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Clinical Testing of an Alternate Method of Inserting Bone-Implanted Fiducial Markers

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Abstract

Background—Deep brain stimulation (DBS) surgery utilizes image-guidance via bone-implanted fiducial markers to achieve the desired submillimetric accuracy and to provide means for attaching microstereotactic frames. For maximal benefit, the markers must be inserted to the correct depth since over-insertion leads to stripping and under-insertion leads to instability.

Purpose—Test clinically a depth-release drive system, the PosiSeat™, versus manual insertion (pilot hole followed by manual screwing until tactile determined correct seating) for implanting fiducial markers into the bone.

Methods—With institutional review board approval, the PosiSeat™ was used to implant markers in 15 DBS patients (57 fiducials). On post-insertion CT scans, the depth of the gap between the shoulder of the fiducial markers and the closest bone surface was measured. Similar depth measurements were performed on the CT scans of 64 DBS patients (250 fiducials), who underwent manual fiducial insertion.

Results—Median of shoulder-to-bone distance for PosiSeat™ and manual insertion group were 0.03 mm and 1.06 mm, respectively. Fifty percent of the fiducials had the shoulder-to-bone

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Human Subjects Participation Statements: All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1975, as revised in 2008 (5).

Informed consent was obtained from all patients for being included in the study.

distances within 0.01-0.09 mm range for the PosiSeat group and 0.04-1.45 mm range for the manual insertion group. These differences were statistically significant.

Conclusions—A depth-release drive system achieves more consistent placement of bone-implanted fiducial markers than manual insertion.

Keywords

Fiducial markers; Deep brain stimulation; Stereotactic surgery; Computerized tomography; Image-guided surgery; PosiSeat

Introduction

Image-guided surgery (IGS) is being used more and more to guide intracranial navigations. One such application is deep brain stimulation (DBS) surgery where electrodes are placed deep in the brain to treat patients with Parkinson's disease and essential tremor [1, 2]. Core to IGS is the registration of surgical anatomy to radiographic images, which is the process of finding the transformation that maps a point in physical space with a corresponding point in the radiographic image. Registration methods commonly used for IGS include point-based registration and surface-based registration [3]. The highest degree of accuracy in IGS is achieved with point-based registration that employs bone-implanted fiducial markers, which are screwed directly into the cranium [4]. To reduce the likelihood of error in any stereotactic system, the reference markers must remain fixed and immovable in order to ensure accurate registration during the surgery. Furthermore, when using such markers as an anchor by which the stereotactic frame is secured to the head [5], it is equally important that the markers do not dislodge, resulting in frame shift. When a screw is under tightened and thus not fully seated against the bone, the screw and any attachments to it (i.e., the stereotactic frame) could become unstable since the threads alone offer less stability than when the shoulder (junction of head of screw with threads) rests against the bone. Conversely, when the screw is over tightened, stripping may occur leading to a loose fit allowing movement of fiducial markers during procedure. Thus, if a screw is under tightened or over tightened, it could cause movement of marker after imaging and prior to completion of surgery that would result in registration error and inaccurate intraoperative targeting.

DBS surgeries involve placing electrodes within a small deep-brain nucleus such as the subthalamic nucleus or the ventral intermediate nucleus. Typically, pre-operative computed tomography (CT) and magnetic resonance images (MRI) of the patient are acquired. A target position is chosen based on these pre-operative images. To accurately place electrodes at the chosen target region, fixtures such as traditional stereotactic frames (a.k.a. N –frames), or microstereotactic frames (e.g. NexFrame (Medtronic Inc., Minneapolis, MN) and Waypoint Stereotactic System (a.k.a. – StarFix platform; FHC Inc., Bowdoin, ME)) are utilized. Based on previously published accuracy studies, the StarFix device provides the best targeting accuracy of 0.42 mm [6] compared to 1 mm to 2 mm for the traditional stereotactic frames [7-10] and 1.25 mm for the NexFrame [11]. Traditional stereotactic frames are increasingly replaced with the smaller and lighter microstereotactic frames such as the StarFix as they are more convenient to patients and also provide higher accuracy. The

StarFix device is a rapid-prototyped frame that rigidly attaches to anchors screwed into the skull and constrains a probe to a path pre-defined in the pre-operative images. While the StarFix system has a very high degree of accuracy, it is dependent on the rigid attachment of the fixture to the skull, which in turn requires secure attachment of the anchor to the skull. The StarFix frame cannot be adjusted, but to enable intraoperative exploration based on neurophysiological signal feedback, the driver system attached to the frame allows a 22 mm diameter cylindrical zone of exploration. Traditional stereotactic frames including the NexFrame require intraoperative adjustments to align the frame to the planned trajectory, and these adjustments are subject to manual error.

