Frameless stereotaxy using bone fiducial markers for deep brain stimulation

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Object. Functional neurosurgical interventions such as deep brain stimulation (DBS) are traditionally performed with the aid of a stereotactic frame. Although frameless techniques have been perceived as less accurate, data from a recent phantom study of a modified frameless approach demonstrated a laboratory accuracy exceeding that obtained using a common frame system. The present study was conducted to evaluate the accuracy of a frameless system in routine clinical use.

Methods. Deep brain stimulation leads were implanted in 38 patients by using a skull-mounted trajectory guide and an image-guided workstation. Registration was accomplished with bone fiducial markers. Final lead positions were measured on postoperative computerized tomography scans and compared with the planned lead positions. The accuracy of the Leksell frame within the clinical situation has been reported on in a recent study; these raw data served as a comparison data set.

The difference between expected and actual lead locations in the x plane was 1.4 mm in the frame-based procedure and 1.6 mm in the frameless procedure. Similarly, the difference in the y plane was 1.6 mm in the frame-based system and 1.3 mm in the frameless one. The error was greatest in the z plane, that is, 1.7 mm in the frame-based method and 2 mm in the frameless system. Multivariate analysis of variance demonstrated no statistically significant difference in the accuracy of the two methods.

Conclusions. The accuracy of the frame-based and frameless systems was not statistically significantly different (p = 0.22). Note, however, that frameless techniques offer advantages in patient comfort, separation of imaging from surgery, and decreased operating time.

KEY WORDS • deep brain stimulation • frameless stereotaxy • stereotactic technique • computer-assisted therapy • surgical technique

The introduction of image-guided surgical systems during the past decade has had a profound impact on neurosurgical practice. Accurate localization of intracranial targets without the use of stereotactic frames has become commonplace. For procedures such as tumor resection, when real-time feedback regarding intracranial position is helpful, image-guided surgical systems have effectively replaced stereotactic frames. Nevertheless, trajectory-based procedures such as lesioning or stimulation of the deep nuclei for Parkinson disease and tremor are still extensively performed using a frame. The benefit of real-time positional feedback in these procedures is less important than the accurate delivery of a probe to a well-defined target. In addition, functional neurosurgery requires a stable platform to examine the brain with microelectrode recording and stimulation over many hours and through multiple parallel trajectories. Skin fiducial markers as traditionally used in frameless localization do not provide sufficient accuracy, and instrument holders for biopsy or other applications do not provide sufficient rigidity to meet the demands of true stereotactic accuracy. Thus, new thinking and instrumentation is needed to adapt these systems for use in functional neurosurgery.

Theoretical advantages of a fully frameless functional surgery system include improved patient comfort, improved ability to perform intraoperative neurological evaluations, separation of imaging and surgery, real-time electrode tracking with the integration of multiple information sources, and the potential for increased accuracy.8-10 Data from several laboratory studies of image-guided surgical systems demonstrated localization accuracies similar to those achievable with a stereotactic frame. Results of preliminary studies have shown the feasibility of using a surgical navigation system in conjunction with an image-guided microdrive to perform functional neurosurgical procedures with acceptable accuracy.

The NeXframe (Image Guided Neurologics, Inc., Mel-
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bourne, FL) is a skull-mounted platform developed specifically to provide a high degree of targeting stability during frameless trajectory-based procedures. We hypothesized that the placement of DBS electrodes with the aid of a frame would not be significantly more accurate or stable than placement using bone fiducial markers and the NeXframe device. We tested this hypothesis by using a three-phase approach, confirming the accuracy of the device at each stage before proceeding to the next. Phase I consisted of a series of laboratory measurements verifying the application accuracy of the NeXframe in a trial involving 25 centers; these results are reported in a separate publication. The mean localization error was 1.25 mm over 560 measurements, which compares favorably to the error reported with the use of stereotactic frames. This accuracy was believed to be sufficient to proceed to Phase II in which we examined the clinical accuracy of the device when used with a stereotactic frame as backup. In the final phase (Phase III) of the study, the NeXframe was used in a completely frameless setting. In this report we describe the results of Phases II and III.

Clinical Material and Methods

The study protocol was approved by the Institutional Review Board at each participating institution, and informed consent was obtained from each patient prior to participation in the study. Patients who chose not to participate were offered a standard frame-based approach to surgery.

