VIEWPOINT

Directional Leads for Deep Brain Stimulation: Opportunities and Challenges

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During the past three decades, deep brain stimulation (DBS) has become an established treatment for movement disorders and other indications with more than 120,000 patients worldwide currently implanted with a DBS device. The advent of directional leads is a recent technological advance and has the potential to expand the capabilities of DBS. The ability to more accurately target and precisely control stimulation can theoretically improve the effectiveness of DBS while avoiding side effects, but given the novelty of this approach there is currently no firm clinical evidence. Hence, we feel that the thoughts and experiences of the early adopters of this therapy, which are summarized in this viewpoint, may guide the practice of others until more evidence accumulates.

Unlike conventional DBS leads, which use cylindrical electrodes, directional leads comprise radially segmented electrodes that allow the stimulation field to be moved in the plane perpendicular to the lead, or shaped using anodes and cathodes to steer stimulation in a particular direction, based on the needs of individual patients (Fig. 1). There are currently two commercially available systems with similar electrode designs. A principal differentiator is how they deliver current: one uses a single current source, the other multiple independent current sources (Fig. 2). A multiple independent current-controlled system can steer the field toward any of the 360° on the circumference of the lead by shifting current in small increments between adjacent directional contacts. In a single-source system, with three contacts in a segmented row, the field depends on orientation and shape on the impedances of the individual directional contacts. If the impedances of the three contacts are unequal, the current distribution is distorted toward the contacts with lower impedances. This can be problematic if the impedance of a contact unexpectedly changes, as the geometry of activated tissue would be suddenly altered and the clinical effects with it (Fig. 2).

Clinical Opportunities

Directional leads were developed to precisely control the volume of tissue activated (VTA) during DBS, which is directly related to individual outcomes. DBS has been used successfully for many years in movement disorders such as Parkinson's disease (PD),[1-3] yet treatment may sometimes be suboptimal for several different reasons, such as inappropriate patient selection or programming or electrode placement; two referral centers for DBS troubleshooting have reported that therapy failure in half of the evaluated leads was caused by suboptimal positioning.[4] Stimulation of the

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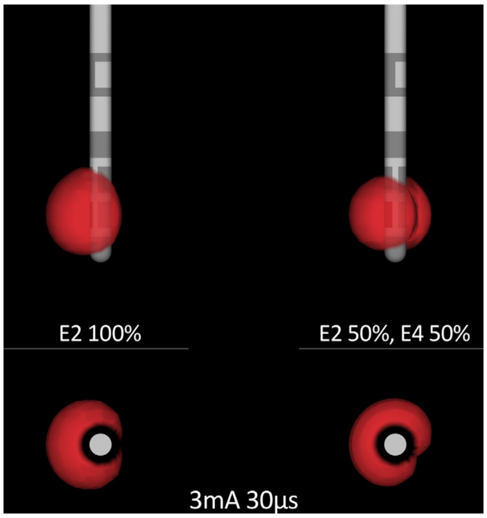

FIG. 1. Visualization of how the size and shape of the volume of tissue activated can be changed by using a directional lead in a multiple, independent, current-controlled system. The images along the top depict a side-on view, whereas those on the bottom display a bottom-up view. The images on the left show all the current on a single directional contact (E2 = 100%), whereas those on the right show the current being split equally between two adjacent contacts within a segmented row (E2 = 50% and E4 = 50%). The directional leads are stimulated with 3 mA at a pulse width of 30 µs.

dorsolateral subthalamic nucleus (STN) is associated with best motor symptom control,[5,6] but excessive stimulation of adjacent fiber tracts can cause adverse effects such as disturbances in speech and fine-motor control.[7,8] Small lead deviations from the intended functional target play an important role in suboptimal efficacy[6] and side effects,[9] even in experienced surgical centers.[6] Even with a seemingly optimal lead position, functional targets vary from patient to patient, and axial displacements may still lead to adverse effects. Some stimulation targets, such as fiber tracts, tend to be nonspherical, making them more difficult to optimally capture with conventional lead geometries. These difficulties can be a challenge for clinicians during patient follow-up.[6]