At our institution, the StarFix is commonly used for DBS surgeries. The description of our experience using this method of stereotaxy in 263 patients over a 6 year period is described in [5]. Briefly, the procedure involves implanting three or four fiducial anchors into the skull of the patient several days prior to surgery just prior to acquisition of a CT scan. Common placement locations for the anchors are usually located outside the intended area of the burr hole and yet above the crown of the skull, similar to placement of other traditional stereotactic frames (e.g.right-anterior, right-posterior, left-anterior, and left-posterior scalp locations). The anchors act both as fiducial markers used to register the preoperative images of the patient to the patient in the operating room and also as a means to attach the StarFix to the patient. The markers are easily seen and localized in the CT scan, and based on the location of markers and the trajectory planned by the surgeon, a customized StarFix platform is designed. The software used for planning is typical of other stereotactic planning software that allows the surgeon to not only determine the fiducial locations, but co-register additional MRI images from the patient and plan a trajectory through the skull and brain to reach a target such as the subthalamic nucleus. The Starfix platform design file is submitted to the manufacturer (FHC Inc.), and the rapid-prototyped frame is then manufactured over a 3 day period and sent back to the hospital for use during the DBS surgery. During the surgery, the StarFix platform mounts on the bone markers which align the path of the electrode to the planned trajectory. Because of the small size of the target region (usually less than 2 mm) within which the electrode must be placed, it is important that submillimetric accuracy be achieved. Hence, it is critical that the bone-implanted fiducial markers be well-seated in the skull providing the requisite imaging accuracy and mechanical stability. This concept is also present with other traditional stereotactic frames using skull mounted pins to attach a frame to the skull [12,13].

In addition to the targeting error introduced by fixtures such as the StarFix, the presence of soft tissue in the brain could affect the accuracy of placement of the electrodes. Although the tissue of the brain is not thought to meaningfully deviate the electrode, the most significant inaccuracy is the shifting of the brain during surgery causing the actual brain structure to shift away from the intended spatial target. This manuscript does not address that source of inaccuracy. Our presumption is that maximizing spatial accuracy (not to mention frame stability) is a necessary first step to successful targeting accuracy and a successful clinical outcome.

The standard practice today for placement of bone-implanted fiducials consists of manually drilling a pilot hole following which the fiducial is screwed into the bone using tactile and

visual feedback to assure appropriate depth. Outside of the possible human error involved with insertion, this manual technique is complicated by inhomogeneous bone density making tactile feedback inconsistent and by visual obstruction by blood and tissue at the site limiting visual confirmation of correct placement.

Our group has developed an alternate technique that depends neither on tactile nor visual feedback by using a depth-release driver called the PosiSeat™. This device, shown in Figure 1 and detailed in a previous publication [14], consists of a stem, which is a spring loaded depth-release drive, coupling a driver to an end effector that matches the shape of the fiducial marker (e.g. hex or Phillips head). The end effector is rotated by the stem that interfaces with a hand-operated driver or a motorized driver such as the Stryker electric driver (Stryker; Kalamazoo, MI, USA) or Osteomed electric driver (Osteomed; Adison, TX, USA). The coupling mechanism that connects the stem to the end effector is designed to disengage after the fiducial is inserted into the bone to a certain depth. This occurs as the outer rim of the end effector touches the bone surface and is pushed backwards as the anchor is driven forward. Depth of insertion is chosen as the length of the screw portion of the fiducial marker to assure optimal insertion and ensure that the shoulder of the fiducial head contacts the surface of the bone. Once this specified depth is reached, the coupling mechanism disengages allowing the driver to spin freely while the end effector and the attached fiducial no longer spin. It is this free-spinning of the driver without motion of the end effector that specifies optimal insertion has been achieved. As with other bone-implanted fiducial marker insertion techniques, the operator needs to ensure that the skull is of adequate thickness for insertion.

We sought to compare the manual insertion technique with the PosiSeat™ through analysis of post-marker implantation CT scans.

Materials and Methods

Evaluation of the methods via CT scans

For each patient undergoing fiducial marker placement, a CT scan with voxel size approximately 0.59 × 0.59 × 0.75 mm was acquired after fiducial placement as standard of care. The scans of patients were analyzed with 3D Slicer Version 3.4, an open-source image analysis tool, developed by National Alliance for Medical Image Computing (NAMIC) and funded by the National Institutes of Health (NIH) (Grant U54 EB005149). Additional coding was developed to specifically localize fiducial markers and measure the shortest distance from the underside shoulder of the fiducial to the closest skull surface (Figure 2). This distance, called the shoulder-to-bone distance, was measured for all fiducials in all patients in the study.

