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REVIEW ARTICLE

Stereotactic implantation of deep brain stimulation electrodes: a review of technical systems, methods and emerging tools

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Abstract Deep brain stimulation (DBS) has become increasingly important for the treatment and relief of neurological disorders such as Parkinson's disease, tremor, dystonia and psychiatric illness. As DBS implantations and any other stereotactic and functional surgical procedure require accurate, precise and safe targeting of the brain structure, the technical aids for preoperative planning, intervention and postoperative follow-up have become increasingly important. The aim of this paper was to give an overview, from a biomedical engineering perspective, of a typical implantation procedure and current supporting techniques. Furthermore, emerging technical aids not yet clinically established are presented. This includes the state-of-the-art of neuroimaging and navigation, patient-specific simulation of DBS electric field, optical methods for intracerebral guidance, movement pattern analysis, intraoperative data visualisation and trends related to new stimulation devices. As DBS surgery already today is an information technology intensive domain, an "intuitive visualisation" interface for improving management of these data in relation to surgery is suggested.

Keywords Stereotactic and functional neurosurgery · Deep brain stimulation · Neuroimaging · Safety

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Abbreviations

AC PC	Anterior and the posterior commissure
DBS	Deep brain stimulation
DTI	Diffusion tensor imaging
FEM	Finite element method
GPi	Globus pallidus internus
LDPM	Laser Doppler perfusion monitoring
MER	Microelectrode recording
PPN	Pedunculopontine nucleus
RF	Radiofrequency
SAR	Specific absorption rate
STN	Subthalamic nucleus
UPDRS	Unified Parkinson's disease rating scale
Vim	Nucleus ventrointermedius of the thalamus
Zi	Zona incerta

1 Introduction

Implantable neurostimulation devices have become increasingly important as tools for the improved treatment of neurological disorders. Technological advances have made it possible for patients suffering from a wide range of neurological symptoms to receive effective relief by means of cochlear implants, cortical and deep brain stimulators, and systems for spinal cord, vagus and gastric nerve stimulation [102]. Among these techniques, deep brain stimulation (DBS) has become one of the most important interventional methods in functional neurosurgery today, and more than 40,000 DBS implant procedures have been performed worldwide [11]. Research on DBS is currently being performed in many clinics, and over 4,400 scientific publications (PubMed, April, 2010) related to DBS have

been published, but only very few of them are technical ones.

Other interventional methods used for similar therapeutic purposes are radiofrequency (RF)-lesioning [48, 73], targeted drug therapy and neural cell grafting [74]. RF-lesioning is sometimes suggested as an option together with DBS in order to tailor the patient treatment [16, 41]. Targeted drug therapy and neural cell grafting are procedures assumed to have major potential applications for the future though it has not yet become established clinically. Thus, DBS implantation is expected to remain the main surgical mode of treatment for Parkinson's disease and related movement disorders for at least the next decade.

As DBS implantations and any other stereotactic and functional intervention procedure require accurate, precise and safe targeting of the brain structure for optimal clinical outcome, the technical aids have become increasingly important. The concept of stereotactic and functional neurosurgery has a history back to the 1940 [36] when the first lesioning procedures were commenced due to the development of stereotactic frames and later on the introduction of brain atlases with well-defined landmarks. Recent improvements of biomedical imaging and intraoperative measurement techniques have contributed to a fast increase in the number of stereotactic procedures and thus DBS implantations. The aim of this paper was to give an overview, from a biomedical engineering perspective, of the current technical aids and future trends in stereotactic DBS implantation procedures.

2 Target areas and clinical symptoms in deep brain stimulation

As the target area, often located in the basal ganglia or thalamus, is usually only slightly larger than the DBS-electrode itself (diameter 1.27 mm Medtronic Model 3389, while the target diameter ranges from a few mm to about 1 cm), the positioning of the electrode is of utmost importance if an optimal clinical outcome, with minimal side-effects, is to be achieved. The structures deep within the brain that are commonly used as targets for the reduction of motor Parkinsonian manifestations are, for tremor and rigidity, the subthalamic nucleus (STN); for tremor alone, the nucleus ventrointermedius of the thalamus (Vim); and for rigidity, for L-DOPA-induced dyskinesia or for dystonia (characterised by involuntary muscle contractions), the globus pallidus internus (GPi). Depending on the particular motor manifestations that are to be treated, other structures can be targeted as well, such as the zona incerta (Zi) or a thalamic subnucleus. Additional targets for deep brain stimulation are currently the subject of intensive research, and it can thus be expected that further types of neurological disturbances will become treatable with DBS. Examples of newer target areas include the pedunculopontine nucleus (PPN, for Parkinsonian manifestations such as impaired gait and balance) [106], the internal capsule (for obsessive–compulsive disorder) [23, 126] and Brodmann area 25 (for depression) [88, 126]. Other disorders that are under trial for DBS are epilepsy [124], Tourette syndrome [1, 126], cluster headache [80] and schizophrenia [92]. Thus, the future clinical applications of DBS are expected to include stimulation not just in the already identified targets, but also in a wide range of brain structures and nuclei, each target corresponding to a particular clinical manifestation or set of manifestations to be treated or reduced. The concept of DBS is thus expected to go towards a more general concept of "BS"—brain stimulation.

