EVALUATION OF TARGETING FRAMES FOR DEEP-BRAIN STIMULATION USING VIRTUAL TARGETS

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ABSTRACT

Surgery for deep-brain stimulation (DBS) requires implanting of stimulators at target positions with submillimetric accuracy, typically via stereotactic frames. A recent innovation replaces the large, universal frame with a miniature frame customized per patient. We present a method for evaluating the accuracy of these new frames using “virtual targets” to avoid collision of implant with target. We implement virtual targets by mounting fiducial markers on an artificial skull and defining the targets relative to that fiducial system. The fiducial system is designed such that it surrounds the targets, thereby reducing the overall effect of fiducial localization inaccuracies. It also provides the transformation from image to physical space. Target selection is based on an atlas of stimulation targets from a set of 31 DBS patients. The measured error is the displacement between phantom implant and virtual target. The new frame was found to have submillimetric accuracy with 0.45 mm RMS error.

Keywords: Surgery, Medical treatment, Image registration, Error analysis

1. INTRODUCTION

Deep brain stimulation (DBS) is a surgical procedure for the treatment of tremor, rigidity, and drug-induced side effects in patients with Parkinson’s disease and essential tremor. The first FDA approval for DBS was granted in 1998. Since then the procedure has gained recognition for treatment of movement disorders [1, 2]. The procedure requires placing a 4-contact electrode within deep-brain targets ranging from 4 to 12 mm in diameter. This placement requires stereotactic neurosurgical methodology. The electrode must be placed centrally within the desired target nucleus for effective stimulation [3], preferably with two contacts above the target and two below. If the contacts are away from the target by 3-4 mm, then the stimulation is ineffective because (a) it fails to stimulate the desired group of neurons, (b) undesired areas are stimulated resulting in unpleasant stimulation, or (c) it requires higher currents to produce the desired effect, thereby reducing the battery life of the implant. When the center of the electrode is placed within about 1 mm of the targeted neurons, these problems are avoided. Thus submillimetric error is the goal.

Implantation of the DBS electrode is a step-wise process [4]: (1) determining the approximate location of surgical targets preoperatively, (2) mapping the key features associated with the intended target during the surgery, (3) adjusting the final target of implantation by appropriate shifts in three-dimensional space, and (4) implanting the 4-contact electrode with the contacts surrounding the final desired target. The surgical targets include the Ventral intermediate nucleus (Vim), the subthalamic nucleus (STN), or the Ventrocaudalis nucleus. They are not visible clearly in CT or MR images and are selected preoperatively based on the nearby structures that are visible in the images [5]. The surgeon then adjusts the target position intraoperatively. Error can be introduced in each of the steps during the implantation.

Figure 1. A dual-target microTargeting® Platform.
Stereotactic frames are traditionally employed to guide the target localization and implantation process [4]. A recently developed alternative is a customized, miniature frame—the StarFix microTargeting® Platform (FDA 510(K), Number: K003776, Feb 23, 2001, FHC, INC; Bowdoin, ME, USA) (Figure 1). Depending on the type of frame, three or four anchors (WayPoint™, FHC, INC) are implanted into the patient’s skull, and CT and/or MR images are obtained. A frame, customized for the specific patient and specific procedure, is then fabricated based on the specific position of the anchors, desired entry point, and surgical target for that patient [6]. During the surgery the frame is mounted on the anchors and then used to guide the implantation. It has these advantages over the traditional frame: (1) The image acquisition and the target planning can be done prior to the day of the surgery. (2) The smaller and lighter frame allows freedom of movement to the patient, who for movement evaluation is awake during the procedure. (3) Bilateral implantations can be performed during one procedure.

The customized frame was shown to have submillimetric accuracy in reaching the target by its manufacturer for FDA testing. They used a phantom that included a physical target, and they reported difficulty with measurements due to collisions between the probe and target. An IRB-approved study was subsequently conducted by some of us [4] to measure the accuracy of the system in a clinical setting. That study measured the electrode placement error, which is the distance between the planned target location and the initial electrode placement (i.e., before correction based on intra-operative evaluation). The mean error for 20 implantations was found to be 2.8 mm. This error reflected the error involved in the entire surgical process plus a post-operative image-registration step. In an effort to reduce overall error, it is important to isolate individual error contributions. The goal of the work reported here is to determine the frame’s contribution. We report results based on a study using skull phantoms.

2. METHODS

A direct method to determine the accuracy of the frame would be to insert a probe and measure its distance from a physical target. However, with that method the probe is at risk of colliding with the target, thereby increasing the measured error. In this study we overcome this problem by replacing physical targets with virtual targets, which are points defined geometrically relative to a fiducial system.