The fiducial marker used for the DBS patients in this study was made of titanium and has a hexagonal head (Figure 1) of height 4 mm and diameter 5 mm with a screw of length 4 mm. The fiducial marker was automatically localized by fitting a three-dimensional model of the marker [15] using a two-step process. In the first step, candidate positions for each marker was determined by automatically processing the entire CT scan to find contiguous region whose intensity was above a threshold and whose size and shape were similar to the known

parameters of the marker design. For the scans used in this study, 2500 was used as the intensity threshold for the marker. In the second step, the three-dimensional model of the marker was placed at each candidate position and the location was adjusted iteratively using the matching method called “optical flow” [15]. The difference between the model and the actual image was reduced at each iteration until the relative movement between each iteration was below a set threshold or a maximum number of steps has been reached. The relative movement between each iteration was calculated as the maximum distance that any point on the object moves between iteration divided by the largest dimension of the object. The threshold for this relative movement was set as 0.03 and the maximum number of iteration was set as 20 for this study. The location of the marker can be determined using this method within 0.25 mm accuracy [16]. The top center of the marker identified (Figure 2) was then visually confirmed by the user. If a marker was not identified by the completely automatic method, a semi-automatic method was used in which the user manually picks the candidate position (first step of the fiducial marker localization) that was then provided as input to the second step.

Once the marker location was identified, it was possible to determine the underside shoulder of the marker using the model of the marker. The region between this underside shoulder of the marker and the tip of the screw, which is the region bounded by the box with white-dotted outline in Figure 2 (b), was then identified. Bone in that region was determined using an intensity threshold. Bone intensity ranged around 1000-1500 in the CT scans. The difference in the intensity range for bone and fiducials made it possible to differentiate bone from the fiducial marker. Distance between the underside shoulder of the marker to the bone points were calculated. The minimum of those computed distances was then recorded as the shoulder-to-bone distance of that marker. This method was tested on computer-simulated images with known shoulder-to-bone distance. The computed location of the fiducial markers and the shoulder-to-bone distances were visually verified in the patient CT scans.

Subjects and procedures

Prior to conducting this study, institutional review board (IRB) approval was obtained for all aspects of this research.

PosiSeat insertion method—A total of 17 patients were consented and enrolled for the PosiSeat phase of this study from June ’08 to May ’09. For eleven patients, the fiducials were implanted by one nurse practitioner, and for the other six patients, the fiducials were implanted by the surgeons, who typically do not perform this task and thus were inexperienced for the purposes of this study. Total number of fiducials implanted with PosiSeat was 57. Time taken to implant the fiducial markers was recorded during the insertions for the patients enrolled in the PosiSeat group.

Manual insertion method—To compare the use of PosiSeat™ to the standard method, we analyzed the CT scans of patients who had fiducial markers implanted using the standard manual method. To minimize inter-surgical variability, we analyzed data only from those patients who had fiducial markers implanted by the nurse practitioner within the neurosurgery session, who performed most of the PosiSeat insertions. In an effort to

eliminate surgical experience bias, fiducial marker control cases were selected from three implant time periods.

1. Manual-Pre: Implantations for this first group were performed from May ’07 to November ’07 (prior to the PosiSeat™ implant period). The nurse practitioner who did these implants was not experienced in manual insertions, having started performing these procedures in May ’07. This group comprised of 79 manually-inserted fiducials (20 patients; 19 of 20 (95%) each had 4 manually-inserted fiducials and 1 (5%) had 3 manually-inserted fiducials).
2. Manual-Simultaneous: These implantations were performed from June ’08 to May ’09 (during the same period that the PosiSeat™ implants were being conducted) and contained a mixed level of surgical experience. The 11 previously described manual insertions that were conducted on the sample of patients enrolled in the PosiSeat group were added in this group. This group comprised of 91 manually-inserted fiducials (24 patients; 22 of 24 (92%) each had 4 manually-inserted fiducials, 1 (4%) had 2 manually-inserted fiducials , 1 (4%) had 1 manually-inserted fiducial).
3. Manual-Post: Implantations for this third group were performed from August ’09 to October ’09. By this time, the nurse practitioner conducting these implants was considered to be ‘experienced’. This group of implants was selected as a follow-up to the previous manual insertions to assess whether experience with the PosiSeat™ affected subsequent manual insertions. This group comprised of 80 manually-inserted fiducials (20 patients; all 20 (100%) each had 4 manually-inserted fiducials).

