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Review

Innovative Developments in Deep Brain Stimulation Devices

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Abstract: Technological advances in DBS hardware and software represent a significant growth area in functional neurosurgery. These advancements have the potential to significantly enhance treatment outcomes and expand the scope of neurological disorders that can be effectively addressed through DBS interventions. The advent of directional deep brain stimulation (DBS) ushers in a new era in neuromodulation, providing enhanced benefits to individuals with Parkinson's disease, optimizing clinical outcomes more efficiently, and targeting treatment for stubborn symptoms using data-driven approaches. Implementing a multimodal programming strategy and incorporating cutting-edge current fractionation technology and image-guided tools for lead localization and brain sensing reduces reliance on traditional trial-and-error programming methods. This paves the way for a more predictive application of this therapy. These advancements are poised to propel the development of advanced closed-loop stimulation systems that seamlessly integrate continuous data streams, ultimately leading to improved patient care.

Keywords: deep brain stimulation; directional leads; neuromodulation

1. Introduction

Deep Brain Stimulation (DBS) stands as a well-established treatment modality for a spectrum of movement disorders, including Parkinson's Disease, Essential Tremor, Dystonia, and Tourette syndrome, as well as for epilepsy and certain psychiatric disorders such as Obsessive-Compulsive Disorder (OCD) and Major Depression (MD). Regrettably, the somewhat stagnant evolution of neurostimulation devices has hindered clinical success. However, in recent years, DBS has witnessed rapid expansion, driven by numerous technological advancements that promise to enhance safety, efficacy, and precision. In this concise review, we aim to highlight the latest findings in DBS device hardware and software components, showcasing their potential to significantly improve treatment outcomes and broaden the scope of neurological disorders amenable to intervention.

2. Hardware developments

a) Directional leads

Traditional DBS systems utilize circular electrodes, producing a roughly spherical electrical field. With these systems, the ability to control the activated tissue volume is limited to adjusting the polarity and stimulation pulse parameters [1]. While advanced programming techniques provide some flexibility in shaping the electrical field along the longitudinal axis of a multi-contact ring electrode, they do not allow for direct current manipulation within the horizontal plane. In contrast, directional leads consist of electrodes segmented radially, enabling the stimulation field to be moved in the plane perpendicular to the lead or shaped using anodes and cathodes to steer stimulation in a specific direction tailored to individual patients. This innovative approach reduces the risk of adverse effects and enhances the efficacy of DBS [2]. Directional leads were developed to precisely control the tissue-activated (VTA) volume during DBS, directly related to individual outcomes. Directional leads are designed with multiple contacts, allowing for precise neural structure targeting. By delivering electrical stimulation in specific directions, clinicians can more effectively target the areas of the nervous system responsible for pain, tremors, or other symptoms. Overall, directional leads represent an essential advance in neuromodulation technology, allowing for more precise and effective treatments for various neurological and pain conditions [3]. These leads can widen the therapeutic window by lowering the efficacy threshold and increasing the side-effect threshold. 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. When increasing the stimulation amplitude, optimizing DBS efficacy during follow-up is essential [4].

The need to conform an electric field to the ever-changing anatomy of the brain target has led to the development of various electrode contact designs. One such design is the "Vercise Cartesia" lead by Boston Scientific, which incorporates a multi-lumen structure. This lead features eight contacts spanning a distance of 15.5 mm, with a spacing of 0.5 mm. The utilization of this design may contribute to enhanced durability and longevity of the entire system, consequently reducing the need for replacement procedures. Additionally, the "Vercise Cartesia" lead allows for individual current settings for each of its eight contacts, enabling stimulation with a pulse width below 60 µs. Moreover, it offers the flexibility of independent frequency adjustments in different areas along a single lead. Another innovative lead, known as the "DirectSTIM" by Aleva Neurotherapeutics, is a quadripolar lead consisting of four rings. Each ring is divided into three independent compartments, with orientations at 0°, 120°, and 240°. This unique configuration enables independent stimulation in specific directions, a technique called current steering. The "SureSTIM" (Sapiens) consists of 32 contacts distributed around the lead that may be activated group-wise. This system allows for accurate sculpting of the stimulation field to maximize relief and avoid side effects. The "Infinity" (St. Jude Medical) is a cylindric quadripolar lead with two middle contacts sectorized into three independent, adjustable directional electrodes. The "SenSight™ directional lead (Medtronic) is quadripolar lead with two external rings contact and two intermediate contacts, each of them consisting of three independent compartments with its orientation; the SenSight directional information combines the benefits of directionality with the power of sensing brain signals.

