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REVIEWS

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Ultra High Field MRI-Guided Deep Brain Stimulation

Birte U. Forstmann,[1,2,*] Bethany R. Isaacs,[1,3] and Yasin Temel[3,4]

Deep brain stimulation (DBS) is a neurosurgical treatment for neurological disorders often planned with 1.5-T or 3-T MRI. The clinical efficacy of DBS can be improved using ultrahigh-field (UHF) MRI for planning by increasing the level of precision required for an individualized approach.

DBS in Parkinson's Disease (PD)

> My neurologist has advised me to think about DBS-surgery, and when I see the reports on TV I would do it immediately, but reading the negative stories on this forum, I get doubts . . .

A DBS candidate posted the above quotation on a web-based forum for patients with PD (http://forum.parkinson-vereniging.nl). The quotation illustrates that, although the effectiveness of DBS of the subthalamic nucleus (STN) as a treatment for PD has been extensively established, this does not necessarily equate to an increased quality of life as perceived by patients who have either undergone or are candidates for DBS surgery [1,2]. Such negative perceptions stem from the fact that STN DBS is not equally effective in all patients. For instance, a fraction of patients will exhibit little to no change in their motor symptoms while others may develop psychiatric side effects such as cognitive decline, associative disturbances, or emotional disorders, all of which may be attributed to suboptimal placement of DBS leads [3].

Benefits and Accessibility of UHF MRI

Here we discuss how utilizing UHF MRI in preoperative planning for DBS can improve both the clinical outcome and the public's perception of the treatment. The main advantages of UHF MRI are an increased spatial resolution, contrast, and signal that can be achieved in a clinically acceptable timeframe. We explain that by adopting a patient-specific approach to DBS targeting with UHF MRI, we can maximize the clinical efficacy of the treatment for each individual patient while simultaneously eliminating the development of associated side effects.

In The Netherlands there are six active DBS centers (http://www.nfu.nl). Each center is located near a UHF MRI site, offering the opportunity to apply UHF MRI and advance its use for clinical purposes, including DBS, with the added benefit of potential direct collaborations with specialized neuroimaging departments associated with these UHF MRI sites. With this multidisciplinary setup, UHF MRI can become a standard clinical tool for DBS surgeries in The Netherlands, and eventually worldwide (Figure 1).

MRI technology has advanced greatly over the past three decades through higher field strengths and specialized sequences (Figure 2). However, subcortical imaging remains more challenging as these nuclei are scarcely represented in standardized anatomical atlases, are lacking in postmortem validation and at present, require labor-intensive and expert analysis for accurate identification. This is problematic given that the majority of DBS targets are small and deeply situated subcortical nuclei that cannot be reliably nor reproducibly imaged with the clinically utilized 1.5-T and 3-T MRI (Figure 2) [4,5]. However, efforts to create automated parcellation procedures with multimodal contrasts are being made with UHF MRI, which would be of great benefit to DBS targeting [6,7]. Forstmann and colleagues provide a more detailed review on UHF MRI advances in data acquisition and analyses [8,9].

UHF MRI-Guided DBS

Successful application of DBS requires precise localization of the optimal target structure, which is achieved by either preoperative patient-specific MRI or standardized atlases, as well as intraoperative microelectrode recordings (MERs). However, there are two crucial

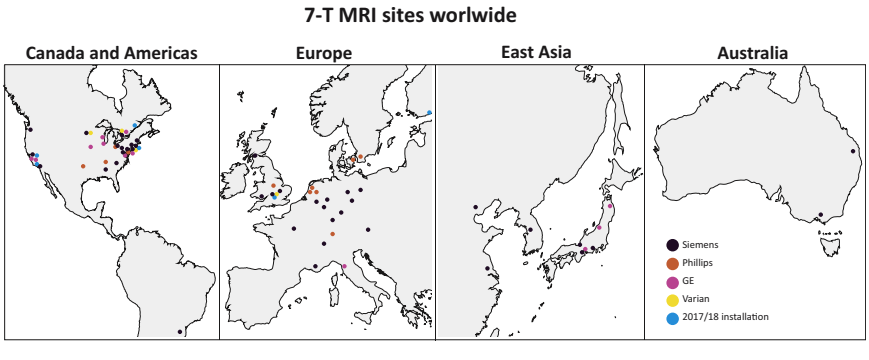

Figure 1. 7-T MRI Sites Worldwide. The figure depicts the locations of all known 7-T MRI sites worldwide. The MR sites are color coded regarding the vendor, where purple represents a Siemens MR scanner location, orange represents a Phillips scanner location, pink represents a GE scanner location, yellow represents a Varian scanner location, and blue represents locations that are planning to install a 7-T MRI system between 2017 and 2018. To date there are 42 7-T Siemens scanners, 12 Phillips scanners, 11 GE scanners, and four Varian scanners, totaling at least 71 whole-body 7-T MR sites worldwide, each either in close proximity to or within a deep brain stimulation (DBS) center.