Phase II

Following verification of laboratory accuracy in Phase I, the NeXframe was used in conjunction with a stereotactic frame to evaluate clinical targeting accuracy compared with the gold standard for localization accuracy. Five centers participated in this phase of the study, with a total of 19 enrolled patients. Eleven patients underwent thalamic DBS and eight patients underwent subthalamic DBS. Volumetric T2-weighted MR images of the entire head as well as coronal T2-weighted slabs through the STN (in patients undergoing subthalamic DBS) were obtained 2 to 30 days prior to the procedure. On the day of surgery, the stereotactic frame (Cosman-Roberts-Wells or Leksell) and four to six bone fiducial markers (Stryker-Leibinger, Kalamazoo, MI) were applied to the skull. Radiopaque markers were placed atop each fiducial screw, and the carbon fiber N-bar fiducial system for the frame system was applied to the base ring. Serial CT scans of either 1- or 2-mm slice thickness were obtained throughout the cranial volume, and all image data sets were loaded into the StealthStation FrameLink software package. Computerized tomography and MR images were fused and the appropriate nucleus was targeted in the usual fashion. The center of each skull fiducial marker was localized on the CT scans. The N-bar fiducial rods were marked and a frame target was derived. A CT scan was used as the reference in all cases. The use of microelectrode recording varied according to surgeon preference. One of the investigators performed the procedure in the CT scanning suite and monitored lead placement using the CT scanner; all other investigators performed the surgery in the operating suite and monitored lead locations with fluoroscopy.

The radiopaque spheres were removed from the skull fiducial markers, and stainless-steel localizing divots were placed. Following sterile preparation and drape, target coordinates were entered into the stereotactic frame and the arc was rotated posteriorly to allow localization with the NeXframe. A StealthStation reference arc was attached to the frame or directly to the skull, and each fiducial marker was touched in turn by using a passive planar probe equipped with reflective spheres, which could be tracked by the cameras of the StealthStation. Registration was successful in all cases. A guide tube equipped with light-emitting diodes was then attached to the NeXframe, and alignment with the previously planned trajectory was accomplished. To verify alignment, the arc and ring angles of the frame were changed to match the preplanned trajectory. A stainless-steel mandrel (outside diameter 6.3246 mm: +0 mm/−0.0254 mm) was passed through the instrument holder of the frame system, and alignment was verified if the mandrel passed through the bushing of the NeXframe (inside diameter 6.3551 mm: +0.0127 mm/−0 mm) without resistance.

If the trajectory was successfully verified, the arc was again moved posteriorly and the remainder of the procedure performed using the NeXframe to guide the cannula and electrode into place. If, based on intraoperative physiological features, the DBS lead was implanted at a location other than the initial target, the final expected lead location was reported in coordinates relative to the midpoint of the AC–PC plane.

Immediately following surgery, a CT scan was obtained to evaluate lead position, assess postoperative pneumocephalus, and rule out asymptomatic hemorrhage. This CT scan was loaded onto the StealthStation, and image fusion was performed with the preoperative MR and CT images. The final lead location was identified as the center of the beam-hardening artifact representing the deepest electrode contact. The difference between the expected lead location and the CT scanning–verified lead location was expressed as a signed distance in each of the x, y, and z coordinates, with negative values indicating medial, posterior, and deep deviations.

Phase III

After completing Phase II as well as an analysis of its results, we proceeded to Phase III testing. Again, 19 patients (six VIM, 12 STN, and one GPI) from five centers were enrolled in this phase, which involved a completely frameless approach, thus entirely eliminating the use of the stereotactic headframe. Magnetic resonance images were obtained 2 to 30 days preoperatively, as described previously. The day prior to surgery, four to six bone fiducial markers were placed after application of a local anesthetic agent with or without sedation prior to obtaining a fine-cut CT scan, as described earlier. The MR image was fused to the reference CT scan, and targeting was performed. The patient was secured in position by using one of several methods. Initially, a Mayfield headholder was used to maintain rigid fixation. As the investigators gained comfort with the technique, this holder was replaced by a Xomed noninvasive head restraint (Fig. 1), and finally by a head cradle with a cervical collar providing moderate immobilization (Fig. 2). A nonsterile reference arc was attached to the head restraint, and each fiducial marker was touched with a registration probe. Entry points were marked on the scalp, and the patient was prepared and draped in a sterile fashion. Following burr hole
placement, the NeXframe was attached and a sterile reference arc was fastened to the base of the tower (Fig. 3). Registration was again performed by touching each fiducial marker through the drape (Fig. 4). In each case the sphere of predicted 1-mm accuracy encompassed the entire cranial volume (Fig. 5). Microelectrode recording was performed according to each institution’s usual protocol. If, based on intraoperative physiological characteristics, the DBS lead was implanted at a location other than the initial target, the expected lead location was reported in AC–PC coordinates reflecting these changes. A postoperative CT scan was obtained, and the distance between expected and actual lead placements was measured, as described previously. The difference between the expected lead location and the CT scanning–verified lead location was expressed as a signed distance in each of the x, y, and z coordinates, with negative values indicating medial, posterior, and deep deviations.