Table 1 summarizes the number of patients and fiducials in different insertion groups.

Statistical analysis

Descriptive and graphical methods were used to summarize shoulder-to-bone distances for all markers implanted using the PosiSeat method, as well as for the three subsets of markers implanted manually. These distributions were extremely skewed in that while a majority of the distances may have been around a central point, there was a considerable “tail” or number of outliers which will be apparent in the box plots presented with the results. Thus, median and 25^{th} – 75^{th} interquartile ranges representing the middle 50% of the values regardless of the shape of the distribution are used to describe the distances. Linear mixed modeling analysis was used to test for differences between technique and among insertion time periods (both between subject factors), as well as location of the anchors (within subject factor). The linear mixed analysis approach adjusts the standard errors for the fact that as many as four fiducial markers (4 locations) were implanted on each patient. An alpha of 0.05 was used for determining statistical significance. To maintain an overall Type I error rate of 0.05, post-hoc analysis of statistically significant overall tests were conducted using Bonferroni adjusted pairwise comparisons.

Results

Summary of the procedural findings. While each of the 17 patient enrolled for the PosiSeat™ procedure had four fiducials implanted (*N*=68), 11 fiducials (4 fiducials in 2 patients, 2 fiducials in one patient, and 1 fiducial in one patient) were actually placed using the manual technique. The reasons for which the nurse practitioner switched to manual insertion within procedure included: (1) Due to the evolution of the PosiSeat™ technique, a low-torque driver was initially used (Osteomed electric driver). This driver did not provide the necessary power to always ensure implantation, and after difficulty placing the fiducials with the low-torque driver, the four fiducials were implanted using the manual method. A high torque driver was utilized for the remaining patients (Stryker electric driver). (2) For one of the patients, two fiducials were implanted using the manual method and the other two fiducials were implanted using the PosiSeat™ method. This decision was made *a priori* to allow a direct comparison between the two methods on the same patient. (3) Due to an unexpected issue with a battery for the high-torque driver, the manual method was necessary for implantation of four fiducials of a single patient. (4) For a fiducial anchor of one of the patients, the PosiSeat™ driver never stopped spinning and it was determined that the fiducial was not rigidly attached to the skull. As a result, this fiducial was removed and a new fiducial was manually placed at a nearby location. This particular case was considered as a failure of the PosiSeat™ system. Therefore, useable distances computed from CT for the PosiSeat™ insertions included 15 patients with a total of 57 fiducials (total 68 - 11 manually-implanted fiducials).

One fiducial anchor—after having been placed by the high-torque driver plus PosiSeat™ and then validated by pre-operative CT scan (Figure 2)—subsequently fell out during DBS surgery. The shoulder-to-bone distance was determined to be 1.06 mm for that anchor. Though we hypothesize that this fiducial distracted due to an external force, we do not have record of this occurring and thus include it as a failure of the PosiSeat™ system. Combining this fiducial with the one that was not stable after implantation using the PosiSeat™ and had to be re-implanted using the manual method, we had two failures for the PosiSeat™ system out of 58 fiducials (57 fiducials implanted using the PosiSeat™ and analyzed in the CT scan plus one fiducial for which the Posiseat™ failed during implantation and had to be implanted using the manual method) for a success rate of 96.6% (*N* = 58).

For six of the 57 successfully implanted fiducials (three patients) the PosiSeat™ end effector never stopped driving indicating that the fiducial never reached the optimal seating depth. These six fiducials were manually assessed by tactile feedback and were found to have acceptable seating and thus required no further action. The shoulder-to-bone distance for three fiducials (one patient) were 1.02 mm, 1.31 mm, and 1.48 mm indicating that the fiducials were not optimally seated. The shoulder-to-bone distances for the other three fiducials were less than 0.10 mm indicating that the screws of the anchors were almost entirely implanted into bone (i.e. complete seating of the fiducial anchor).