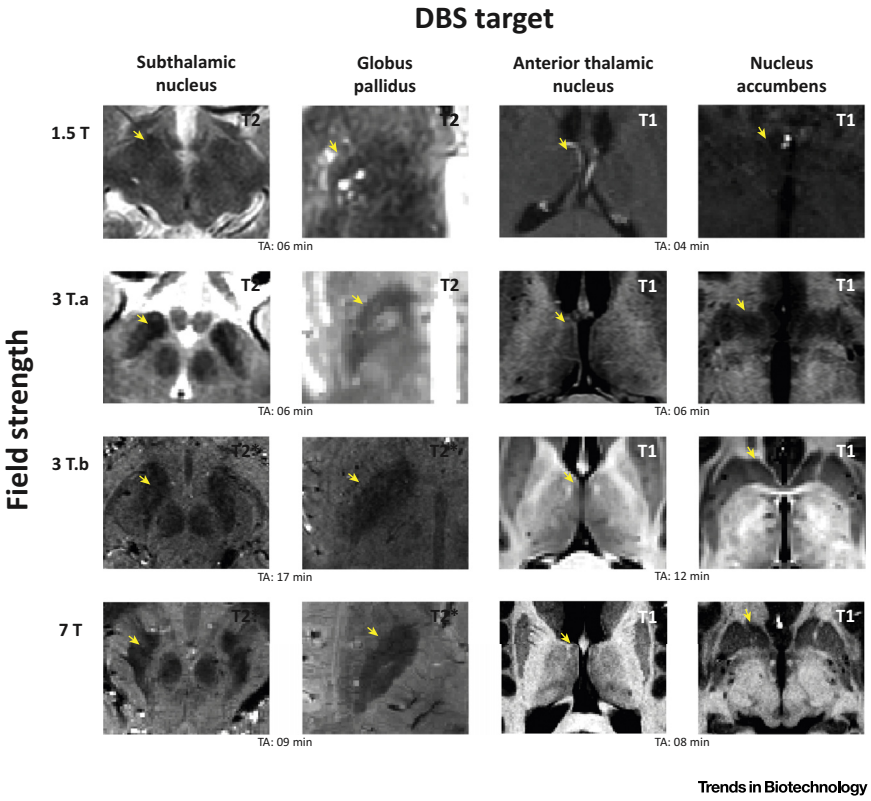

Figure 2. Deep Brain Stimulation (DBS) Targets. The figure illustrates multiple DBS target nuclei across field strengths that require different contrasts. 1.5-T T1 and T2 images were obtained from a 52-year-old male Parkinson's patient at the Maastricht University Medical Centre (MUMC) and 3-T.a images were obtained from 57-year-old male Parkinson's patient with a standard preoperative clinical scan at the MUMC radiological department; the 7-T images also came from this patient. 3-T.b images were obtained from a healthy male subject at Amsterdam's Spinoza Centre for Neuroimaging and are representative of what can be achieved with a longer, optimized sequence. All images are shown in the axial plane and are present in their native space with no post-processing to replicate the visualization of each nucleus as performed on neurosurgical planning software [e.g., the StealthStation® surgical navigation system (Medtronic, MN, USA)]. The T1 contrasts remain constant across field strength for the anterior thalamic nucleus (ANT) and nucleus accumbens (NC). The subthalamic nucleus (STN) and globus pallidus (GP), however, are shown with a T2 contrast at 1.5 T and for the clinically utilized 3-T scan (3 T.a) but with a T2* contrast for an optimized 3-T and a 7-T scan. The acquisition times (TA) for each scan are included to highlight the fact that while an optimized 3-T sequence (3 T.b) may provide high-quality images similar to those at 7 T, they take nearly twice as long to obtain, a factor that is not always clinically feasible. While the STN and GP are visible in both the 3 T.a and 3 T.b images, the contrast and sharpness of borders, especially along the lateral and posterior borders, certainly increases at 7 T. Further, while the ventral intermediate nucleus (VIM), commonly targeted for motor disorders such as tremor, does not show clear delineation along its borders in any field strength, the contrast is increased between other intrathalamic structures at 7 T as seen in the ANT T1 7-T image. Thus, the VIM may be identified through landmark identification of surrounding structures. Therefore, even when a 3-T sequence is optimized, it is clear here that the 7-T images are superior for each nucleus, regardless of contrast. These are representative images shown with permission from the MUMC and Amsterdam Spinoza Centre.

as-yet-unmet requirements for optimal DBS, which are high-precision individualized targeting and reduced operation time.