3 Surgical implantation and current supporting techniques

Until now Medtronic Corporation (Minneapolis, MN, USA) provides the only DBS system approved by the FDA for clinical use of Parkinson's disease and related movement disorders. This is expected to change in the future as several companies are known to do research and development in the area. The most commonly used DBS electrodes have four contacts (Medtronic's leads and electrode models 3389 and 3387). The voltage is often set at a value between 1 and 4 V; the frequency is set between 130 and 185 Hz; the pulse width is between 60 and 450 μs; and the stimulation mode can be mono- or bipolar. Uni- or bilateral implantation is used depending on symptoms and target areas. The surgical procedure is divided in two steps: the implantation of the DBS electrode and the pulse generator. This paper focuses on the DBS implantation. However, the way in which different clinical centres perform DBS electrode implantations often differs. In general, the procedure can be distinguished according to preoperative planning, surgical procedure and postoperative follow-up [85, 111, 123, 132]. Figure 1 summarises the current supporting techniques in form of a diagram. Figure 2 shows typical stereotactic planning and postoperative control images.

3.1 Preoperative planning

The first part is preoperative planning where the specific target in the brain and the trajectory to reach this target are planned on preoperative anatomical images**.** In general, fiducials are affixed to the skull of the patient via a stereotactic system in order to introduce a reference system to the images. Different frameless fiducial systems for DBS implantation have been described and compared with frame-based systems [9, 14, 26, 32, 60, 81, 110], but stereotactic

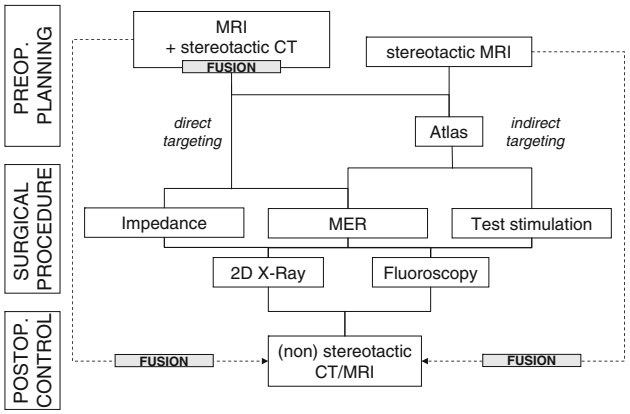

Fig. 1 Current supporting techniques for DBS surgery

frame-based systems remain the gold standard. In consequence, this article will concentrate on the procedures using the stereotactic frame. Comparing the implantation procedures in different clinical centres, differences in the preoperative part can especially be found in the stereotactic system, the imaging modality, the moment of image acquisition and the targeting technique.

Concerning the *stereotactic systems*, differences do exist such as the type of coordinate system used, either a Cartesian coordinate system with x, y and z coordinates (G frame, Leksell Stereotactic Systems®)[84] or a polar coordinate system describing the target by angles to horizontal and vertical plane and the distance to a reference point (Cosman-Robert-Wells CRW frame, Riechert-Mundinger frame) [70]. Furthermore, sometimes a phantom base exists to confirm accuracy of coordinate adjustment and integrity of the entire stereotactic system (CRW, Riechert-Mundinger frame). The coordinate calculation is usually performed with a commercially available stereotactic software: iPlan (BrainLab AG, Munich, Germany), SurgiPlan (Elekta Instrument AB, Stockholm, Sweden), Framelink (Medtronic Incorporation, Minneapolis, MN, USA) and STP (Stereotactic Treatment Planning System; Howmedica Leibinger GmbH, Freiburg, Germany).

Concerning the *imaging modalities*, ventriculography has historically been the gold standard based on its highly reliable identification of the anterior and the posterior commissure (AC, PC) used as references for atlas-based indirect targeting. Today it has been replaced by CT and MR imaging [111, 123]. MRI is the imaging modality of choice to visualise the anatomic targets. The sequence used depends on the chosen target structure: T_1 [24] or proton density imaging [57] is especially used for targeting of the globus pallidus; T_2 imaging for STN targeting [49, 111, 115]; inversion recovery images are also beneficial for direct targeting of GPi and STN [107]. Figure 2a shows a stereotactic T_2 MR image and 2b the planned trajectories.

Moments of image acquisition can be different. Some centres acquire stereotactic MRI on the day of implantation just before surgery [25], while others perform the MRI on the day before surgery and reposition the stereotactic frame on the day of surgery [79]. More often, an MRI is acquired some days before the implantation to be merged with a stereotactic CT on the day of surgery [95, 118].

Furthermore, there are two types of *targeting techniques*. The planning, i.e. the way the definition of entry point, trajectory and target takes place is sometimes based on MR or, CT and MR data alone [25, 49] which is called "direct targeting" (Fig. 2b). Other groups prefer using anatomical brain atlases created from dissected brains and superimposing them to the MRI ("indirect targeting") to improve the identification of nuclei in the thalamus or basal ganglia (e.g. STN, GPi), or other invisible or hardly identifiable structures of the deep brain. Modern versions of the Schaltenbrandt-Wahren and the Talairach atlases [99] as well as for Morel's atlas [96], a specific stereotactic atlas of the human thalamus and basal ganglia, are available for