The mean localization errors were calculated for both phases of the study in each of the x, y, and z directions by using both signed and absolute values. Vector localization errors were also calculated using the formula \((x^2 + y^2 + z^2)^{1/2}\) for each localization, and the mean of these aggregate localization errors was reported for each phase.

**Comparative Frame Data Set**

Starr, et al.,\(^{16}\) reported on a series of 76 deep brain stimulators that had been placed in the STN by using the Leksell frame. Their report included data on the deviation of the DBS lead from the expected location of the final track, which had been assessed using the same techniques described in the present study. The expected final lead location was specified by noting the location of the final track in reference to the original target. The AC–PC coordinates of the tip of the DBS lead on the postoperative scan were recorded and compared with the expected location. Errors in the x, y, and z directions were noted and a vector localization error was calculated, as described previously. Raw data from this report serve as a reference for the clinical accuracy of the frame-based system.

**Statistical Analysis**

Biostatistical analysis was performed for the direct measurements, namely the x, y, and z coordinates of error, the absolute values of these coordinates, and the derived length of the vectors. A MANOVA was applied to compare the difference in the accuracy between the frame-based and frameless systems. The MANOVA simultaneously compared the three signed measurements (x, y, and z). A 95% confidence ellipsoid around the mean was generated for both of the systems.
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Analysis of the absolute x, y, and z errors provides more accurate information about the magnitude of the errors because it does not allow a positive error to cancel out a negative error (for example, a medial error in one patient does not cancel out a lateral error in another patient). Nevertheless, the signed values provide information about the centering of data around the zero point, which represents the locus of no error. The mean lengths of the vectors in the frame-based and frameless groups were compared using a t-test. In all analyses an assumption of normality was made; this assumption was verified using the usual diagnostics. The skewness and kurtosis were compared with those that

Fig. 3. Photograph showing the NeXframe secured over the burr hole with bone screws and the Stealth spinal reference arc rigidly fixed to the tower.

Fig. 4. Photograph illustrating how registration is performed by touching the center of the divot of each fiducial marker, which corresponds to the center of the fiducial sphere on imaging.
would be expected in normality, and a test of normality using the Shapiro–Wilk test was performed. In addition, normal probability plots and box plots were examined.

Results

A total of 47 electrodes were implanted in 38 patients: 23 in Phase II and 24 in Phase III. Twenty-six of these were implanted with the aid of microelectrode recording. The targeted nucleus was the VIM in 16 cases, the STN in 29, and the GPI in two. Forty-two postoperative coordinates were available for error analysis, although the coordinates could not be assessed in four patients. Two patients did not undergo electrode implantation (see Protocol Deviations). Two patients whose postoperative CT scans had been performed incorrectly (using slice thicknesses of 10 mm rather than 1–2 mm) were not included in analysis. The outcomes in these patients were similar to those in whom postoperative coordinates were obtained.

During Phase II, patients underwent frameless placement of the DBS electrodes with the frame as a backup. In every instance there was a good match of the stereotactic frame

TABLE 1

Comparison of the accuracy demonstrated in Phase II (combined frame-based and frameless methods) and Phase III (completely frameless methods)*