As previously mentioned, DBS targets are typically visualized with either 1.5-T or 3-T MRI. However, these lower field strengths are often suboptimal compared with 7-T MRI in imaging both entire nuclei, such as the STN or the nucleus accumbens (NC) and subcomponents of thalamic and pallidal structures, such as the anterior thalamic nucleus (ANT), ventral intermediate nucleus (VIM), and globus pallidus interna (GPi) and externa (GPe) [5,10]. Additionally, clinical scans obtained via routine practice are often shorter than those used for research purposes due to limitations in scanning time and therefore differ in quality. While optimized 3-T sequences may allow reasonable visualization of subcortical nuclei, they require a longer acquisition time than an analogous 7-T sequence (Figure 2). Even when low field MRI is optimized for specific nuclei such as the STN, we often fail to achieve consistent volumetric measurements or accurate identification of the cognitive, limbic, and motor subcomponents that are more consistently observed with UHF MRI and which are known to differ both functionally and structurally across individuals [3,4,5,11,12]. Such findings strongly support the use of patient-specific UHF MRI for optimal DBS lead placement, for which the same logic may extend to other types of stereotaxic neurosurgery [12,13].

Additionally, clinical identification of subcortical DBS targets is largely achieved via anatomical landmarks and *a priori*-defined assumptions, especially when a nucleus such as the VIM or ANT is not directly observable. Such an approach to identification is likely to vary from surgeon to surgeon. Therefore, to avoid subjectivity it is important to accurately image not only the target nucleus but also its surrounding structures, such as the internal capsule and mammillothalamic tracts, which are best achieved by the increased signal and contrast afforded by UHF MRI.

Furthermore, the viability of the DBS target must be either confirmed or modified with time-consuming and invasive intraoperative electrophysiological methods obtained during implantation, such as microelectrode recordings, macrostimulation, and behavioral feedback in the awake patient [4]. If surgery were planned using UHF MRI, target nuclei could be more reliably and objectively identified,

limiting the chance of having to remove and/or re-implant suboptimally placed DBS leads. Further, high-precision imaging would reduce operation time and allow the patient to be placed under general sedation where behavioral assessments can be conducted postoperatively, ultimately maximizing patient comfort.

An additional factor to consider is whether stimulation of the targeted nucleus will result in the optimal clinical outcome. The choice of DBS target depends on the clinical presentation of symptoms, which can vary within the same disease across patients and is highly dependent on individual differences in neuroanatomy. The number of different DBS targets that exist for the same disorder illustrates this variation. For PD and related movement disorders, DBS targets include not only the STN but also the substantia nigra, GPi, and VIM. In epilepsy, the hippocampus, ANT, or centromedian thalamic nucleus and seizure foci themselves are possible neurostimulation targets, and for obsessive compulsive disorder (OCD) possible targets include the medial thalamus, the anterior limb or ventral part of the internal capsule and the NC [2]. Such findings call into question the accuracy and reproducibility of low field MRI and raise several questions. How do we choose the target nucleus for each disorder and is this target different for each patient?

We believe each issue described here can be overcome by applying patient-specific UHF MRI. UHF MRI allows more anatomically correct imaging and accounts for subtle individual differences in neuroanatomy that cannot be captured with lower field strengths. Specialized sequences already exist for complex structures such as intrathalamic subnuclei, which could greatly aid preoperative planning for DBS in OCD, tremor, Tourette's, and epilepsy [5]. UHF functional MRI and diffusion-weighted imaging may be used to determine the nature of structural and functional connectivity for subcomponents of target nuclei, facilitating, for example, the identification of the motor portion of the STN for PD patients, which would maximize the efficacy of treatment while minimizing the occurrence of psychiatric side effects [12,13]. Further, high-precision imaging should also result in the elimination of intraoperative testing, permitting surgery to be performed under general anesthesia, which maximizes patient comfort as well as minimizing the related anxiety often reported by potential DBS candidates.

Remaining Challenges

Despite the advantages discussed above, the application of UHF MRI in neurosurgical targeting is not yet FDA approved and is very much an experimental technique, requiring a more advanced knowledge than is typical in the field of clinical radiology. Moreover, the aforementioned practices remain to be standardized or implemented on conventional scanners. Numerous challenges exist regarding increased geometric distortions, specific absorption rate, power deposition and artifacts, inhomogeneity of the B1 field, incompatible coils, and contraindicative metal implants [14]. Ongoing technical developments to harmonize the B1 field with specially designed coils, as well as the development of UHF coils that are compatible with stereotaxic coordinate frames along with corresponding fusion protocols, optimization of sequences, radiofrequency shimming, post-processing, and multimodal methods, are under way to counter such challenges [14,15].

Concluding Remarks

UHF MRI should be the new gold standard for stereotaxic neurosurgical procedures such as DBS. Before this can become reality, UHF MRI must be confirmed as a superior method for localizing surgical targets. For this, MR researchers and neuroscientists must collaborate with neurosurgeons and clinics to start consistently utilizing UHF MRI for DBS preoperative planning. Then we can begin to assess postoperative lead placement and behavioral outcome to determine whether targeting at UHFs does indeed significantly increase the efficacy of the treatment as well as reduce the occurrence of associated side effects compared with targeting with clinical MR. The promotion of such a vision will further require a systematic and updated review of the various stereotactic methods, targeting techniques, MR parameters utilized for preoperative planning, and intraoperative CT verification, as well postoperative confirmation of DBS lead location.

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