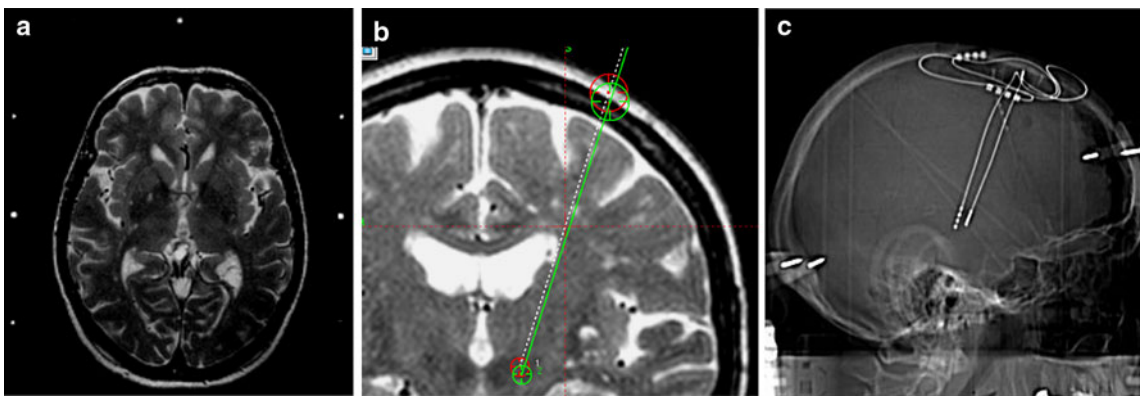

Fig. 2 **a** Stereotactic T_2-weighted 1.5 T axial MR image, **b** T_2-weighted 1.5 T MR image including the planned trajectories and **c** CT image with implanted electrodes in Vim and STN. CT and MR images to Figs. 2 and 5 have been used with kind permission from Patric Blomstedt MD, PhD, Department of Neurosurgery, Umeå University Hospital

computer use and as 3D image reconstructions. Another approach to perform an accurate 3D multiplane analysis is manual segmentation with the help of stereotactic books and 4.7 Tesla MRI anatomy software [79].

3.2 Surgical procedure

The second part of the procedure is the intervention itself. It can be performed under local or general anaesthesia depending on if the patient's feedback is needed for specific testing or not. In the first case, supplementary techniques are used to get additional information about the target area; in the latter, the DBS electrode is directly implanted at the target chosen during the preoperative planning phase.

For a number of reasons, including individual variability regarding brain anatomy, several problems may arise during a DBS implantation. One of these is the "brain shift" that occurs in conjunction with trepanation. It can cause a deviation from the pre-planned target coordinates resulting in suboptimal anatomical location with side disorders or with haemorrhage if the stereotactic probe injures a blood vessel [46, 67]. This is one of the reasons in addition to the varying brain anatomy why intraoperative measurements are often performed. Such complementary intraoperative data acquisition methods can be for example *impedance measurements* while creating the trajectory for the DBS electrode, giving an idea of the surrounding structures passed [72, 133]. Another often used method is *microelectrode recording* (MER) which is based on registering neuronal activity [28, 42]. Registration is recorded along 1–5 trajectories in the volume of interest to identify the different structure boundaries. In general, these measurements are performed in millimetre steps before reaching the target and often measurements even go beyond the target structure. Most centres using microelectrode recording perform, as well, *intraoperative stimulation* along the trajectory using the microelectrodes stimulating in the microampere range [26, 34, 118] or macroelectrodes stimulating in the milliampere range for example using RF- or DBS stimulation electrodes [14, 95, 115]. In general, this is done at the same measurement points as for MER to evaluate the clinical effects with increasing stimulation current and to determine symptom reduction, the clinical therapeutic and side effect thresholds at each measurement point.

The interpretation of all the intraoperative data in order to take a decision on the final surgical target is in general done by the neurosurgeon or neurologist by "mental imagination", i.e. interpreting mentally and combining the anatomic position of each measurement value with the results of MER and test stimulation including clinical efficacy, therapeutic stimulation threshold, side effects and stimulation range. During the surgery, some groups perform an intraoperative position control in order to check the absence of deviation of the electrode from the planned trajectory. This can be an intraoperative conventional 2D-X-Ray or a fluoroscopic control [25, 28, 112]. Some groups do compensation due to their experience.

3.3 Postoperative follow-up

Postoperatively, a control of the final electrode position and the absence of haemorrhage via CT or MRI [53, 108, 115] is commonly part of the protocol (Fig. 2c). This is then done directly after the implantation procedure with or without the frame on. Due to the electrode artefacts on the postoperative images hiding parts of the anatomical structures, pre- and postoperative images are often merged using stereotactic planning software—sometimes as well with anatomical atlases—in order to be able to identify the anatomical structures around each electrode contact. Furthermore, this image fusion is part of a quality control as it makes possible a comparison between the planned and the final electrode position.

The patient follow-up is as well part of the postoperative follow-up; it consists of regular consultations. Especially at the early stage, stimulation parameters have to be adapted individually: stimulated contacts, pulse width, frequency and voltage have to be programmed. When an ON/OFF effect (immediate disappearance and reappearance respectively of symptoms) exists, as is the case for tremor, many centres perform a test session where all the four electrode contacts are successively activated with increasing voltage to identify first the therapeutically effective contacts. Furthermore, the "symptom arrest threshold", i.e. the lowest voltage for which symptoms disappear, and the "side effect threshold", i.e. the lowest voltage for which side effects start to occur [28], can be determined. When the therapeutic effect is not immediate and may take days to several months, as for dystonia, a long lasting test period is needed in searching for the optimal stimulation parameters. In these cases, the choice of the first parameter configuration is based on experience and can be guided by the anatomic contact position, especially when postoperative MRI could be performed [25, 28].