Directional leads—within limits—may address these issues, allowing stimulation to be directed toward the functional target and away from side-effect structures. As such, these novel leads can widen the therapeutic window by lowering the efficacy threshold and increasing the side-effect threshold,[10,11] as indicated in a recent pilot study.[12] A larger therapeutic window allows greater programming flexibility, as the expected beneficial effects of DBS may be reached at a lower current amplitude or higher current amplitudes could be attainable before side effects appear[11]—this is important when increasing the stimulation amplitude to optimize DBS efficacy during follow-up.[13] When used chronically, directional DBS may reduce the incidence of side effects that cannot be tested intraoperatively (eg, gait, cognitive, or behavioral disturbances)[10] and in patients with a narrow therapeutic window despite good location of the lead as verified by intraoperative testing, microrecordings, or imaging, as well as in patients operated under general anesthesia precluding clinical testing (eg, for dysarthria). By using a directional lead, it may thus be possible to improve outcomes and cause fewer adverse effects, including dyskinesia in patients with low thresholds for stimulation-induced dyskinesia. Moreover, in addition to current steering modification of pulse width and frequency combined with directional stimulation opens even more strategies to test for the best therapeutic window. However, if a concentric spherical VTA perfectly covers the target, directional stimulation is not needed. Therefore, if the lead is optimally placed in the horizontal plane, all three contacts in a segmented row can be activated at equal amplitudes to functionally simulate a cylindrical electrode ("ring mode"). More clinical evidence for the postulated and theoretically plausible advantages of directional DBS is needed.

It may also be time to examine the standard parameters used for DBS, which may change in a directional system. For example, in general patients may currently receive more than the minimum necessary stimulation;[14] a directional lead could improve this, as directed stimulation may selectively capture target volumes at lower amplitudes. In addition, the selectivity of DBS within the VTA may be further improved by adjusting temporal parameters such as pulse width and frequency.[15,16] Moreover, within the target region, different symptoms tend to correspond to different substructures[7] (eg, tremor regions are distinct from bradykinesia regions). Directional leads enable further study of the structure and shape of the targets as well as the pathophysiological role of microstructures within by directing the VTA toward new subtargets. This may foster our understanding of motor and nonmotor effects of DBS and of the physiology of movement, cognition, and mood.[10]

Directional DBS may also be useful in smaller or nonspherical targets that are currently investigated for other disorders, such as the fornix for dementia,[17] nonmotor STN for obsessive-compulsive disorder,[18] medial forebrain bundle in psychiatric disorders such as major depression,[19] and the thalamus or the pallidum for Tourette syndrome.[20] The fornix, for example, is too small and thus vulnerable as a target to be directly implanted but is stimulated by a lead adjacent to the fiber tract. Directional DBS seems a compelling approach for this geometry. The ability to shape and steer the VTA in the plane perpendicular to the lead could help advance the use of DBS in these and other potential indications.

Challenges and Future Needs

There are challenges that need to be overcome when using directional leads. Although the surgical procedure for a directional lead is equivalent to a conventional