The conventional parameters utilized in Deep Brain Stimulation (DBS) might undergo alterations in a directional system. Currently, patients often receive stimulation exceeding the minimum required; however, directional leads offer potential enhancements. Directed stimulation can precisely target specific volumes with lower amplitudes, thus optimizing therapeutic efficacy [5]. Furthermore, adjusting temporal parameters such as pulse width and frequency could enhance the selectivity of directional DBS within the Ventral Tegmental Area (VTA). Different substructures within the target region correspond to various symptoms, necessitating precise targeting. Directional leads facilitate detailed exploration of the target structure and microstructural pathophysiology, potentially deepening our understanding of DBS's motor and nonmotor effects, as well as the underlying physiology of movement, cognition, and mood [6]. Directional DBS holds promise for smaller or nonspherical targets currently under investigation, such as the fornix for dementia, nonmotor Subthalamic Nucleus (STN) for obsessive-compulsive disorder, medial forebrain bundle for psychiatric disorders like major depression, and the thalamus or pallidum for Tourette syndrome. For instance, the fornix, being too small and delicate for direct implantation, can be stimulated by a lead adjacent to the fiber tract. Directional DBS presents an appealing approach for such geometries. The capability to shape and guide the VTA in the plane perpendicular to the lead may advance DBS utilization in these and other potential indications [7]. The bioelectrical parameters of Deep Brain Stimulation (DBS), such as therapeutic impedance and surface current density, are significantly influenced by the electrode surface and undergo inevitable changes when activating a single segment. Consequently, implementing "directional" stimulation necessitates several adjustments: reducing intensity to prevent excessive increases in current density (current intensity divided by electrode surface) and fine-tuning stimulation adjustments with a smaller step-size amplitude (0.1–0.3 mA compared to the traditional 0.5 mA). Moreover, given that electrical current tends to flow out of the electrode through its edges, the lateral extension of the Ventral Tegmental Area (VTA) is broader than the surface covered by the electrode. This aspect must be considered, as simultaneous activation of multiple adjacent segmented electrodes may compromise directionality to some extent. [8,9].

a) Closed-loop DBS (Adaptive DBS)

Presently, existing Deep Brain Stimulation (DBS) systems operate in an 'open-loop' configuration, with parameters set empirically for the duration of stimulation. Closed-loop DBS (CLDBS) introduces a novel approach that holds the potential to overcome current limitations by autonomously adjusting stimulation parameters as needed.

Utilizing real-time feedback, closed-loop DBS systems dynamically adjust stimulation parameters based on the patient's neural activity. This allows for more precise and personalized stimulation, thereby reducing the risk of side effects. Unlike traditional DBS, which delivers constant stimulation to the brain, closed-loop DBS employs sensors to detect and respond to changes in biomarker activity within the basal ganglia. Consequently, treatment can be tailored more precisely to the individual's requirements in real-time [10–12].

In open-loop DBS, manual adjustment of stimulation parameters occurs every 3-12 months following implantation. In contrast, closed-loop DBS automatically programs stimulation parameters based on measured biomarker activity. This necessitates a control algorithm that learns and optimizes stimulation parameters using both an “amplitude–responsive strategy” and a “phase-responsive strategy.” In the former, stimulations are guided by increments in the biomarker signal, while in the latter, they are influenced by the phase (timing) of the biomarker signal [13].

The operation of a closed-loop DBS system revolves around detecting variations in biomarker activity. Various electrophysiological biomarkers, such as Action Potentials (APs), ElectroCorticography (ECoG), and Local Field Potentials (LFPs), are considered in the feedback loop of the adaptive system. The selection of biomarkers depends on factors such as disease type and symptoms, signal-to-noise ratio, stability, and resistance to external artifacts like movement and cognitive processes [14–16]. LFPs, in particular, are commonly used as feedback signals due to their ability to capture excitatory and inhibitory potentials from nearby neurons, making them less susceptible to tissue reactions post-electrode implantation. These LFPs are categorized into frequency bands (e.g., delta, theta, alpha, beta, gamma, high frequency), with beta frequency bands showing promise in Parkinson's disease. CLDBS may administer stimulation "on demand" only when exaggerated synchronization in the beta band compromises system performance. The relationship between LFP frequency bands and symptoms in other conditions is still evolving. However, existing data suggests associations between theta/alpha bands with tremors and low-frequency bands with dystonia [17].