4 Emerging techniques and future trends

Already today, DBS surgery is a technology-intensive domain. A high quantity of data is recorded before, during and after the intervention. Information technology is the key to improving management and visualisations of these data, and to implement new supporting technologies in order to optimise the trajectory planning and final stimulation target choice. Examples of emerging tools with great potential but still not established in clinical routine are patient-specific

electric field modelling and simulation, optical intracerebral measurements and quantitative indicators for intraoperative surgical planning and postoperative surgical outcome investigation of movement pattern. Furthermore, new stimulation systems and improved biomedical imaging technologies will play a significant future role. The "mental imagination" of neurosurgeons during surgery of the optimal stimulation target, based on anatomy and on the intraoperative measurements, is expected to be replaced by user-friendly visualising tools facilitating final target choice, "intuitive visualisation". Emerging techniques, not yet clinical routine, are briefly presented below.

4.1 Neuroimaging and navigation

During the last decade, biomedical imaging has gained more and more importance for surgical planning of deep brain stimulation surgery [132]. With the introduction of 3T MR scanners, it has become possible to further increase the image quality and resolution [119], and 7T images may follow in the future [21]. Nevertheless, the choice of the imaging sequence still remains essential to visualise the different targets as illustrated in Sect. 3 of this article.

In order to provide real-time image guidance, interventional MRI has recently been used in some centres performing DBS surgery. One approach is to use an open MRI, but due to low image quality of 0.2 T MRI scans, which are sub-optimal for anatomical localisation, image fusion with pre-operative higher quality scan is necessary [27]. Another approach is reported by Starr and colleagues [75, 87, 116]. They use a skull-mounted aiming device, the NeXframe system, in a standard configuration 1.5 T MR imaging unit, where also the entire surgical procedure is accomplished. In this way, surgical planning, guided implantation and final electrode position check is performed intraoperatively. Other alternatives to the traditional frames are the Eljamel-Tulley stereotactic cube [32] and the STarFix^{TM} microtargeting Platform [9, 26]. The STarFix^{TM} platform uses titanium anchors which are implanted into the patient's skull before imaging. Based on the results from high-resolution preoperative CT and MR images, a patient- and treatment-specific platform is constructed. During surgery, the platform is mounted on the anchors together with a guide tube which is used for insertion of the DBS electrode.

Concerning postoperative MR scanning there has been a considerable debate about the safety in patients with DBS systems. Following manufacturer guidelines [91], imaging is possible only with a 1.5 Tesla horizontal bore MRI, a transmit/receive head coil and when limiting the average head-specific absorption rate (SAR) to 0.1 W/kg or less even if this implicates a lower imaging quality. Otherwise heating, magnetic field interactions or induced stimulation for example can be the consequence [111]. Experiences from MRI of implanted deep brain stimulators on a large patient material have been presented by several groups [76, 98].

Diffusion tensor imaging (DTI) represents another possibility to obtain data using MRI. It is used to measure the water diffusion in multiple directions, which has been proposed to represent the electrical conductivity of the tissue, and can be used to visualise nerve bundles in the brain. For the moment, DTI is still in the state of evaluation, i.e. images are acquired preoperatively to deep brain stimulation, and they are analysed postoperatively concerning target position and interstructure connections [45, 100, 113].

Transcranial sonography has started to be applied for the placement of DBS electrodes in dystonic [125] and Parkinsonian patients [97]. Transcranial sonography can display echogenic deep brain structures such as the GPi in dystonic patients and the substantia nigra. Also the STN has been identified considering its topographic relationship with the substantia nigra [97]. For the moment, highly echogenic imaging artefacts of the metal parts of the electrode do exist.

4.2 Patient-specific models and simulations of the DBS electric field

The finite element method (FEM) has been used in order to develop computer models of DBS electrodes and to create simulations of the electric field surrounding DBS electrodes [4, 54, 89, 131]. The equation for steady currents is used in order to calculate the electric potential distribution in the vicinity of the electrode. The first generation of DBS models were used to visualise the electric field for different stimulation settings (monopolar and bipolar) and with reference to the pre-selected stereotactic target area and anatomy, e.g. the GPi [54] and the STN [89]. Other studies focused on the influence from tissue type in the vicinity of the stimulation area, e.g. cerebrospinal filled cysts [4] or the electrode-brain interface [130]. McIntyre et al. [89] also used FEM simulations together with an axon model in order to study the axonal tissue around the STN directly activated by DBS.

The second generation of modelling techniques is patient- and treatment-specific, i.e. based on individual input data and electrode settings [7, 18, 120]. Butson et al. [18] were, by using DTI as input for handling potential anisotropic tissue, able to study in detail the electric potential when stimulating in the STN. The technique has been further developed and used in patients in order to identify and visualise the theoretical volume of activated tissue around the STN [86, 93]. The activated volume around the GPi has been studied and visualised with a computational stereotactic model by Vasques et al. [120]. An approach based on

the individual patient's preoperative MR batch of images, in order to classify the electrical conductivity for different tissue types, has been developed by Åström et al. [7]. With the help of treatment-specific positioning of the DBS electrode in relation to the postoperative MR images, the method allows for investigations of the relative electric field changes in relation to anatomy and DBS settings (Fig. 3). The latter technique has been used for evaluation of speech intelligibility and movement in patients with Parkinson's disease where DBS electrodes were implanted in the STN [5].