Summary of the distance findings. Table 1 provides the median and 25^{th}-75^{th} interquartile range of the measured shoulder-to-bone distance values for the different groups. The median shoulder-to-bone distance for all of the manual insertions (*N*=250) was 1.06 mm. Fifty

percent of the fiducials had distances between 0.04 and 1.45 mm and the maximum distance of all measured distances 2.43 mm. The respective distances for the 57 fiducials inserted using the PosiSeat™ technique were a median shoulder-to-bone distance of 0.03 mm with 50% of the distances between 0.01 and 0.09 mm. The maximum distance for all PosiSeat™ insertions was 1.48 mm. The CT scan of the single patient who had two fiducials implanted by the manual technique and two fiducials by the PosiSeat™ technique revealed a shoulder-to-bone distance for one of the manually-implanted fiducials of 0.85 mm and shoulder-to-bone distances of less than 0.10mm for the other three fiducials.

The difference between the manually inserted and PosiSeat™ inserted shoulder-to-bone distances was statistically significant ($p<0.001$). Furthermore, pairwise comparisons of the PosiSeat™ distances to each of the manual groups (Manual-Pre, Simultaneous, and Post) were each statistically significant ($p < 0.001$). Figure 3 illustrates these findings. This analysis also revealed a statistically significant difference in shoulder-to-bone distances among the four insertion locations ($p = 0.038$). Post-hoc analysis revealed distances for left-anterior anchors were less than those of the left-posterior anchors ($p = 0.033$). A similar pattern was observed regardless of the technique used (Figure 4).

For 43 of 57 fiducials implanted using the PosiSeat™ and 11 manually-implanted fiducial anchors (from the patients enrolled for the PosiSeat™ insertion) data was available on time taken to implant. It took an average of 9.05 ± 5.36 seconds to implant a fiducial using the PosiSeat™, whereas it took an average of 62.33 ± 7.45 seconds to implant a fiducial using the manual method.

Conclusions

We sought to compare the manual insertion method for bone-implanted fiducial marker placement to a semi-automated, depth-release drive system, the PosiSeat™, in patients undergoing image-guided, neurosurgical interventions. The depth-release device, the PosiSeat™, is a relatively simple mechanical design which has been previously described [14]. In short, the device has a mechanical clutch which disengages the distal end effector from the motor of a handheld driver when the fiducial marker has penetrated bone to a specified depth. The data contained herein shows that the PosiSeat™ places fiducials significantly deeper into bone without stripping as compared to manual insertion (manual pilot hole followed by manually screwing). The PosiSeat™ allowed better depth placement both by experienced and inexperienced users.

The limited time data implies that the PosiSeat™ allowed faster placement of bone-implanted fiducials. However, as the timing was not an original study variable, no statistical significance could be inferred due to the possible influence of outside variables such as a longer set-up time for the manual method once the PosiSeat™ method was abandoned. Despite the insufficiency of control for significance testing, the time data was striking enough to present in this paper.

Among the different manual groups across the three different periods, the second group (Manual-Simultaneous) had the lowest average shoulder-to-bone distance. The difference

among the manual groups over time does not appear to be due to experience since we chose the same practitioner for all manual insertions. Therefore, this finding seems to be attributable to the Hawthorne effect indicating that the insertions were different because the practitioner knew they were being tested.

While this system is highly robust, as evidenced by the 96.6% success rate, it can fail to disengage if soft tissue comes between the shoulder of the screw and the skull thus preventing the screw from reaching the specified depth. We believe that it was because of this reason (presence of soft tissue between the shoulder of the screw and the skull) that the PosiSeat™ never disengaged for one of the failed PosiSeat™ insertions (for which manual insertion was chosen) and the six other PosiSeat™ inserted fiducials that were “successful”, i.e. remained rigidly attached to the skull. Notable is the fact that one of the fiducials placed using the PosiSeat™ fell out during subsequent surgery despite adequate seating seen in the post-insertion CT scan. For this particular case, the surgery did not get affected as the surgeon was able to mount the StarFix frame on the remaining three fiducials and did not feel there was any frame wobble. Furthermore, the surgical team was able to identify the deep brain nucleus physiologically consistent with the planned target to reassure the surgeon that the intended target had been reached. However such occurrences of anchor falling out after CT scan and before intraoperative placement of electrodes are disruptive as—if the microstereotactic frame cannot be adequately secured using the other fiducial anchors—the surgical procedure has to be rescheduled after the fiducial anchor is replaced. The neurosurgical co-authors recall occasional “fall-out” from manually-inserted anchors and estimate its occurrence at < 1%. A previous report on the use of StarFix frame for DBS surgeries using a now outdated fiducial system with extenders attached to the anchors reported anchor dislodgement in 1.1% of patients [5]. Anchor dislodgement was noted to be more prominent in patients with violent movement disorder associated with Parkinson's disease.