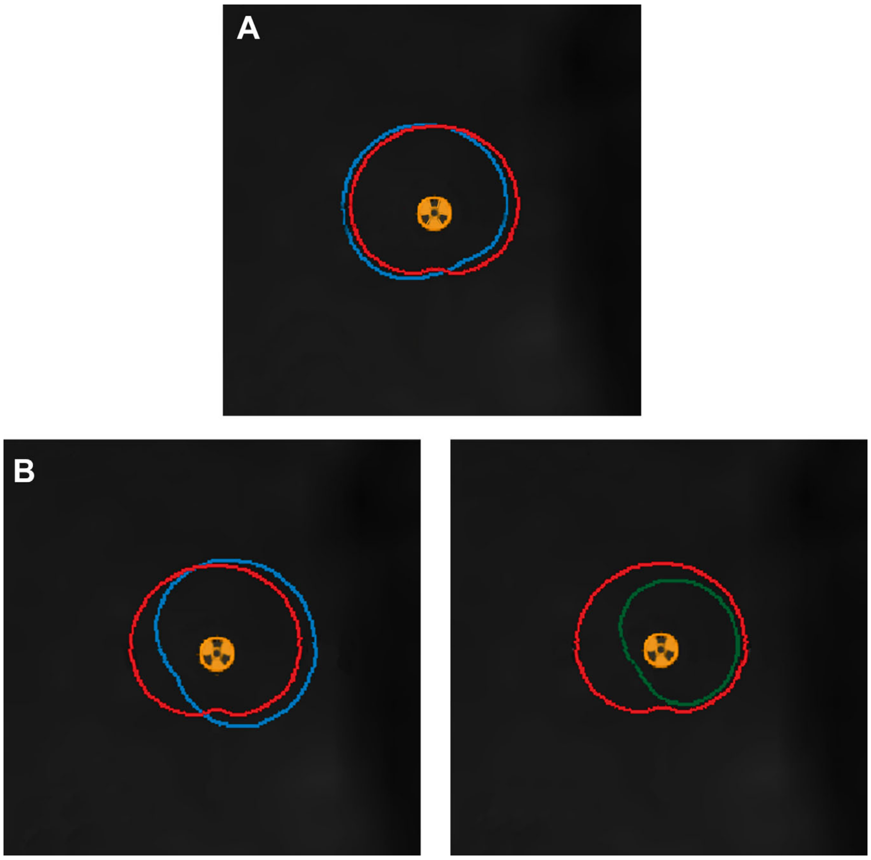

FIG. 2. Multiple independent current source versus single current source systems. A level of three directional contacts in 120° distance around an electrode is shown. In all figures, the view is perpendicular to the electrode (drawn in orange). Of the three contacts, two are activated. The intended distribution of the stimulation current between the two adjacent activated directional contacts is 50:50. (**a**) Depicts a case where the impedance is 3 kOhm on one contact and 1.5 kOhm on the other contact. The red stimulation field model shows the resulting stimulation field using a multiple independent current control system; the blue contact shows the stimulation field using a single source system. The change in stimulation field from red to blue indicates what may happen where the single source system is used and the impedance is initially equal at both contacts, but changes over time to a 3:1.5 kOhm ratio. (**b**) Depicts a case where there is an open circuit leading to one of the contacts. The red stimulation field was the original stimulation field (assuming equal impedance at both contacts). The blue in the left figure illustrates what happens with a single source system, when all of the stimulation (3 mA) is sent to the other, nonopen contact. The green in the right figure shows the same scenario, but with a multiple independent current control system; in this case, the amount of current sent to the nonopen contact remains the same (1.5 mA).

lead, lead rotation should be controlled using a marker against patient-centric anatomical landmarks using X-ray if possible. Targeting and intraoperative standards should not be altered from current practice, although future visualization technology may benefit from incorporating patient-specific anatomical and electrophysiological data. In a note of caution, the directional lead must not be used as an excuse for lowering the precision of surgical lead placement. Although a directional lead may theoretically be used to compensate for suboptimal placement, more clinical evidence for the corrective potential of directional DBS is needed.

Another challenge is that the finer control over the VTA afforded by directional DBS entails a more complex and thus potentially more time-consuming search for best parameter settings. Assisted programming using patient-specific imaging and electrophysiological data including local field potentials will help compensate for the greater complexity of programming. Although the use of directional settings may initially be more demanding in centers that wish to explore the full stimulation space, fewer reprogramming sessions may be required as understanding increases regarding best practices for directional lead programming. Patient preference is a significant part of therapy, and allowing different settings from which they can choose (within clinician-set parameters) may provide DBS programs tailored to specific situations; it may also assist and therefore shorten the clinician's search for the best parameter settings. Initially, use of a directional lead is essentially the same as a conventional lead; monopolar review can be begun in ring mode, following the same steps used with a conventional 4-row lead. It is important at the outset to define the "best" outcome for each individual patient, and a benchmark for PD patients is the levodopa response, with the exception of tremor that may not respond to levodopa while responding to DBS. If the "best" outcome cannot be matched in ring mode before side effects occur, further programming options should be used.