<table>
<thead>
<tr>
<th>Group</th>
<th>X</th>
<th>Y</th>
<th>Z</th>
<th>Vector</th>
</tr>
</thead>
<tbody>
<tr>
<td>Phase II study</td>
<td>1.7 ± 1.0</td>
<td>1.0 ± 0.8</td>
<td>2.4 ± 1.5</td>
<td>3.3 ± 1.5</td>
</tr>
<tr>
<td>Phase III study</td>
<td>1.5 ± 0.9</td>
<td>1.5 ± 1.2</td>
<td>1.6 ± 1.1</td>
<td>3.0 ± 1.2</td>
</tr>
<tr>
<td>combined</td>
<td>1.6 ± 1.0</td>
<td>1.3 ± 1.0</td>
<td>2.0 ± 1.3</td>
<td>3.2 ± 1.4</td>
</tr>
<tr>
<td>p value</td>
<td>0.1†</td>
<td>0.4§</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* Values represent the absolute errors ± standard deviations and were calculated by comparing the absolute difference in the expected lead location and the CT scanning–verified location in each plane.
† The 3D vector of these errors was calculated using the formula \((x^2 + y^2 + z^2)^{1/2}\).
§ The x, y, and z values were compared simultaneously with a MANOVA.

TABLE 2

Absolute errors for the frame-based and frameless systems*

<table>
<thead>
<tr>
<th>Group</th>
<th>X</th>
<th>Y</th>
<th>Z</th>
<th>Vector</th>
</tr>
</thead>
<tbody>
<tr>
<td>frame-based</td>
<td>1.4 ± 0.9</td>
<td>1.6 ± 1.1</td>
<td>1.7 ± 1.5</td>
<td>3.2 ± 1.4</td>
</tr>
<tr>
<td>frameless</td>
<td>1.6 ± 1.0</td>
<td>1.3 ± 1.0</td>
<td>2.0 ± 1.3</td>
<td>3.2 ± 1.4</td>
</tr>
<tr>
<td>p value</td>
<td>0.21†</td>
<td>0.95§</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* Values represent the absolute errors ± standard deviations and were calculated by comparing the absolute difference in the expected lead location and the CT scanning–verified location in each plane.
† The 3D vector of these errors was calculated using the formula \((x^2 + y^2 + z^2)^{1/2}\).
§ The x, y, and z values were compared simultaneously with a MANOVA.
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During Phase II, patients underwent frameless placement of the DBS electrodes with the frame as a backup. In every instance there was a good match of the stereotactic frame.
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TABLE 3

Stereotactic errors in the x, y, and z planes

<table>
<thead>
<tr>
<th>Group</th>
<th>X</th>
<th>Y</th>
<th>Z</th>
</tr>
</thead>
<tbody>
<tr>
<td>frame-based</td>
<td>−0.75 (−1.1 to −0.38)</td>
<td>0.76 (0.36 to 1.17)</td>
<td>−0.69 (−1.21 to −0.18)</td>
</tr>
<tr>
<td>frameless</td>
<td>−0.44 (−0.94 to 0.05)</td>
<td>−0.06 (−0.60 to 0.49)</td>
<td>0.42 (−0.27 to 1.11)</td>
</tr>
</tbody>
</table>

trajectory and the NeXframe trajectory. Therefore, all electrodes in Phase II were placed using the frameless trajectory. Absolute errors in each dimension for each study phase as well as the combined data are reported in Table 1. A MANOVA was calculated to look for evidence of differences in the accuracy between the two study phases, and none was found. Thus, the combined data, which includes 42 data points, were then compared with the 76 data points from the frame-based study (Table 2). The difference between expected and actual lead locations in the x plane was 1.4 mm for the frame-based procedure and 1.6 mm for the frameless method; the difference in the y plane was 1.6 mm for the frame-based system and 1.3 mm for the frameless one. The error was greatest in the z plane: 1.7 mm, frame-based system; and 2 mm, frameless system. The derived vectors were 3.15 for the Leksell frame and 3.15 for the frameless system. A MANOVA was performed to test the null hypothesis that the centers of the ellipsoids of the absolute errors for the two procedure groups were equal. The accuracy of the frame-based and frameless systems was not statistically significantly different (p = 0.22).

Next, we considered directional errors, which consisted of the errors in the x, y, and z planes where negative values equaled medial, positive, and deep deviations. A 95% confidence ellipsoid of the 3D data can be described and provides information about the centering of the data around the zero point, which represents the locus of no error. The MANOVA comparing the center of the ellipsoid of the frame-based group to that of the frameless group demonstrated a statistically significant difference (p < 0.008). The frameless group was centered closer to zero than the frame-based group. Looking at each axis separately by using post-hoc t-tests revealed that the difference was statistically significant in the y and z axes (p = 0.018 and 0.01, respectively) but not in the x axis (p = 0.32). The CIs for the frame-based group did not include 0, whereas those for the frameless group did. These findings demonstrated that the error in the frameless group was not only closer to zero but was also centered around zero. The extent of the CIs of the data were greater in the case of the frameless system compared with those in the frame-based system. This was believed to be due mainly to the larger sample size in the frame-based group. The center and the 95% confidence ellipsoid for the two procedure groups are presented in Table 3.