The PerceptTM PC neurostimulator, featuring BrainSenseTM technology, captures brain signals (LFPs) using implanted DBS leads. These signals can be recorded simultaneously with therapeutic stimulation inside and outside clinical settings. Physicians can correlate brain signals with stimulation and events, including medication intake, symptoms, or side effects, to provide personalized, data-driven treatment and adjust stimulation according to patients’ evolving needs.

In summary, Closed-loop DBS has demonstrated promising results in clinical trials, with some studies suggesting improvements in symptom management and reductions in side effects compared to traditional DBS. However, this therapy is still in the early stages of development and is not yet widely available. Its implementation also necessitates specialized training and expertise in neurostimulator implantation, programming, and data interpretation [18].

a) Current Steering Technologies

Accurate targeting of the precise brain structure is imperative for optimizing the clinical efficacy of Deep Brain Stimulation (DBS) therapy. However, the target structure is often minute, irregularly shaped, with intricate substructures, and surrounded by adjacent structures. Stimulation of these neighboring structures during therapy can lead to undesirable side effects. Achieving optimal therapy outcomes without triggering such side effects poses a significant challenge if the lead placement is suboptimal [19]. A recent advancement in DBS technology introduces radially segmented electrodes. Modeling and preclinical studies indicate that stimulation through segmented electrodes enables the axial steering of current toward the therapy target while avoiding regions

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prone to producing side effects. Pilot studies employing segmented DBS leads have showcased improved outcomes by empowering clinicians to tailor and shape stimulation according to individual patient anatomies. With segmented lead systems, using a single-activated electrode (single-segment activation or SSA) often generates customized axially asymmetric directional fields. However, in cases where a higher degree of customization of the activated tissue is desired, current fractionalization techniques can be employed. Current fractionalization involves distributing currents through two or more electrodes. While this allows for a high level of user control over the activated tissue, it also increases programming complexity and may reduce the lifespan of the implantable pulse generator (IPG) [20]. Presently, two current fractionalization approaches are available for clinical use. The first approach, known as multi-stim set (MSS) or "interleaving," rapidly alternates multiple stimulation sets with different parameters apart from a shared stimulation frequency. MSS is employed in systems with a single current source to facilitate current fractionalization [20]. The second approach, multiple independent current control (MICC), involves capping the total current amount and independently distributing portions of the total current through two or more electrodes. Some systems allow for concurrent activation of multiple electrodes through parallel hardware connection, referred to as "coactivation." While coactivation can decrease overall electrode impedance and potentially reduce power utilization in current-controlled systems, it may also result in variable directionality of the volume of tissue activation (VTA) based on interelectrode impedance. Thus, coactivation is considered a limited current fractionalization technique [21].

a) Multiple independent current control (MICC)

In contrast to voltage-controlled DBS systems, current-controlled DBS regulates the current passing through the electrode-tissue interface. The voltages generated within the targeted brain tissues by current-controlled DBS remain relatively unaffected by variations in electrode impedance. However, despite the precision offered by directional leads in neural targeting, it's challenging to program individual lead contacts with a single-source system, potentially resulting in inadvertent stimulation of unintended areas. Multiple Independent Current Control (MICC) technology addresses this limitation by allowing the manipulation of the electric field center between adjacent DBS contacts and independently distributing the total current across two or more contacts, enhancing spatial precision. Integrating MICC with directional leads enhances current adaptability, facilitating more efficient targeting of desired structures. A novel MICC directional lead has been developed to improve clinical outcomes by enabling vertical and horizontal current steering in Subthalamic Nucleus (STN) DBS for Parkinson's disease (PD). Horizontal current steering extends the therapeutic window, improving PD cardinal symptoms while mitigating stimulation-induced adverse effects in real-world clinical settings. Additionally, vertical steering aids in addressing dyskinesia by providing additional stimulation to the dorsal STN area and, in some cases, alleviating tremors. Vertical steering is primarily utilized to address dyskinesia and tremors, while horizontal steering helps avoid stimulation-induced adverse effects. Even in instances of lead misplacement, significant horizontal current steering compensates for surgical errors. Post-microlesion effect elimination, current steering becomes particularly crucial in DBS interventions. The Vercise System represents a breakthrough in DBS technology, offering Multiple Independent Current Controls (MICC) for precise stimulation positioning and shaping via steerable current delivery. With dedicated power sources for each electrode (up to 16) on the lead, the Vercise DBS System enables highly accurate targeting to minimize unwanted stimulation side effects and maintain therapy effectiveness over time. MICC provides precise control over the size and shape of the stimulation field, allowing for tailored treatment for individual patients. Moreover, by utilizing Multiple Independent Current Controls instead of voltage control, the Vercise DBS system is designed to adapt to impedance changes automatically, ensuring therapy continuity over time.