4.3 Optical intracerebral measurements

Optical intracerebral measurement is a technique for real-time presentation of grey-white tissue boundaries during stereotactic procedures. A thin probe with dimensions adapted to the stereotactic system and with optical fibres aligned along the interior side of the probe towards the tip is connected to the optical system. The probe is used to create tracts for the DBS electrodes along the precalculated trajectories; at the same time as the reflected light intensity, i.e. tissue type is recorded, processed and displayed in real time.

In this manner, reflectance spectroscopy measurements in the near infrared region have been performed by several investigators in order to discriminate between white and grey brain matter during both experimental and clinical stereotactic neurosurgery [3, 38]. Up to date, the spectral measurements during clinical implantations of DBS electrodes have been used by Giller et al. [37] in more than 200 implantation procedures and also been compared with microelectrode recording. The concept developed by Wårdell and colleagues, which is based on both laser Doppler perfusion monitoring (LDPM) [127] and diffuse reflection spectroscopy [2], have been clinically evaluated on more than 50 DBS lead implantations and compared to impedance recordings [62]. This group extracts curve data from specific wavelength intervals, e.g. around 573 nm (blood content) and 780 nm (grey-white boundaries), the latter wavelength also applicable in the LDPM system, whereas Giller and co-workers are using the tilt of the curve within an interval in the near infrared region. Despite slightly different signal processing, both research groups present similar optical signatures along trajectories towards the STN and the thalamus. In general, all time-curves start with a low intensity value in cortex and increases to a maximum intensity value when passing the subcortical white matter. The last section differs depending on the target area aimed at. For the GPi a characteristic "double peak", representing light intensity changes during insertion through the white lamina surrounding the Putamen, GPe and GPi has been identified [62] (Fig. 4). This is possible due to the fact that white matter is more opaque than grey matter, and thus the white matter lamina in grey matter is easier to detect than grey matter nuclei in white matter.

In general, the light interaction with tissue, and thus the measurement depth, is affected by several aspects such as probe design, light source and the tissue's scattering and absorption characteristics. Experimental investigations and Monte Carlo simulations show that the optical sampling depth in brain tissue is less than 1 mm [63, 77, 109]. Qian et al. [109] studied the "look ahead distance" in brain matter by means of Monte Carlo simulation, and found that in the near infrared region and for small fibre separation, grey matter is expected to have a slightly increased "look ahead distance" than white matter. This was confirmed by Johansson et al. [63].

4.4 Movement pattern analysis

In order to make analysis of Parkinson's disease symptoms (tremor, bradykinesia, rigidity and postural instability) and dyskinesia more objective, several centres have introduced movement pattern analysis to their clinical evaluation procedure. It exists in a variety of laboratory-based systems to quantitatively measure and analyse body movement. This includes systems for movement analysis of dystonia

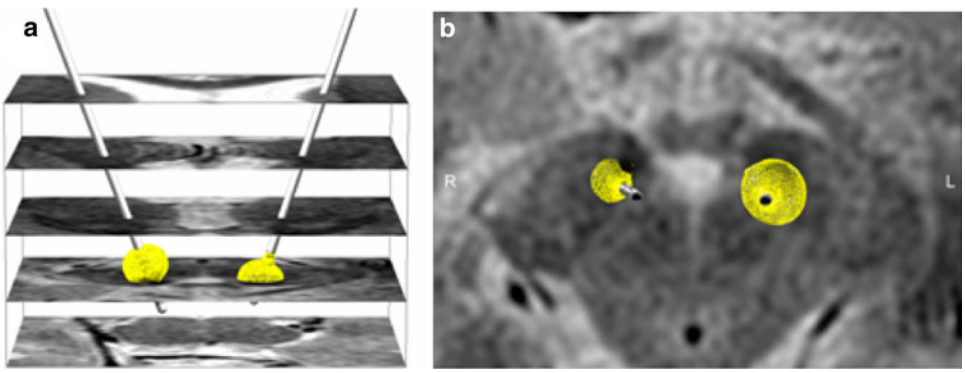

Fig. 3 Patient-specific simulation of bilateral DBS in the STN during clinically effective stimulation settings. **a** The electric field is visualised with isosurfaces at 0.2 V/mm. **b** Axial model slice visualising the electric field isolevel at 0.2 V/mm together with the anatomy [7]

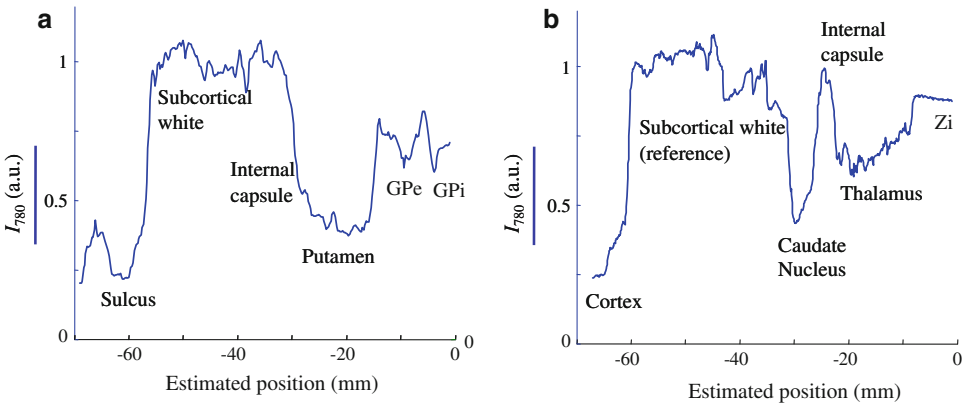

Fig. 4 Continuous light intensity measurements from cortex along the pre-calculated trajectory towards the target area: **a** GPi and **b** Zi. The optical signals are processed for presentation at the wavelength 780 nm. The intensity values represent the changes in tissue grey-whiteness during insertion of the probe [63]

[78], tremor [12, 35, 103], bradykinesia [31, 71], gait [8, 51, 66] and levodopa-induced dyskinesias [39, 59].

