



## Stereotactic registration using cone-beam computed tomography

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### ARTICLE INFO

#### Keywords:

Deep brain stimulation  
Surgical accuracy  
Cone-Beam computed tomography  
Stereotactic techniques

### ABSTRACT

**Objective:** Stereotactic registration for deep brain stimulation surgery is often performed after halo placement on an MRI or CT with fiducials. Cone-beam computed tomography scanners (CBCT) have been used for lead confirmation in DBS surgery. A new CBCT scanner has an enlarged field of view now allowing for visualization of fiducials, and the potential for intraoperative registration. The aim of this retrospective study was to evaluate the accuracy and precision of stereotactic registration using images obtained in intraoperative CBCT.

**Patients and Methods:** The registration accuracy and precision of CBCT (O-arm O2, Medtronic, Dublin, Ireland) was compared to CT registration study obtained in the same patient (n = 10). Stereotactic coordinate differences were compared. In a second analysis the end-to-end accuracy and precision between the surgical target and lead position was analyzed on postoperative MRI in cases where CBCT was used for registration (n = 31 leads).

**Results:** The average radial distance of the stereotactic coordinate using the CBCT and CT registration studies was not clinically different ( $0.46 \pm 0.17$  mm (max 0.81)). The registration image maximum rod error was more accurate for CBCT ( $0.50 \pm 0.12$  mm (max 0.7)), than the CT registration study ( $1.02 \pm 0.63$  mm) (max 1.8) (P = 0.018). On average 26 min was saved using only the CBCT to perform registration (P < 0.001). The radial error in the end-to-end analysis was  $1.07 \pm 0.67$  (max 2.4) measured on postoperative MRI.

**Conclusion:** Registration using a CBCT image is accurate, and using this workflow yields accurate and precise DBS lead placement.

### 1. Introduction

Stereotactic registration has become an automated process within modern targeting software. The software converts a target location on an imaging study (the direct target) into surgical stereotactic coordinates, based on known geometry of a fiducial system. Frame-based registration is often performed on an MRI scan acquired with halo and fiducials system attached, on the day of surgery. Both registration and targeting are performed on the same MRI image.

Another common workflow obtains a preoperative MRI as an outpatient, at a much more convenient time for the patient and surgeon. Then a halo is placed on the day of surgery followed by acquisition of a stereotactic CT registration study. Co-registration of MRI and CT is performed in software, also referred to as image fusion. Automated frame registration is performed on the CT scan, and direct targeting on MRI. In both of these workflows the registration accuracy relies on an undistorted scan to accurately show the geometry of the fiducial rods. In latter workflow, the accuracy also depends of the quality of image fusion. Thus, when one measures the registration accuracy in the latter case, the analysis should also include accuracy of image fusion.

Portable cone-beam computed tomography (CBCT) scanners have become widely adopted for intraoperative imaging and navigation in spine, and also cranial cases. CBCT is now commonly used for intraoperative deep brain stimulation (DBS) lead confirmation. The accuracy of CBCT in DBS lead confirmation has been measured by several groups, including us. [1] Its accuracy is equivalent to postoperative MRI. [1–8] However, early CBCT scanners have limitations in the inability to obtain stereotactic registration images due to small field of view (FOV) that does not include all the fiducial rods.

Advancements in CBCT scanners now permit registration studies to be obtained with a larger field of view, specifically using the O-arm O2 (Medtronic, Dublin, Ireland). Integration of a CBCT for intraoperative registration can change the overall workflow of DBS cases. We developed a new workflow using CBCT to register, once the O-arm O2 was commercially available. We have been routinely using this tool in all DBS cases since. The aim of this retrospective study was to determine if intraoperative registration with CBCT is sufficiently accurate compared to standard registration techniques.

When we first began using the CBCT to perform intraoperative registration we also obtained registration CT images as a backup to the

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<https://doi.org/10.1016/j.clineuro.2019.05.004>

Received 12 March 2019; Received in revised form 3 May 2019; Accepted 7 May 2019

Available online 08 May 2019

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CBCT registration image, to be sure the case would proceed accurately. After 10 cases we performed internal post-market quality analysis of the registration accuracy, as shown in this paper. We found sufficient accuracy of registration that allowed us to proceed with only using the CBCT for intraoperative registration. In a retrospective fashion we also analyzed the end-to-end accuracy of a series of cases using only the O-arm O2 for registration.

The modified workflow adopted in this process performs direct targeting on a preoperative MRI, which is fused to a preoperative CT scan. Then this workflow registers from a CBCT image obtained intraoperatively, that is also fused to the same preoperative CT. There are two image fusion processes in this workflow. It is challenging to determine image fusion accuracy; current software does not report numerical accuracy and only visual inspection is used to confirm the fusion. Thus, to really know that the registration and image fusion process yields accurate stereotactic coordinates we analyzed the overall surgical accuracy, termed the “end-to-end” accuracy. We routinely obtain a CBCT at the conclusion of DBS surgery, to confirm the lead is at the expected location. We record and track these errors as part of internal quality control. And we routinely obtain postoperative MRI to confirm lead location and screen for other complications such as hemorrhage or stroke. Therefore, we hypothesized that the CBCT registration image is sufficiently accurate and precise to perform DBS surgery. To evaluate this, we retrospectively compared the location of the lead on final CBCT images and postoperative MRI, comparing them to the surgical target obtained using this workflow. The logic in this analysis is that, if the leads are placed closed to the planned direct target, then the combination of registration with CBCT and image fusion errors is small.