An interesting question that arose from our data was whether fiducial placement differed in the four quadrants of the patient's skull. Our data showed that the fiducials placed in the left and right anterior quadrants had lower median shoulder-to-bone distances than those in the posterior directions, which is due to the fact that the patient is lying down on their back during the anchor implantation which may have made it more difficult for this practitioner to reach the posterior locations.

While it is clear that the PosiSeat™ allows more consistent placement of bone-implanted fiducial markers, the clinical significance of this is not as clear. While it logically makes sense that more secure fiducial markers result in more accurate image-guided intervention, there is limited data to support this conclusion given the heterogeneous density of bone. Because of differences in bone density, more shallow insertions may appear to be well seated, and this perception may explain why an experienced user placed the markers more superficially. From an engineering standpoint, however, deeper penetration allows not only the intraosseous threads to support the fiducial but also the shoulder under the screw head to rest on the surface of the bone and prevent canting.

In summary, as more and more neurosurgical interventions are guided by IGS, it is becoming increasingly more important to minimize error. One way of doing so is to improve the stability of bone-implanted fiducials. While the current standard of practice uses a manual insertion method for fiducial insertion, data contained herein shows a significant difference in favor of a depth-release driver system such as the PosiSeat™.

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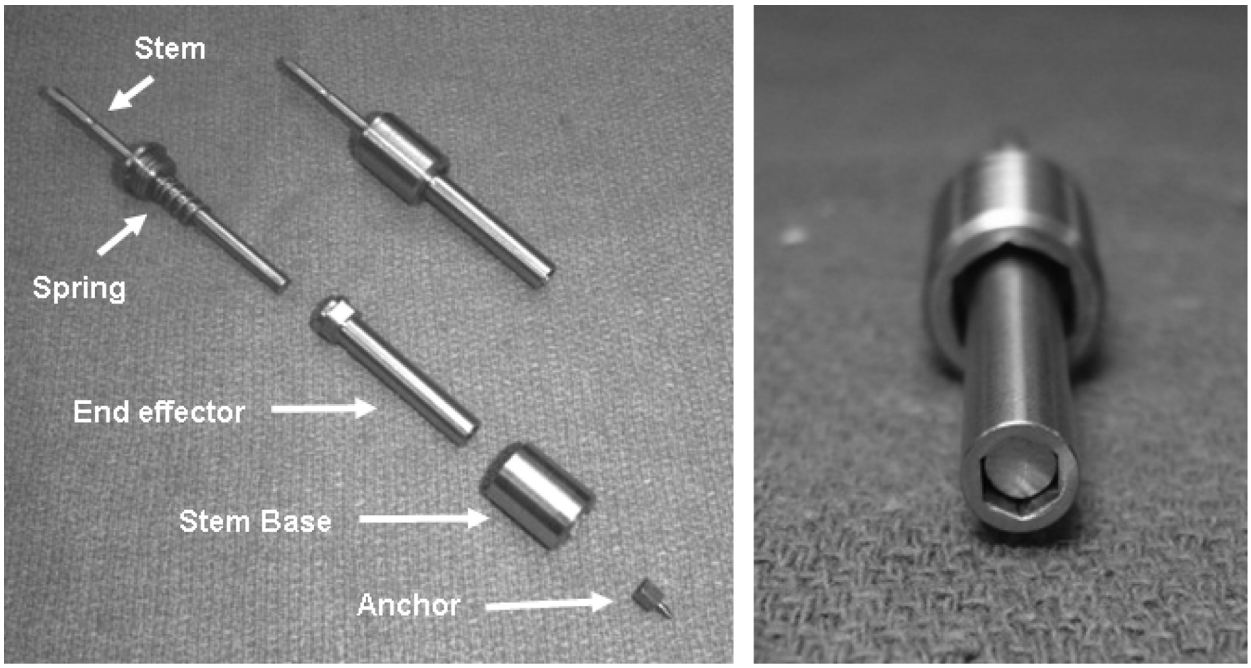

Figure 1.
PosiSeat™. (a) Exploded and unexploded views of the PosiSeat™ built for an anchor, which is a fiducial marker with hexagonal head. (b) End effector that matches the shape of the anchor.