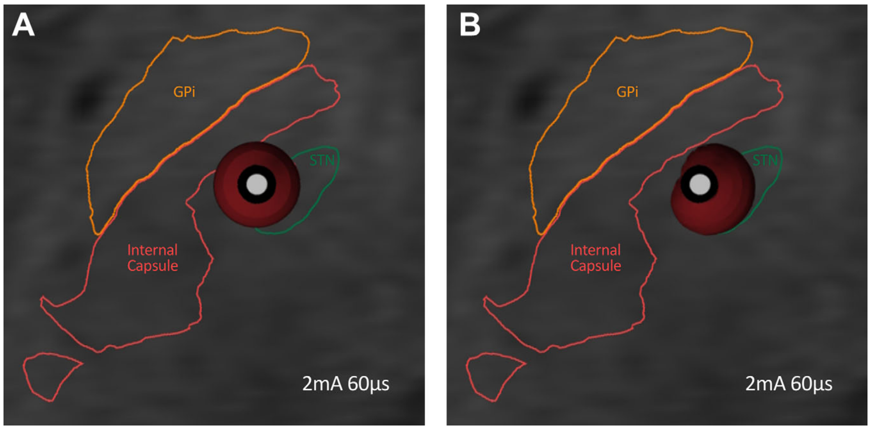

FIG. 3. Example of patient-specific computer modeling. Tissue activation volumes illustrate the potential utility of a directional lead system. In both images, the green anatomical outline shows a cross section of the subthalamic nucleus (STN), the red outline shows the internal capsule, and the orange outline shows the globus pallidus internus (GPi). (**a**) A nondirectional lead is placed in a clinical location, where the volume of tissue activated shows that expected therapeutic stimulation of the STN is impossible without simultaneous activation of the internal capsule. (**b**) A directional lead is placed in the same location and only a single directional contact is active, effectively steering the volume of activated tissue away from the internal capsule. In both images, the tissue is being stimulated with 2 mA at a pulse width of 60 µs. Slices perpendicular to the implanted electrode at the mid-level of the subthalamic nucleus are shown; the z-coordinate is 2.5 mm inferior.

At present, when directional settings are required, the current programming methodology relies primarily on experienced clinical intuition and minimal use of visual or computational guidance, potentially requiring multiple programming sessions with the patient to achieve optimal results.[21] With increasing experience using directional leads, programming strategies and guidelines will become available to aid neurologists and reduce programming time. An algorithm needs to be developed, potentially using imaging or electrophysiological data, to allow clinicians to quickly identify the best initial settings, which can be refined according to each patient's response.

Nevertheless, clinical identification of optimal stimulation parameters may not be intuitively obvious without computational assistance as it is inconceivable to clinically evaluate all available stimulation settings. Furthermore, some symptoms (eg, bradykinesia) may require time to respond to changes in stimulation settings. Current patient-specific visualization and computer modeling software (Fig. 3) needs to be further developed to reliably assist the choice of the most appropriate initial parameters based on the patient's anatomy, thereby simplifying clinical programming associated with directional DBS.[14,21,22] In addition, stimulation adjustment may be facilitated by patients' use of technology-based devices for ongoing and objective assessment of symptoms such as postural control, tremor, bradykinesia, freezing, dyskinesia, and gait.[23]

A constant effect of DBS is crucial and depends on technological aspects of the system used. Electrode impedance can vary from one electrode to another and change over time.[24] In a voltage-controlled system, electrodes with fluctuating impedance will deliver different amounts of stimulation at the same voltage level; in a constant-current system, the amount of stimulation delivered is always known, making it simpler to maintain a constant VTA. However, when multiple electrodes are used with a single-source generator, current will flow through the path of least resistance. If there is an inopportune arrangement of impedances, a single source system may not support the selection of the most advantageous field. If there are unexpected changes in impedance, the stimulation field will shift unexpectedly as a result. Thus, a multiple independent current-controlled system may be the preferred paradigm, where each electrode is individually controlled by a dedicated current source and impedance is not a factor. Also, as segmented electrodes are smaller and thus inherently have higher impedance,[25] energy consumption may be increased when using a single segmented electrode compared to a single conventional cylindrical electrode at the same amplitude. However, with a directional lead equivalent activation in a preferential direction would require lower amplitudes, thus reducing the energy requirement. The potential for higher voltage output and greater charge density[25] with small contacts may be a concern. Therefore, safeguards must be present within directional systems to protect against any tissue damage. Charge density is only explicitly controlled with a multiple independent current-controlled system.

As clinical evidence gathers on directional lead systems, the demonstration of a clinical advantage over conventional DBS is challenging. Because DBS is a very effective therapy, incremental improvements by using directional stimulation will statistically best be demonstrated in selected patient groups likely to benefit from the new therapeutic option, for example, by choosing a modified enriched-enrolment strategy[26] using a physiological predictor, for example, a narrow therapeutic window during a monopolar review.

Conclusion

The directional lead is a new tool in the armamentarium for DBS that may considerably influence our approach to the therapy. This new technology may help to improve the standard of DBS care for movement disorder patients and may become useful in new targets and indications. As it is not possible to preoperatively predict whether there will be a potential for improvement of DBS outcome with directional stimulation in a given patient, implantation of a directional lead from the outset must be weighed against the resources required. Crucially, clinical evidence that the theoretical possibilities of directional leads indeed translate into better clinical outcomes is needed. ■

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