a) New paradigms of stimulation

Currently, available implanted pulse generators typically produce charge-balanced bipolar square-wave pulses with a fixed, non-adjustable pattern, offering only adjustable parameters such as

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amplitude, frequency, and pulse width. However, recent research suggests that alternative designs could enhance effectiveness and efficiency.

High-frequency stimulation (HFS) and Low-frequency stimulation (LFS) are two promising alternatives for treating Parkinson's disease symptoms. HFS, ranging from 130 to 185 Hz, has effectively addressed appendicular symptoms, whereas LFS, ranging from 60 to 90 Hz, has shown efficacy in alleviating axial symptoms like freezing of gait and balance impairment. Additionally, HFS is believed to promote neural plasticity, potentially restoring function in damaged brain regions.

Interleaving stimulation (IL) is another approach that involves the rapid and alternating activation of two independent stimulation programs on each lead. These programs can differ in amplitudes and pulse widths but are constrained to the same frequency.

A novel stimulation paradigm, the dual-frequency interleave–interlink (IL–IL), has been developed to address axial and appendicular symptoms simultaneously. In IL–IL, two overlapping LFS programs are interleaved on each DBS lead, with the overlapping region centered around the optimal electrode contact. Within this overlapping area, high-frequency stimulation (HFS) is applied to control appendicular symptoms, while the non-overlapping regions receive LFS to mitigate gait freezing and balance issues. This innovative approach aims to provide comprehensive symptom management while preserving motor function and improving overall patient outcomes [24].

3. Software developments

Introducing new software represents a significant advancement in Deep Brain Stimulation (DBS) therapy, enabling personalized reconstruction of DBS leads based on MRI and post-operative CT imaging. This software facilitates the precise delineation of nuclei and fiber tracts neighboring stimulation sites, enhancing the understanding of their spatial relationships. Additionally, the software enables the mapping of intra- and perioperative electrophysiological recordings, providing invaluable insights into the neural activity patterns associated with DBS interventions. By incorporating patient-specific anatomical and physiological data, this innovative software empowers clinicians to tailor DBS treatment strategies with unprecedented precision, ultimately optimizing therapeutic outcomes and minimizing potential side effects.

a) Image registration for localization of DBS electrode

Accurate control over the anatomical positioning of active contacts is crucial for understanding and adapting the effects of neurostimulation. The recent introduction of multidirectional DBS lead systems adds complexity to the programming of stimulation settings. Programming software now requires precise knowledge of the localization of electrodes and their contacts. Typically, registration between preoperative MRI and postoperative CT scans is employed to assess localization. However, the accuracy of this registration depends on the algorithm's quality. Various software programs are available for this purpose, each with slight but significant differences in the calculated coordinates. Some notable examples include VoXim by IVS Solutions Technology GmbH, Framelink v5.4 by Medtronic, NeuroInspire by Renishaw Mayfield, and Elements Stereotaxy by Brainlab [25]. Each program offers unique features and algorithms for precise electrode localization, aiding clinicians in optimizing DBS therapy for individual patients.

a) Computational modeling

Computational modeling plays a pivotal role in enhancing the accuracy of electrode placement and simulating the effects of Deep Brain Stimulation (DBS), ultimately enabling clinicians to optimize stimulation parameters before implantation. This approach can significantly improve the efficacy and safety of DBS procedures while minimizing the need for trial and error during the programming phase. Typically, computational modeling relies on automatic image segmentation algorithms to identify and delineate anatomical structures in image datasets and to model the volume of tissue activated (VTA). Elements Segmentation Algorithms introduce a novel approach by employing a synthetic tissue model to simulate the patient's anatomy and generate an individualized, patient-specific atlas exhibiting the same imaging characteristics as the analyzed image set. This innovative technique enhances segmentation accuracy and more precisely represents the patient's anatomy than traditional fixed atlases. Intraoperative microelectrode recording (MER) has traditionally been the