A majority of the mentioned papers deal with the quantitative evaluation of Parkinsonian symptoms in general. Still, only some of the mentioned movement analysis studies for Parkinson's disease have been performed in relation to DBS. Just to name some of them: Kumru [71] examined the effects of STN-DBS on characteristics of EMG activity of the wrist representative for bradykinesia and akinesia of the agonist muscle; Herzog [55] and Fukuda [35] applied accelerometry to compare between results of thalamic and subthalamic nucleus DBS and to correlate PET imaging (regional cerebral blood flow) with tremor in patients with unilateral Vim-DBS respectively. Sturman [117] examined the efficacy of STN-DBS and medication for resting tremor with accelerometery and EMG; Blahak [15] and Timmermann [118] did the same using an ultrasound-based measuring system (Blahak in addition to EMG). Several studies used quantified gait analysis to demonstrate the impact of STN and GPi stimulation on gait and balance [8].

Most of these studies concern pre-/postoperative or stimulation ON/OFF evaluations that means during preoperative office visits, hospitalisation for surgery, or postoperative follow-up visits. Intraoperative quantitative measurement of the motor manifestations of Parkinson's disease has rarely been proposed. Some groups intraoperatively used accelerometry and/or surface EMG [13, 64], accelerometer-based tremor pens and touch recording plates [104], or gyroscopes [69] to try to objectify the assessment of tremor and bradykinesia. Birdno et al. [13] used intraoperative accelerometry to demonstrate the influence of the periodicity of DBS on tremor, but did apparently not make it a part of their routine surgical protocol. Journee et al. [64] intraoperatively placed two 1D accelerometers on the index finger and analysed amplitude and frequency as tremor parameters. Even if there is no gold standard today for movement pattern analysis, accelerometers seem to be the most frequently used evaluation technique, but this can as well be linked to the fact that tremor is the mostly evaluated Parkinson's disease symptom. Some typical quantitative parameters for tremor and bradykinesia that have been derived from accelerometric measurements in addition to amplitude and frequency [64, 68] are mean magnitude [58, 65], the duration of tremor [68], and poverty of movement [68].

4.5 Intraoperative data visualisation

In Sect. 3.2, we show the quantity of existing data that has to be analysed intraoperatively in order to take a decision on the final surgical target. Most of the clinical groups base their decision on taken notes and the "mental combination" of all these data. Only BrainLab has proposed very recently a software module that allows for processing of intraoperatively acquired micro electrode recording/stimulation data to support the optimum DBS treatment decision through graphical representations. None of the other existing navigation and planning systems seems currently to propose an intraoperative "intuitive visualisation" interface. The StimPilot Software (Medtronic Inc., Minneapolis, MN, USA) [56] allowed a combined visualisation of short MER recordings together with the anatomical information, but it is only commercialised in the US. Only few groups use homemade software for online data collection and visualisation [26, 43, 83]. Most of them use electrophysiological databases of several patients taking into account MER and rarely as well test stimulation results which are non-rigidly registered to the patient's MRI in order to predict preoperative target points. Miocinovic et al. [94] have added a feature predicting the volume of tissue activated for a given electrode position and stimulation parameter setting. The aim in the future should be to set up an interface that supports management and visualisation of all data achieved during planning and surgery, including new emerging technologies (Fig. 5).