The distribution error can be seen using a spinning box plot (Fig. 6) or a bubble chart (Fig. 7). The x, y, and z coordinates of each error are plotted separately for the frame-based and frameless groups in a 3D spinning box plot (Fig. 6). The zero point or origin represents the locus of no error; a negative value indicates posterior, deep, or medial deviations. Similarly, Fig. 7 shows both sets of errors in a single graph in which x and y errors are indicated by the location of the bubble along each axis and the z (depth) error is indicated by the size of the bubble.

To verify the assumption of normality, formal tests were applied and indicated no departure from normality for most of the variables. These tests were performed separately for each group. There was moderate departure from normality only in the absolute measurements in the frame-based group. The type of departure from normality observed would typically underestimate the probability values. Given that the conclusions for the absolute measurements provided no evidence to reject the null hypothesis, this moderate departure from normality is inconsequential. Visual presentations of the distributions of these variables are shown in the box plots (Fig. 8) whose boxes represent the middle half (50%) of the data.

Protocol Deviations

In one instance early in the series, the lead author (K.L.H.) reverted to frame-based placement to avoid corticomedullary vessels at the entry site. In subsequent cases, this situation was dealt with prior to lead implantation by bipolar cautery of vessels within the planned entry zone. No return to the headframe has since been required for subsequent implants. An alternative method of avoiding a surface vessel is to target with an offset device, which will allow an alternative cortical entry site.

Frameless implantation in one additional patient was attempted and aborted without implantation of the DBS lead because the patient had no intraoperative response to stimulation. Both frameless and frame-based procedures yielded no response to stimulation and equivalent accuracy, which was confirmed with intraoperative x-ray films. No microelectrode recording was performed in this case. The patient was lost to follow-up study.

In a third case, surgery was aborted during microelectrode recording at the patient’s request. The patient was extremely anxious prior to surgery and became progressively more anxious during the lengthy recording procedure. Three microelectrode penetrations had been made without determining an optimal target. The patient subsequently underwent successful frame-based placement of bilateral DBS electrodes with psychological counseling and support during surgery. No evaluation of the localization error could be made in this case.

Early in the study, planning and targeting software had yet to be integrated, thus requiring the creation of a surgical plan in the FrameLink software package and transfer of this plan into the cranial software package to allow navigation. The software was modified during Phase III testing to allow navigation within the FrameLink package. This modification improved the efficiency of the procedure and eliminated the possibility of errors created by writing multiple plans.
in FrameLink and importing an unintended plan into the cranial software package. This process was thought to create two instances of significant z (depth) error, which have not recurred since the software has been modified. Because these errors were detected and corrected intraoperatively, they are not reflected in the postoperative DBS location data set. There was no additional incidence of significant z (depth) errors in the subsequent 44 implants.

Discussion

In this multicenter study, we found no difference between the accuracy of frameless navigation and that of the stereotactic frame, as cited in the literature. The mean vector difference between an expected target and an actual lead location was 3.15 mm for both procedure groups. The error was greatest in the z plane: 1.7 mm for the frame-based system and 2 mm for the frameless system. The difference in the x and y planes was 1.4 to 1.6 mm for both systems. Although there was no difference between the vector errors in the two procedure groups, results of MANOVA demonstrated that the center of the error ellipsoid in the frameless group was not only closer to zero but also better centered around zero than that for the frame-based data.

Phantom studies have demonstrated the mean accuracy of the Cosman-Roberts-Wells and Leksell frames to be 1.7 ± 0.1 and 1.8 ± 0.11, respectively, when using 1-mm CT slice thickness and no weight bearing. The increased error seen in the clinical situation is expected for several reasons, including weight bearing by the frame, mobility of the brain within the cranial cavity, loss of cerebrospinal fluid with subsequent brain shift, inaccuracies of localization introduced by selection of the lead tip and the AC–PC coordinates on postoperative imaging, and deviations of the microelectrode or DBS as it passes through the brain substance.