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gold standard for optimal electrode placement in DBS procedures. However, modern imaging technology, such as the Elements Segmentation Basal Ganglia algorithm, enables patient-specific 3D visualization of the target through advanced MRI-based automatic segmentation. This approach improves surgical planning and intraoperative visualization, ultimately enhancing the accuracy of DBS electrode placement. Postoperatively, visualization software like the Boston Scientific Guide™ Deep Brain Stimulation Visualization System and the Medtronic SureTune™3 software for DBS enables clinicians to optimize DBS programming by visualizing the implanted lead and its anatomical surroundings in 3D. These systems provide patient-specific visualization of the lead location and simulated volume of neural activation, facilitating precise and efficient treatment while improving patient management. These advanced computational modeling and visualization technologies represent significant advancements in DBS therapy, enabling clinicians to tailor treatment more effectively to individual patient needs and ultimately improving patient outcomes.

4. Conclusions

The current advancements in hardware and software for Deep Brain Stimulation (DBS) represent a significant area of growth within functional neurosurgery, holding promise for substantially enhancing outcomes and broadening the scope of neurological disorders treatable via DBS. The advent of directional DBS (dDBS) marks a pivotal moment in neuromodulation, offering the potential to augment benefits for Parkinson's disease (PD) patients, optimize clinical outcomes more effectively, and address refractory symptoms in a data-driven manner. Through the implementation of a multimodal programming strategy that integrates novel current fractionation technology with image-guided tools for lead localization and brain sensing, dDBS stands to diminish reliance on conventional trial-and-error programming approaches. Instead, it introduces a potentially predictive method for applying therapy. These advancements pave the way for developing robust closed-loop stimulation systems, also known as adaptive DBS, capable of seamlessly integrating continuous data streams on disease state dynamics. However, further research is imperative to evaluate these novel technologies' safety and efficacy comprehensively. Ongoing investigations will refine these innovations, ensuring they adhere to the highest safety and efficacy standards, ultimately benefiting patients undergoing DBS therapy.

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References

1. Foutz TJ, McIntyre CC. Evaluation of novel stimulus waveforms for deep brain stimulation. J Neural Eng. 2010 Dec;7(6):066008. doi: 10.1088/1741-2560/7/6/066008. Epub 2010 Nov 17. PMID: 21084732; PMCID: PMC3018699.
2. Schüpbach WMM, Chabardes S, Matthies C, Pollo C, Steigerwald F, Timmermann L, Visser Vandewalle V, Volkmann J, Schuurman PR. Directional leads for deep brain stimulation: Opportunities and challenges. Mov Disord. 2017 Oct;32(10):1371-1375. doi: 10.1002/mds.27096. Epub 2017 Aug 26. PMID: 28843016.
3. Lavano A, Torre AD, Guzzi G (2016) Directional Deep Brain Stimulation. Brain Disord The 5: 220. doi:10.4172/2168-975X.1000220
4. Hell F, Palleis C, Mehrkens JH, Koeglsperger T, Bötzel K. Deep Brain Stimulation Programming 2.0: Future Perspectives for Target Identification and Adaptive Closed Loop Stimulation. Front Neurol. 2019 Apr 3;10:314. doi: 10.3389/fneur.2019.00314. PMID: 31001196; PMCID: PMC6456744.
5. Wårdell K, Nordin T, Vogel D, Zsigmond P, Westin CF, Hariz M, Hemm S. Deep Brain Stimulation: Emerging Tools for Simulation, Data Analysis, and Visualization. Front Neurosci. 2022 Apr 11;16:834026. doi: 10.3389/fnins.2022.834026. PMID: 35478842; PMCID: PMC9036439.