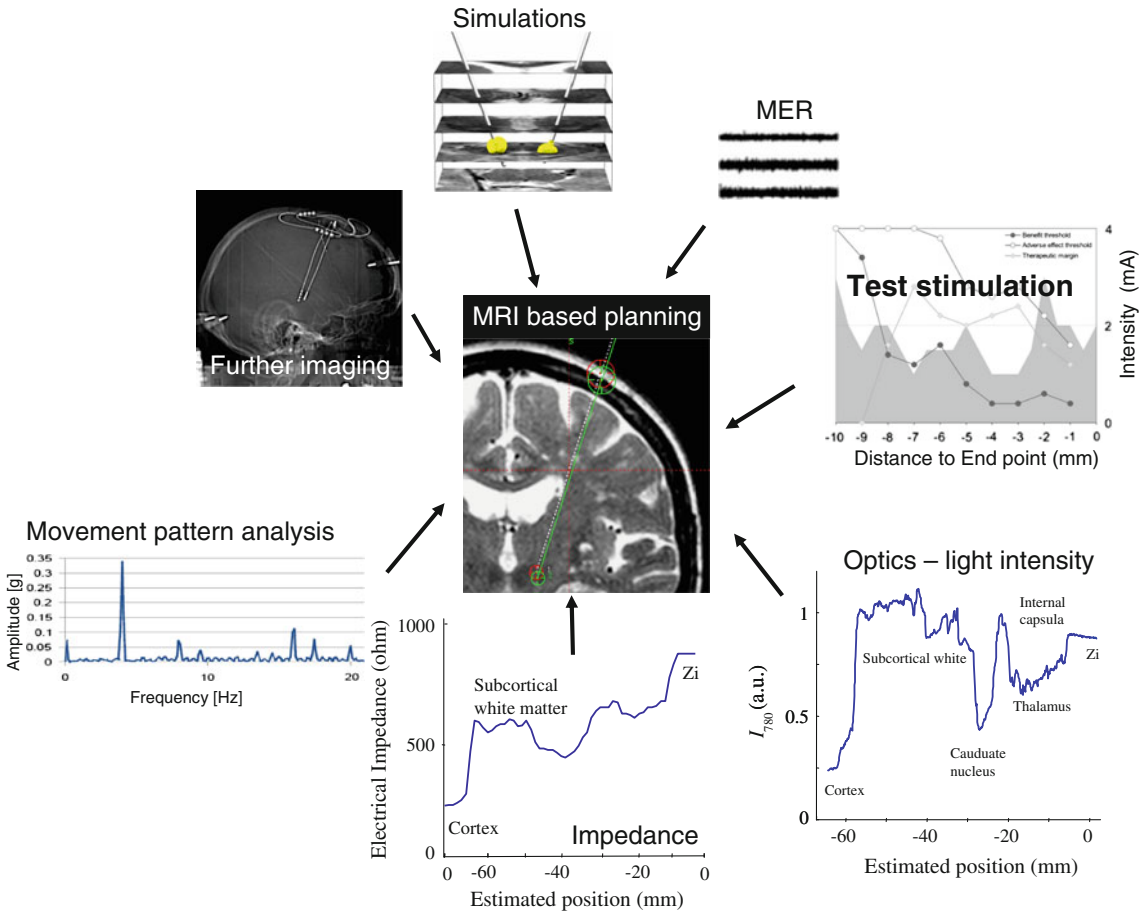

Fig. 5 From "mental imagination" to "intuitive visualisation": the objective in the long term should be to replace the mental interpretation of the high quantity of intraoperatively obtained data by a software-guided data presentation [42, 79]

4.6 New stimulation systems

For the last 20 years, the market has been dominated by the Medtronic DBS-system [22]. At the moment, several companies and research groups show strong interest in development and improvement of neurostimulation devices [102]. Among these, St. Jude Medical has received the European CE mark approval of the Libra® and Libra*XP*™ deep brain stimulation systems for treating symptoms of Parkinson's disease, and the first clinical implantations were done in Europe in 2009 [114]. The device is also approved for Investigational Device Exemption from the FDA to evaluate the efficacy of DBS for the treatment of chronic depression by stimulation in Brodmann Area 25. Further development of established electrode techniques are also expected and suggested improvements include: miniaturised cranial implantable neurostimulators which would allow the entire surgical procedure to be done as one incision procedure; material and leads that make MR imaging safer and reduces the risk of RF-induced heating; and field steering [22]. Steering of the electric field towards a target area of interest has also been simulated. Åström et al. [6] used patient-specific models and simulations of the electric field to visualise a multi-contact asymmetrical voltage steering technique beneficial for reduction of DBS-induced speech deficits, and Butson and McIntyre [19] evaluated the use of current steering for better control of the activated tissue volume during STN-DBS. Other suggestions to improve the stimulation effect include alteration of the stimulation pulses by desynchronisation [52].

5 Discussion and conclusion

A review of the state-of-the art of technical aids for the stereotactic implantation procedure of deep brain stimulation electrodes has been presented. The preoperative planning, surgical intervention and postoperative follow-up of DBS electrodes include many steps and use a range of information-related technologies. A procedure is normally a full day surgery, and this makes it both time- and resource-consuming. As the number of clinical indications and target areas are expected to increase and thus the number of implantation procedures, it is of outmost importance to

make the different steps as effective as possible, but without increasing the surgical risks and jeopardise the final clinical outcome. For any stereotactic procedure, safe, accurate and precise targeting of the brain structure to be treated is essential for an optimal clinical outcome with minimal side disorders.

In order to judge the implantation accuracy, it is important to be aware of limits and risks of the whole surgical procedure from the planning to the postoperative follow-up. In general, it is possible to distinguish between accuracy of the target identification on the anatomical images and the surgical precision. The former one includes the stereotactic image acquisition and the use of the images. While stereotactic CT acquisitions do not show any geometrical distortion due to the presence of the stereotactic frame, distortions of MR-images and the fiducials cannot be excluded. They have shown to be insignificant for specific MR sequences [10, 17, 122]. To avoid distortion, many centres coregister non-stereotactic MR to stereotactic CT images for the preoperative planning. The accuracy of the coregistration seems to remain in acceptable limits [111, 123], around 1.3 mm for example when applying the mutual information algorithm [30]. Groups using anatomical atlases during the targeting procedure have to be aware of the uncertainties introduced by the non-rigid MRI/atlas fusion [44, 121] due to the interindividual anatomical variations. It has been shown that, especially in case of GPi and STN targeting, the direct method has obvious benefits over indirect atlas-based targeting [85, 105, 123]. Another factor influencing the planning accuracy is the identification of the stereotactic reference system which is the basis for the target calculation. Depending on how many image slices are used for the calculation of the transformation parameters and how the fiducial points are identified, automatically or semi-automatically, target coordinates can slightly differ.