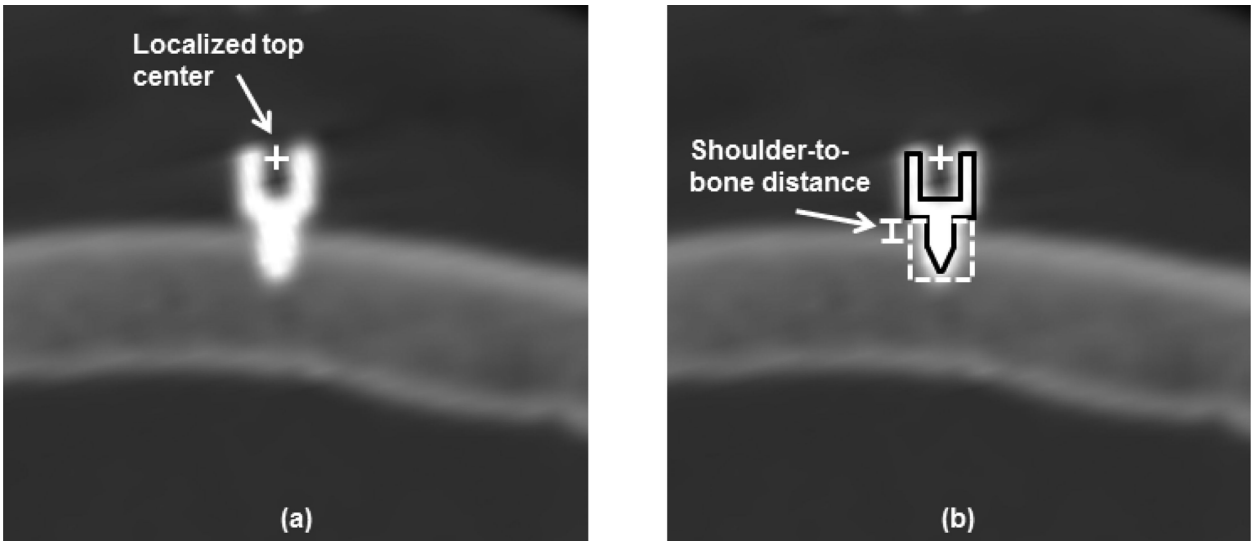

Figure 2.

CT image of a fiducial marker implanted into a patient's skull. (a) The localized top center of the fiducial marker is shown as the plus sign. This particular fiducial was implanted using the PosiSeat™ system and fell out during the surgery despite adequate seating as seen in the CT. (b) Measurement of the shoulder-to-bone distance. The black outline indicates the model of the marker, and the box bounded by the white-dotted dashed line indicates the region between the underside shoulder of the marker and the tip of the screw of the marker.

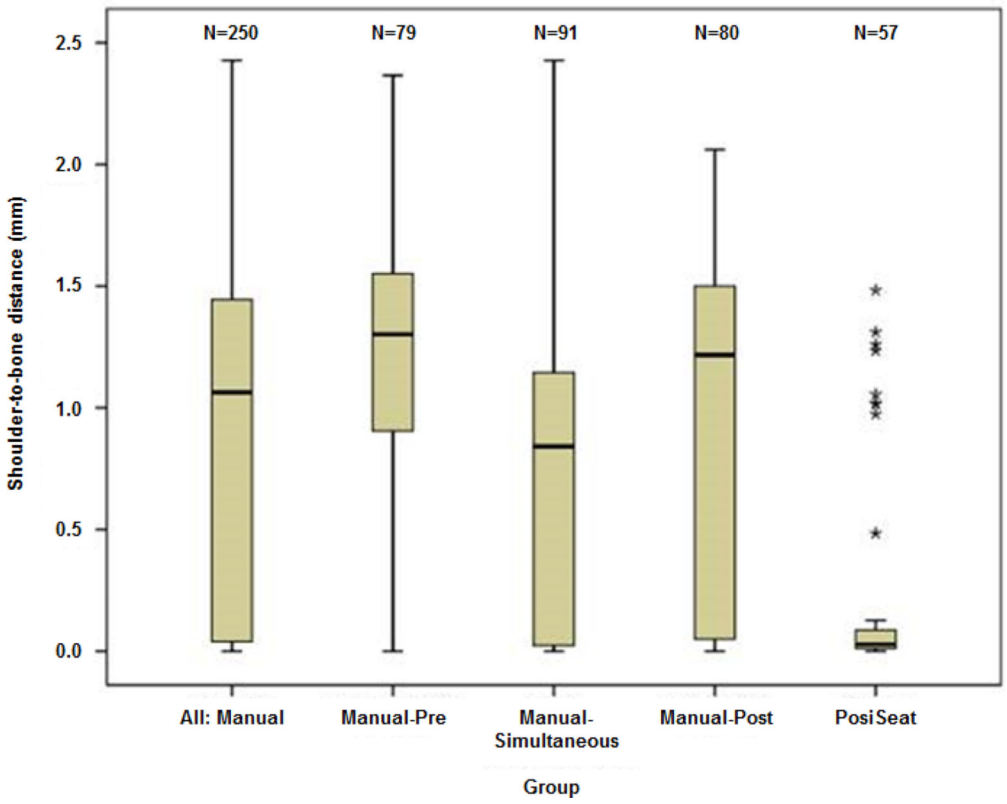

Figure 3.