The accuracy of stereotactic frames and frameless systems has been well studied using phantoms.\cite{1,2,4,6,10,17} Prior to the publication of data obtained by Starr, et al.,\cite{16} however, there had been no similar study of frame-based stereotactic accuracy in the clinical situation.\cite{2,8} Such studies require a marker for actual target localization, with an internal (AC–PC coordinates) or external (frame) reference system on the postoperative scan to compare expected with actual target locations. Alternatively, this process can be accomplished with image fusion, which is a relatively recent development. Starr and colleagues carefully assessed the postoperative coordinates of 76 STN DBS electrodes that had been placed using a Leksell frame and found a mean deviation of 3.15 mm from the expected target location. Similar results have been reported by other authors.\cite{11,13} The University of California Los Angeles group evaluated the discrepancy between expected and actual targets in 217 DBS cases. There was a mean vector error of 2.9 mm (range 0.1–6.44 mm) for VIM, 2.3 mm (range 0–7.61 mm) for STN, and 2.2 mm (range 0.03–4.5 mm) for GPI targets.\cite{11} O’Leary, et al.,\cite{11} analyzed intraoperative radiographic data on 109 microelectrode tracks and found a 2.1-mm discrepancy between the theoretical microelectrode target and the values obtained from intraoperative fluoroscopic images. Dorward and colleagues assessed the error between expected and actual target locations of biopsy sites by using the infrared guide system by Philips. The location of the biopsy site was identifiable on postoperative MR images, which were fused to the preoperative images, and the deviation from the planned target was measured. These data were collected in 15 patients who had undergone biopsy based on 3-mm axial CT scans or 1.5- to 2-mm MR images. The vector of the mean error of localization was 4.8 mm. This result contrasts with a 1.3- to 1.7-mm error demonstrated on phantoms using the same technique.\cite{2} The clinical accuracy of frameless systems using skin fiducial markers has the additional error introduced by mobile or nonfixed marks and the accuracy data reflect this result.

In our study, the mean registration error reported when using the FrameLink software after patient registration with skull fiducial markers was 0.6 ± 0.2 mm. In contrast, the mean registration error using skin fiducial markers, in our hands, is generally in the range of 1.5 to 2 mm. Germano, et al.,\cite{1} assessed registration error using skin fiducial markers during surgical cases by comparing the computer-estim
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![Bubble chart depicting the distribution of the error along the x and y axes of each error. Medial and posterior deviations are negative on the x and y axes, respectively. The magnitude of the error in the z plane is indicated by the size of the bubble. Frame-based data are plotted as open circles, with the heavier outlines indicating positive or superficial errors and lighter outlines indicating negative or deep errors. Frameless data are represented by hatched circles. Vertical hatching indicates positive or superficial z depth errors, and horizontal hatching represents negative or deep errors.](image)

Fig. 7. Bubble chart depicting the distribution of the error along the x and y axes of each error. Medial and posterior deviations are negative on the x and y axes, respectively. The magnitude of the error in the z plane is indicated by the size of the bubble. Frame-based data are plotted as open circles, with the heavier outlines indicating positive or superficial errors and lighter outlines indicating negative or deep errors. Frameless data are represented by hatched circles. Vertical hatching indicates positive or superficial z depth errors, and horizontal hatching represents negative or deep errors.

![Box plots of error variables demonstrating normality for all, except for a mild departure from normality for the absolute values of error for the frame-based system. Boxes represent the middle 50% of the data; diamonds represent the mean; the horizontal line inside the box represents the median; and the whiskers extend to the minimum and maximum. Observations that are 1.5 times larger than the interquartile range are represented by dots and are potential outliers. The bracket shows the middle 50% of the data under normality. Notice that the bracket generally overlaps the box in almost all cases, except for the absolute measurements in the frame group.](image)

Fig. 8. Box plots of error variables demonstrating normality for all, except for a mild departure from normality for the absolute values of error for the frame-based system. Boxes represent the middle 50% of the data; diamonds represent the mean; the horizontal line inside the box represents the median; and the whiskers extend to the minimum and maximum. Observations that are 1.5 times larger than the interquartile range are represented by dots and are potential outliers. The bracket shows the middle 50% of the data under normality. Notice that the bracket generally overlaps the box in almost all cases, except for the absolute measurements in the frame group.