In addition to all these factors influencing the planning accuracy, especially two aspects have to be considered concerning the surgical accuracy. First, there is the application accuracy of the frame systems themselves, i.e. the targeting precision, which has been estimated for the different probe positions and stereotactic frames by Zylka et al. [134]. They studied imaging accuracy and mechanical errors and came to the result that frame systems equipped with a phantom base allow compensating for mechanical inaccuracies and errors. The second phenomenon introducing an inaccuracy, but difficult to predict, is the "brain shift". The only way to reduce the causing liquid loss is to keep the burr hole as small as possible and to perform the surgery as fast as possible [61]. Intracerebral measurements can help the surgeon to compensate for the "brain shift".

The paper has also reviewed a number of emerging tools, several of them being research prototypes today but with great potential to become available in the health care system in the near future. Among these, further development of established brain stimulation electrodes and new stimulation devices developed for specific treatments are expected to push the use of DBS. Miniaturised cranial implantable pulse generators are suggested in order to make the entire surgical procedure as one incision [22] and steering of the electric field for tailoring the treatment and reduce potential side disorders [6, 19]. However, even with such improvements, the implantation procedure of DBS electrodes will still require stereotactic surgery and support from technical aids. Furthermore, imaging quality related to MRI and DTI is expected to improve and may in the future make "invisible" structures possible to visualise. Transcranial sonography may become as well an interesting and promising complementary monitoring technique if the highly echogenic imaging artefacts of the metal parts of the electrode can be reduced. It may allow further intraoperative refinement of the electrode position as well as simultaneous prevention of haemorrhages.

Despite this, the "brain shift" will still be an obstacle to overcome, and intraoperative measurements will therefore still be required. To date, microelectrode recording is the most commonly used technique for intracerebal identification of the DBS target areas. Being well established, MER is however sometimes questioned, and some researchers point out that the thin needles used may increase the risk of bleeding and does not guarantee proper targeting [47, 101]. Furthermore, MER can be relatively time-consuming; as the signals are in general studied in the time domain, they may be difficult to interpret in real time. Optical measurements [37, 62, 127] are a highly interesting alternative to MER. It has the advantage of real time presentation of grey-white boundaries passed during probe insertion. A recording is done within minutes. In addition to grey-white boundary determination, vessels in the vicinity to, and along the trajectory, may be detected by means of simultaneous microvascular recordings with laser Doppler technique [128]. By using a multipurpose probe, the optical measurements can be combined with impedance recordings [62]. The optical alternative to MER could be especially beneficial for newer target areas, where well-defined grey-white matter boundaries are passed as the tissue is "seen" before it is reached.

An additional promising tool for exploring new target areas is the use of patient-specific models and simulations of the electric field [7, 18]. These can also be used to advance and optimise the treatment of an individual patient, and act as a tool for training and for simulation of electric field in target areas before the actual surgical procedure is done. Such simulations can allow for 3D visualisations of the electric field influenced by the stimulation and match it to the patient's clinical outcome [5, 86]. As DBS has become more commonly used, there

have been increasing reports of postoperative neuropsychiatric complications, including depression, behaviour problems, aggression and language disturbances [20, 50, 129]. Even though several hypothesis of the fundamental mechanisms exist underlying both the therapeutic effects and the adverse side effects of DBS, the mechanism remains largely unknown [29, 40, 82, 90].

In a broader context, simulations can, together with, e.g. neuroimaging, biochemical monitoring and neuronal mapping, be one additional corner stone for increased knowledge of the DBS mechanisms. Another important and self-evident basis of the analysis of the mechanism of action of DBS is the obtained clinical result. Here appears the problem of the comparability of the evaluations performed by different medical doctors and in different medical centres. For Parkinson patients, for example, it is crucial to assess the severity of the cardinal Parkinson disease symptoms (tremor, bradykinesia, rigidity and postural instability) and dyskinesia to document the clinical changes quantitatively. Current methods such as the Unified Parkinson's Disease Rating Scale (UPDRS) [33] are mainly semi-quantitative and not fully objective: these clinical scales rely on ordinal ratings based on descriptive terms such as "mild", "moderate" and "severe". The literature review has shown that many groups have worked on quantitative movement pattern analysis, but that there is no gold standard and no complete pre- and postoperative evaluation of all Parkinson's disease symptoms. This is valid as well for the intraoperative evaluation process. Only few groups have tried to introduce quantitative measurement methods in the operating theatre which could further increase the precision of the target choice. For other disorders treated with DBS, such as psychiatric illness, techniques in parallel to movement pattern monitoring should be developed in order to optimise the objectivity of the clinical evaluation.

Another key point which could improve the surgical decision-making process would be to introduce data and information technologies in the DBS procedure, i.e. by means of "intuitive visualisation" of parameters and images recorded in relation to the intervention. As already mentioned, existing homemade and commercialised software provides in general an integration of microelectrode recordings with the patients MR images and sometimes as well with the test stimulation results. An extended system for visualisation of additional parameters could include presentation of the patient MR batch of images together with the DBS electric field simulation or physiological information such as tissue impedance, neural activity recorded by MER, grey-white boundaries, microvascular perfusion related to small vessel structures or tissue chromophores measured by optics. Furthermore, depending on clinical symptoms for the implantation procedure, movement pattern could be included. In consequence, there still seems to be a high potential to optimise the surgery and its precision by means of objectification and improved data management for patients suffering from various movement disorders or other diseases treated by deep brain stimulation.

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