Box-and-whisker plot of the shoulder-to-bone distances for the manual and PosiSeat™ insertion methods. The bottom and top of the box indicate the 25th and 75th percentile and the band inside the box indicate the 50th percentile (median). The two ends of the whiskers indicate the lowest and highest distance value that is within the 1.5 interquartile range (IQR) of the lower and upper quartile respectively. The asterisks indicate the outliers that are outside the 1.5 IQR. The leftmost and rightmost plots show the descriptive statistics of the distances for all fiducials implanted using the manual and PosiSeat method, respectively. The middle three plots show descriptive statistics of the distances for the three different subgroups within the manual group—Manual-Pre, Manual-Simultaneous, and Manual-Post.

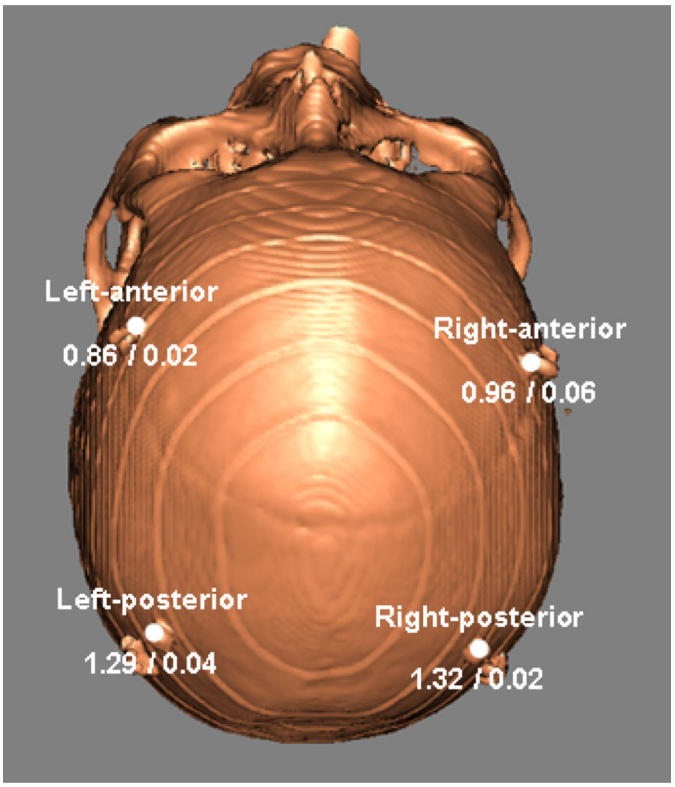

Figure 4.
Median shoulder-to-bone distances at typical anchor locations. The anchor locations are shown as white circles. The two values associated with each location indicate the median value of the shoulder-to-bone distance in mm using the manual method and the PosiSeat method respectively.

Table 1

Measured shoulder-to-bone distances for different insertion groups.

Method of insertion	Group name	Period	Number of patients	Number of patients scans used	Number of fiducials used for analysis	Shoulder-to-bone distance (mm)	
						Median	25th-75th interquartile range
Manual	Manual-Pre	May-Nov '07	20	20	79	1.30	0.89-1.56
	Manual-Simultaneous	June '08-May '09	24 (20 + 4)*	24*	91	0.84	0.02-1.16
	Manual-Post	Aug-Oct '09	20	20	80	1.22	0.04-1.50
PosiSeat	PosiSeat	June '08-May '09	15 (17 - 2)*	15*	57	0.03	0.01-0.09

* For two patients enrolled in the PosiSeat study, all the four anchors were implanted using the manual method due to technical issues with the driver for the PosiSeat. Since these two patients were enrolled in the same period during Manual- Simultaneous, these patients were considered as part of the Manual- Simultaneous group. For one patient, two fiducials were implanted using the PosiSeat and two fiducials using the manual method for a direct comparison. This patient was hence considered as part of both Manual- Simultaneous and PosiSeat group. For one another patient, a fiducial was implanted using the manual method since the PosiSeat never stopped spinning and the anchor was not considered to be rigidly attached to the bone. This patient was hence considered as part of both Manual-Simultaneous and PosiSeat group.