6. Paff M, Loh A, Sarica C, Lozano AM, Fasano A. Update on Current Technologies for Deep Brain Stimulation in Parkinson's Disease. J Mov Disord. 2020 Sep;13(3):185-198. doi: 10.14802/jmd.20052. Epub 2020 Aug 31. PMID: 32854482; PMCID: PMC7502302.
7. Johansson JD, Zsigmond P. Comparison between patient-specific deep brain stimulation simulations and commercial system SureTune3. Biomed Phys Eng Express. 2021 Jul 1;7(5). doi: 10.1088/2057-1976/ac0dcd. PMID: 34161929.
8. McIntyre CC, Foutz TJ. Computational modeling of deep brain stimulation. Handb Clin Neurol. 2013;116:55-61. doi: 10.1016/B978-0-444-53497-2.00005-X. PMID: 24112884; PMCID: PMC5570759.
9. Maks CB, Butson CR, Walter BL, Vitek JL, McIntyre CC. Deep brain stimulation activation volumes and their association with neurophysiological mapping and therapeutic outcomes. J Neurol Neurosurg Psychiatry. 2009 Jun;80(6):659-66. doi: 10.1136/jnnp.2007.126219. Epub 2008 Apr 10. PMID: 18403440; PMCID: PMC2859444.
10. Parastarfeizabadi M, Kouzani AZ. Advances in closed-loop deep brain stimulation devices. J Neuroeng Rehabil. 2017 Aug 11;14(1):79. doi: 10.1186/s12984-017-0295-1. PMID: 28800738; PMCID: PMC5553781.
11. Priori A, Foffani G, Rossi L, Marceglia S. Adaptive deep brain stimulation (aDBS) controlled by local field potential oscillations. Exp Neurol. 2013 Jul;245:77-86. doi: 10.1016/j.expneurol.2012.09.013. Epub 2012 Sep 27. PMID: 23022916.
12. Schüpbach WMM, Chabardes S, Matthies C, Pollo C, Steigerwald F, Timmermann L, Visser Vandewalle V, Volkmann J, Schuurman PR. Directional leads for deep brain stimulation: Opportunities and challenges. Mov Disord. 2017 Oct;32(10):1371-1375. doi: 10.1002/mds.27096. Epub 2017 Aug 26. PMID: 28843016.
13. Polanski WH, Zolal A, Sitoci-Ficici KH, Hiepe P, Schackert G, Sobottka SB. Comparison of Automatic Segmentation Algorithms for the Subthalamic Nucleus. Stereotact Funct Neurosurg. 2020;98(4):256-262. doi: 10.1159/000507028. Epub 2020 May 5. PMID: 32369819.
14. Reinacher PC, Várkuti B, Krüger MT, Piroth T, Egger K, Roelz R, Coenen VA. Automatic Segmentation of the Subthalamic Nucleus: A Viable Option to Support Planning and Visualization of Patient-Specific Targeting in Deep Brain Stimulation. Oper Neurosurg (Hagerstown). 2019 Nov 1;17(5):497-502. doi: 10.1093/ons/opz015. PMID: 30860266.
15. Maiti TK, Konar S, Bir S, Kalakoti P, Nanda A. Intra-operative micro-electrode recording in functional neurosurgery: Past, present, future. J Clin Neurosci. 2016 Oct;32:166-72. doi: 10.1016/j.jocn.2016.03.028. Epub 2016 Jul 5. PMID: 27396672.
16. Engelhardt J, Guehl D, Damon-Perrière N, Branchard O, Burbaud P, Cuny E. Localization of Deep Brain Stimulation Electrode by Image Registration Is Software Dependent: A Comparative Study between Four Widely Used Software Programs. Stereotact Funct Neurosurg. 2018;96(6):364-369. doi: 10.1159/000494982. Epub 2018 Dec 19. PMID: 30566953.
17. Peeters J, Boogers A, Van Bogaert T, Gransier R, Wouters J, Nuttin B, Mc Laughlin M. Current Steering Using Multiple Independent Current Control Deep Brain Stimulation Technology Results in Distinct Neurophysiological Responses in Parkinson's Disease Patients. Front Hum Neurosci. 2022 Jun 2;16:896435. doi: 10.3389/fnhum.2022.896435. PMID: 35721356; PMCID: PMC9203070.
18. Vitek JL, Jain R, Chen L, Tröster AI, Schrock LE, House PA, Giroux ML, Hebb AO, Farris SM, Whiting DM, Leichliter TA, Ostrem JL, San Luciano M, Galifianakis N, Verhagen Metman L, Sani S, Karl JA, Siddiqui MS, Tatter SB, Ul Haq I, Machado AG, Gostkowski M, Tagliati M, Mamelak AN, Okun MS, Foote KD, Moguel-Cobos G, Ponce FA, Pahwa R, Nazzaro JM, Buetefisch CM, Gross RE, Luca CC, Jagid JR, Revuelta GJ, Takacs I, Pourfar MH, Mogilner AY, Duker AP, Mandybur GT, Rosenow JM, Cooper SE, Park MC, Khandhar SM, Sedrak M, Phibbs FT, Pilitsis JG, Uitti RJ, Starr PA. Subthalamic nucleus deep brain stimulation with a multiple independent constant current-controlled device in Parkinson's disease (INTREPID): a multicentre, double-blind, randomized, sham-controlled study. Lancet Neurol. 2020 Jun;19(6):491-501. doi: 10.1016/S1474-4422(20)30108-3. Epub 2020 May 26. Erratum in: Lancet Neurol. 2020 Sep;19(9):e8. PMID: 32470421.
19. Brücke C, Kempf F, Kupsch A, Schneider GH, Krauss JK, Aziz T, Yarrow K, Pogosyan A, Brown P, Kühn AA. Movement-related synchronization of gamma activity is lateralized in patients with dystonia. Eur J Neurosci. 2008 May;27(9):2322-9. doi: 10.1111/j.1460-9568.2008.06203.x. Epub 2008 Apr 22. PMID: 18430031.