Rohlfing and coworkers found a decrease in the accuracy of stereotactic frames because of torque introduced by the effect of weight bearing on the frame. They assessed the effects of the mechanical loading of the frame and a change
in patient position on localization error within the clinical situation. They chose to compare scans obtained while the patient was prone and supine, maximizing the adverse effect of linear mechanical loading. Computerized tomography scans were obtained in 14 patients placed in the Brown-Roberts-Wells frame while supine and then prone, and the registration transformations were compared. The mean error was 0.97 mm (standard deviation 0.38), but the registration error was greater than 1.5 mm in eight of 14 patients. The authors noted that the errors from positioning and mechanical loading were additive with other sources of error.

There are numerous pitfalls involved in attempting to measure postoperative lead locations accurately. First among these is the difficulty in locating the precise center and depth of the lead as it relates to the intended target. Both magnetic susceptibility artifact (on MR imaging) and beam-hardening artifact (on CT scanning) conceal the lead and require estimation or interpolation of the electrode position. Papavassiliou, et al., evaluated DBS lead locations in eight cases by using both CT and MR imaging studies. They found differences between the two techniques ranging anywhere from −2.4 to 2.6 mm; the mean of these signed values was 0.1 to 0.3 mm and was not significant. Furthermore, because the last contact of a Medtronic DBS lead lies 1.5 mm from the actual tip of the electrode, determining its location on either modality can be difficult. Because the DBS trajectory is not perpendicular to the AC–PC plane, an error in localizing the electrode tip can lead to errors not only in z (depth) but also in the x and y directions, depending on the approach angle (Fig. 9). Even if the lead position can be accurately determined on postoperative imaging, relating this position to the intended target requires a translation method such as image fusion or coordinate transfer, each of which has potential inaccuracies. Thus, some of the errors in this study and the study by Starr and colleagues were most likely due to inaccuracies of the entire process of relating the intended target to the postoperative lead location.

An additional category of error can be related directly to errors in lead placement. Some examples include deflection of the lead during implantation, slippage of the lead during anchoring, and various inaccuracies in stereotactic localization, which have been described elsewhere. Direct measurement of localization errors in phantom studies eliminates the step of translating postoperative imaging to preoperative targeting, which may be a major contributor to the relatively decreased accuracy noted in clinical studies, compared with phantom studies.

Other factors that can influence localization accuracy include differences in scan slice thickness, MR imaging susceptibility artifact, and differences in scanners and fiducial marker placement. In our phantom and clinical studies, we used 1- to 2-mm slice thicknesses for both CT and MR imaging studies. Although errors could potentially be introduced on image fusion, these errors were usually less than 1 to 2 imaging voxels. Many centers routinely use MR/CT image fusion to correct for MR image distortions, and it was decided that the phantom and subsequent clinical phases should be performed in the same manner to replicate the routine clinical situation as closely as possible. Four to five bone fiducial markers were placed in a generalized pattern around the head for CT scanning and this data set was used as the reference scan; the MR image was fused to this scan. Registration accuracy was not related to localization error. Phantom studies in which the current system was used demonstrated that fiducial markers placed in the four corners of the head and one at the vertex provided a mean accuracy of 1.25 mm at the level of the expected nuclear target lo-
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cations. This arrangement also allows the patient to sleep comfortably with the fiducial markers in place without dislodging them.

Several advantages related to the use of the frameless device were realized during the course of this study. Patients were much less apprehensive when faced with skull fiducial marker placement compared with the application of a stereotactic frame. The ability to apply the fiducial markers one or more days prior to surgery allowed imaging and planning to be separated from the performance of the procedure, decreasing operating room time and enhancing patient comfort given the shorter periods spent without medication. Without rigid fixation to the operating table, patients were allowed greater mobility and appeared better able to tolerate lengthy procedures. Intraoperative examination of the patient was easier without the bulky frame.

Conclusions

In this multicenter study, we found no significant difference between the accuracy of frameless navigation in which bone fiducial markers were used and the accuracy of a stereotactic frame, as reported in the literature. The accuracy of both the NeXframe system and the frame in a clinical situation is less than that reported when using phantom in a laboratory setting.

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Disclosure

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Appendix

The following institutions participated in this study:
Medical College of Virginia Hospital of Virginia Commonwealth University, Richmond, Virginia
Hunter Holmes McGuire Veterans Affairs Medical Center, Richmond, Virginia
St. John Medical Center, Tulsa, Oklahoma
Cleveland Clinic Hospitals, Cleveland, Ohio
Celebration Hospital, Celebration, Florida

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