	4.1	26.1
3	60	3	46.5	127.1	58.6	190.2
5	60	3	80.7	240.9	140.3	436.9
1	120	3	22.5	61.4	12.0	55.3
3	120	3	80.4	243.7	112.4	350.5
5	120	3	151	437.9	262.9	778.6
1	240	3	36.1	95.3	22.7	86.5
3	240	3	133.6	401.3	172.7	522.3
5	240	3	240.9	748.1	398.4	1142.5

Appendix B. Patient-specific settings

Table B1. Patient-specific settings. The lead ID denotes patient number and lead side. Targets: ZI-Zona Incerta, GPi-Globus Pallidus interna, STN-SubThalamic Nucleus. *The VTA for M5 right includes a 10 mm³ CSF-filled cyst.

Lead ID	Target	Voltage (V)	Pulse width (μ s)	Number of active contacts	SureTune3	3 μ m axon VTA (mm ³)	FEM	3 μ m axon VTA (mm ³)
					2 μ m axon VTA (mm ³)		2 μ m axon VTA (mm ³)	
1 Left	ZI	1.4	60	1	15.0	44.6	11.9	33.9
2 Left	GPi	2.8	100	1	60.1	169.1	51.8	171.8
3 Left	STN	1.9	60	2	34.8	104.5	33.1	123.1
4 Left	ZI	1.6	60	1	16.3	56.7	14.6	38.5
5 Left	STN	1.8	60	2	37.6	133.7	27.4	93.2
6 Left	ZI	3.8	90	2	118.3	353.8	155.6	433.5
7 Left	STN	2.5	60	1	30.5	88.6	26.2	78.4
8 Left	STN	3.6	60	Bipolar 1+, 2-	33.1	85.5	40.8	91.0
9 Left	ZI	1.2	60	1	13.1	34.2	9.2	25.0
10 Left	ZI	1.7	60	1	18.4	58.1	16.3	45.6
1 Left	ZI	1.7	60	1	17.6	61.5	16.0	44.0
1 Right	ZI	3.4	60	Bipolar 1+, 2-	31.4	80.5	35.4	85.5
2 Right	GPi	2.8	100	2	*92.9	*266.8	*152.1	*552.9
3 Right	STN	0.2	60	2	0.0	0.0	0.0	0.1
5 Right	STN	1.8	60	2	37.6	133.7	27.4	105.2
7 Right	STN	2.0	60	1	22.2	70.7	20.4	55.6
8 Right	STN	3.6	60	Bipolar 1+, 2-	33.1	85.5	38.6	101.45
10 Right	ZI	1.7	60	1	18.4	58.1	15.9	44.8

Appendix C. Median results

Table C1. Median VTA values for different parameter settings.

Parameter setting	Median VTA _{FEM} (mm ³)	Median VTA _{ST} (mm ³)
1 contact-voltage control	91	99
2 contacts-voltage control	174	154
3 contacts-voltage control	253	232
1 contact-current control in grey	76	111
2 contacts-current control in grey	74	108
3 contacts-current control in grey	68	111
1 contact-current control in white	168	111
2 contacts-current control in white	165	108
3 contacts-current control in white	156	111
1 V-voltage control	33	46
3 V-voltage control	194	180
5 V-voltage control	426	336
1 mA-current control in grey	27	33
3 mA-current control in grey	84	126
5 mA-current control in grey	192	237
1 mA-current control in white	31	33
3 mA-current control in white	187	126
5 mA-current control in white	420	237
60 μ s-voltage control	89	78
120 μ s-voltage control	165	148
240 μ s-voltage control	251	239
60 μ s-current control in grey	45	61
120 μ s-current control in grey	85	111
240 μ s-current control in grey	131	181
60 μ s-current control in white	103	61
120 μ s-current control in white	193	111
240 μ s-current control in white	291	181
2 μ m-voltage control	96	86
3 μ m-voltage control	288	257
2 μ m-current control in grey	54	75
3 μ m-current control in grey	164	229
2 μ m-current control in white	119	75
3 μ m-current control in white	353	229

ORCID iDs

Johannes D Johansson <https://orcid.org/0000-0003-4910-0291>

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