We use an artificial skull (Anatomical Chart Company, Skokie, IL) that is cut so that we have access to the target area for the DBS implants. To enhance the rigidity of the relatively pliable plastic that plays the role of bone, we fill the hollow skull with a ceramic casting compound (Rescor 740, Cotronics Corp., Brooklyn, NY).

Figure 2. Skull filled with ceramic-based casting compound and a circular ring attached. The circular ring has 16 Titanium spheres. Two holes were drilled to allow probes to pass through the skull for CMM measurements.

A circular ring is attached to the inside of the skull with 16 fiducial markers (Figure 2). The fiducials are Titanium spheres of diameter 4.4 mm, whose centers can be localized accurately both in CT space and in physical space. The virtual targets are defined relative to these fiducials, which are arranged to surround the targets, thereby reducing the error due to localization inaccuracies [7].

We obtain target positions by manually registering the skull CT to an atlas, in which a cluster of target locations has been determined from a set of 31 DBS patients [8]. Two target points are defined for the skull—the mean cluster position of the subthalamic nuclei (STN) on the two sides (left STN and right STN). Random perturbations are then selected from a normal distribution matching that of the cluster and applied to these positions to produce the virtual targets in the CT image space. Planning is performed, the plan is emailed to a fabrication location (FHC), and the frame is built and shipped back to us.

The frame is then mounted on the anchors and the entry point(s) are marked on the skull. The frame is removed, and an oversized hole is drilled in the skull to allow free passage of a rigid probe, which plays the role of the DBS electrode implant, from the frame into the interior of the skull. The frame is then remounted on the anchors.

To comply with typical DBS frame dimensions, the frame is constructed such that the distance of the target from the instrument mounting surface of the frame is 120 mm, and the probe is designed so that, once it is fixed to the frame, its shaft will pass through the entry point and its tip will be at the desired target position. The probe tip is a ball of diameter 9.5 mm, whose center is the representative position of the center of the DBS implant. The error of the
frame is now defined as the distance of this center to the virtual target. We call this error the target registration error (TRE) [9].

The virtual target is defined using the set of spherical fiducial markers attached to the skull. These markers are localized both in the image and physical space. Point-based registration [9] is performed between image space and physical space to transform image space points to physical space. The virtual target in physical space is thus obtained.

All physical space data is acquired with a Brown and Sharpe, Chameleon coordinate measuring machine (CMM) (Wright Industries, Nashville, TN, calibration 4/11/06, certificate 4112006029735005) (Figure 3), in particular the centers of the spherical fiducial markers and of the probe tips. The CMM probe touches five or more points on the surface of a sphere to compute its center. The frame error is the distance between the center of the probe tip (measured by the CMM) and the virtual target obtained by transforming the image space target point on the basis of the positions of the fiducials in the two spaces. A TRE, which we label measuredTRE, is computed for each target for each frame. measuredTRE is due to three independent components:

1. FLETRE—due to fiducial localization error (FLE) in the image and physical space
2. TLE—error in the localization of the probe tip in the physical space by the CMM
3. frameTRE—error contributed by the frame.

Thus,
\[
\langle \text{TRE}_{\text{measured}}^2 \rangle = \langle \text{TRE}_{\text{FLE}}^2 \rangle + \langle \text{TLE}^2 \rangle + \langle \text{TRE}_{\text{frame}}^2 \rangle
\]  

(1)

where \( \langle \rangle \) means expected value. TRE_{FLE} at a point \( r \) can be calculated using the equation [9, 10]:

\[
\langle \text{TRE}_{\text{FLE}}^2 (r) \rangle = \frac{\langle \text{FLE}^2 \rangle}{N} \left( 1 + \frac{1}{3} \sum_{k} d_k^2 \right)
\]  

where \( N \) is the number of fiducials, \( d_k \) is the distance of \( r \) from the \( k \)th principal axis of the fiducial set, and \( f_k \) is the RMS distance of the fiducials themselves from the \( k \)th principal axis. \( \langle \text{FLE}^2 \rangle \) can be estimated using the equation [9, 10]:

\[
\langle \text{FLE}^2 \rangle = N \langle \text{FRE}^2 \rangle / (N - 2)
\]  

(3)

where FRE is fiducial registration error, which is the root-mean-square (RMS) distance between corresponding fiducials after a registration. TLE is 0.0055 mm (see next section) and can be ignored in comparison to the other terms in Eq. (1). From TRE_{measured} and TRE_{FLE}, TRE_{frame} can be calculated as follows:

\[
\langle \text{TRE}_{\text{frame}}^2 \rangle = \langle \text{TRE}_{\text{measured}}^2 \rangle - \langle \text{TRE}_{\text{FLE}}^2 \rangle
\]  