Preprints.org (www.preprints.org) | NOT PEER-REVIEWED | Posted: 14 February 2024 doi:10.20944/preprints202402.0800.v1

20. Quinn EJ, Blumenfeld Z, Velisar A, Koop MM, Shreve LA, Trager MH, Hill BC, Kilbane C, Henderson JM, Brontë-Stewart H. Beta oscillations in freely moving Parkinson's subjects are attenuated during deep brain stimulation. Mov Disord. 2015 Nov;30(13):1750-8. doi: 10.1002/mds.26376. Epub 2015 Sep 11. PMID: 26360123.
21. Dergachyova O, Zhao Y, Haegelen C, Jannin P, Essert C. Automatic preoperative planning of DBS electrode placement using anatomo-clinical atlases and volume of tissue activated. Int J Comput Assist Radiol Surg. 2018 Jul;13(7):1117-1128. doi: 10.1007/s11548-018-1724-8. Epub 2018 Mar 20. PMID: 29557997.
22. França C, Carra RB, Diniz JM, Munhoz RP, Cury RG. Deep brain stimulation in Parkinson's disease: state of the art and future perspectives. Arq Neuropsiquiatr. 2022 May;80(5 Suppl 1):105-115. doi: 10.1590/0004-282X-ANP-2022-S133. PMID: 35976323; PMCID: PMC9491408.
23. Mancini F, Guzzi G, Castrioto CF, Cavallo MA, Conti A, Conti C, Della Torre A, Esposito F, Iorio G, Landi A, Lanotte M, Lavano A, Locatelli M, Longhi M, Marruzzo D, Mondani M, Morace R, Pellizzari M, Piacentino M, Picozzi P, Romeo F, Sarrubbo S, Servello D, Somma T, Trezza A, Tringali G, Tufo T, Ricciuti RA. Deep brain stimulation for Parkinson's disease in practice: results of the survey by the Italian Neurosurgery Society. J Neurosurg Sci. 2022 Dec;66(6):526-534. doi: 10.23736/S0390-5616.22.05751-4. Epub 2022 Sep 9. PMID: 36082836.
24. La Torre D, Della Torre A, Chirchiglia D, Volpentesta G, Guzzi G, Lavano A. Deep brain stimulation for treatment-resistant depression: a safe and effective option. Expert Rev Neurother. 2020 May;20(5):449-457. doi: 10.1080/14737175.2020.1749049. Epub 2020 Apr 4. PMID: 32223454.
25. Lavano A, Guzzi G, Della Torre A, Lavano SM, Tiriolo R, Volpentesta G. DBS in Treatment of Post-Traumatic Stress Disorder. Brain Sci. 2018 Jan 20;8(1):18. doi: 10.3390/brainsci8010018. PMID: 29361705; PMCID: PMC5789349.
26. Guzzi G, Della Torre A, Chirchiglia D, Volpentesta G, Lavano A. Critical reappraisal of DBS targeting for movement disorders. J Neurosurg Sci. 2016 Jun;60(2):181-8. Epub 2016 Mar 25. PMID: 27015393.