(4)

3. RESULTS

We report results based on a study using three skulls and nine “dual-target” frames (three frames per skull), which are used to perform bilateral procedures and require four anchors each. Twelve anchors were implanted in each skull with anchor placements selected by a trained neurosurgical resident, and a CT scan was obtained on a Phillips Mx8000 IDT 16 (16-slice acquisition, 120 kVp, 400mA, 750 msec, slice thickness = 0.75mm, pixel sizes = 0.422, 0.404, and 0.586mm for skulls 1, 2, and 3, respectively). We defined two target points—left STN and right STN—and two entry points. The target points were based on the atlas, by randomly varying the mean of the clusters for each target and each frame using the standard deviations of the clusters, which were [0.91, 1.99, 2.05] and [1.24, 1.77, 1.76] mm along the [L, P, S] directions for left STN and right STN respectively. Then three dual-target frames were built for the anchors, using 3 sets of four anchors with no anchor in common. One of the frames was mounted on the anchors, and the two entry points were marked. Then the frame was removed and the oversized holes were drilled.

Each of these three frames was then outfitted with two probes and then attached to the anchors on the skull (Figures 2, 3). The skull was attached to a holder to avoid movement during the CMM measurements and placed on the CMM table (Figure 3).

For the first frame, the location of all sixteen fiducials and the two probe tips were obtained. Then Frame 1 was removed, and Frame 2 was fitted with the same probes and attached to its anchors. For this frame the physical locations of only three fiducials selected from the 16 fiducials and the two probe tips were obtained. A coordinate system was established using these three fiducials (Figure 2). Before the
physical measurements were made with the CMM, the coordinate system for the measurement was oriented to align with the coordinate system used for the measurements with Frame 1 using these 3 spheres. Thus, all the 16 spheres were aligned in the same way for the measurements. Frame 3 was treated similarly to Frame 2. The whole process was repeated for each skull.

The location of the fiducials was also measured in image space. Point-based registration was performed between image and physical space for Frame 1, and the TRE_measured values were computed at the target locations. The image-to-physical RMS(FLE) was found via Eq. (3) to be 0.118 mm which results in an RMS(TRE_FLE) of 0.0315 mm at both of the target positions. The physical-to-physical RMS(FLE) for Frames 2 and 3 was found via Eq. (3) to be 0.00555 mm, which results in a physical-to-physical RMS(TRE_FLE) of 0.00349 mm at the target positions. Combining image-to-physical and physical-to-physical TREs in quadrature gives a total RMS(TRE_FLE) for Frames 2 and 3 of 0.0317 mm. Table 1 reports RMS(TRE_frame). We note that, because of the small size of RMS(TRE_FLE) relative to RMS(TRE_measured) all RMS(TRE_measured) values are, to two significant figures, the same as RMS(TRE_frame). Thus, our evaluation method is quite accurate. Other statistics on TRE_frame are as follows: N = 18 (two targets for each of the nine frames), mean = 0.43 mm, standard deviation = 0.14 mm, maximum = 0.69 mm, minimum = 0.20 mm. If we assume a normal distribution, we find that TRE_frame is less than 0.80mm at 99% and 0.90mm at 99.9%.

Table 1. RMS(TRE_frame) Values

<table>
<thead>
<tr>
<th></th>
<th>Left STN</th>
<th>Right STN</th>
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</thead>
<tbody>
<tr>
<td>Skull 1</td>
<td>0.50 mm</td>
<td>0.30 mm</td>
</tr>
<tr>
<td>Skull 2</td>
<td>0.49 mm</td>
<td>0.46 mm</td>
</tr>
<tr>
<td>Skull 3</td>
<td>0.47 mm</td>
<td>0.47 mm</td>
</tr>
<tr>
<td>All 3 skulls, both targets</td>
<td>0.49 mm</td>
<td>0.42 mm</td>
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4. CONCLUSION

We described in this paper a method based on the concept of the virtual target to evaluate the accuracy of a new stereotactic frame—the microTargeting® Platform—which is currently being used to guide surgeries for deep-brain stimulation. The virtual target eliminates the problem of collisions between the probe, which the frame is designed to place at a target, and the target itself and thus makes the evaluation more accurate. Each virtual target is defined relative to a fiducial system that is arranged such that it surrounds the target, thereby reducing the error due to fiducial localization inaccuracies. The virtual targets are defined using clusters obtained from atlas images based on 31 DBS patients, and the planning procedure is performed similarly as for DBS surgery. Results show with very high probability that for DBS surgery the microTargeting Platform is accurate to submillimetric level.

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6. REFERENCES