## 2. Material and methods

This is a retrospective analysis of registration accuracy, as well as the position of final lead locations based on images obtained in the usual process and techniques of DBS surgery as previously reported. [1] This research was approved by a local Institutional Review Board. Informed consent was waived based on the retrospective nature of the study. Research was conducted in compliance with the Declaration of Helsinki. Patients had Parkinson’s disease ( $n = 7$ ), dystonia ( $n = 4$ ), or essential tremor ( $n = 7$ ). Leads were placed in the subthalamic nucleus ( $n = 17$ ), globus pallidus internus ( $n = 7$ ), and ventrointermedius nucleus of the thalamus ( $n = 7$ ). The Medtronic 3389 lead was implanted in all cases (Medtronic, Dublin, Ireland).

The methods involve image co-registration (image fusion) between six different image sets: preoperative MRI, preoperative outpatient stereotactic CT, preoperative registration CT with halo and fiducials, intraoperative registration CBCT, intraoperative CBCT of lead, and postoperative MRI. The image fusion and targeting accuracy analysis were conducted within Cranial 3.0 software (Medtronic, Dublin, Ireland). In every image fusion process the preoperative CT was used as reference.

The first analysis compared stereotactic coordinates using the preoperative stereotactic CT for registration with halo and fiducials and the CBCT for registration acquired intraoperatively. In this analysis a targeting 3 T MRI was performed in an outpatient setting, one week prior to surgery. The following MRI sequences were used: T1 3D MPRHAGE (256 × 256 matrix) 1 mm thick, T2 (256 × 256 matrix) 2 mm thick. On the day of surgery, a Cosman-Roberts-Wells (CRW, Integra, Burlington, MA) halo was placed under local anesthesia in a conscious patient. The patient was transported down the hallway to the CT scanner and a stereotactic registration CT image obtained (KV 120, mA 300, FOV 250 cm, 1.5 mm thick).

The patient was then transported to the operating room, positioned on the operating table. The CBCT was aligned to the frame, and an CBCT registration image was obtained. The settings for this image were: 3D fluoroscopy mode, 40 cm field of view setting, high definition mode, 192 slices, 0.83 mm thick, KV 120, mA 20. This led to an additional

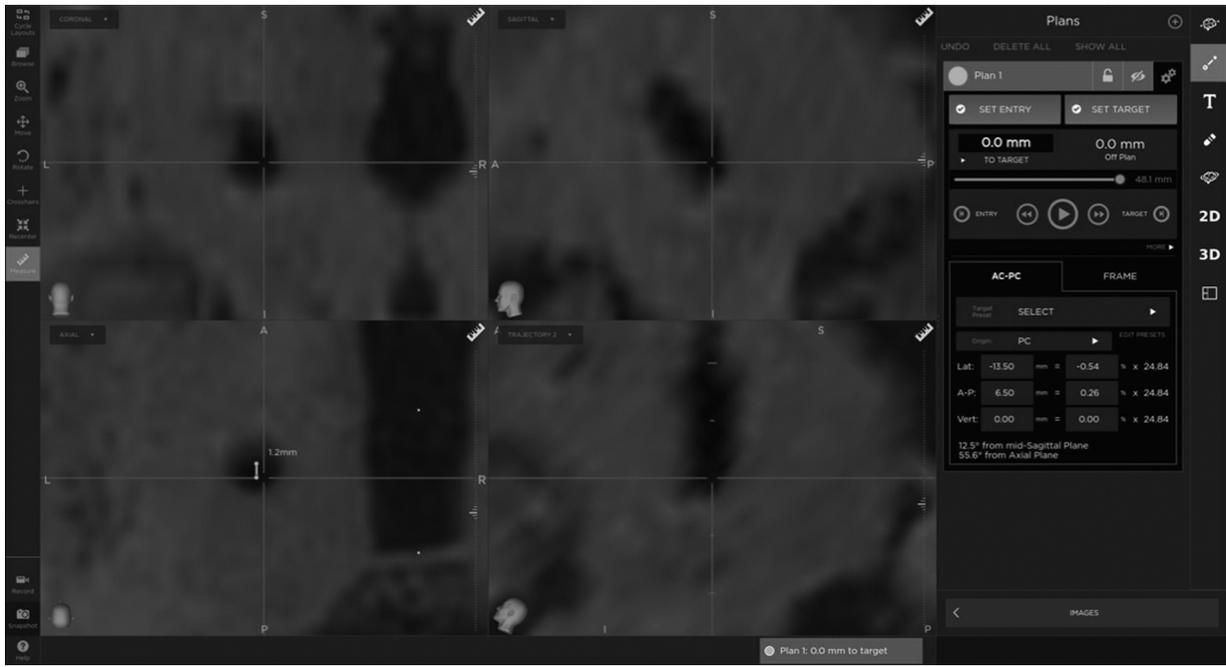
14.7 ± 1.6 mGy radiation exposure, which is approximately 1/5 of a CT scan exposure, or 5 typical fluoroscopy images). The MRI image was fused to the registration CT image, registration was performed on the stereotactic CT, direct targeting was performed on preoperative MRI, and stereotactic coordinates were obtained using Cranial 3.0 software on the S7 workstation (Medtronic, Dublin, Ireland). Then the registration study was switched to the CBCT registration study in Cranial 3.0 software to see if there was a difference in coordinates. These two sets of target coordinates were manually recorded and clinically compared. DBS surgery was performed as previously described which includes microelectrode confirmation of target as well as CBCT confirmation of lead placement. [1] In this fashion we safely adopted the use of CBCT registration, confirming the accuracy of the CBCT image for registration, in a post-market quality assurance analysis.

The second analysis measured the overall surgical accuracy and precision while using only the CBCT registration study. This “end-to-end” analysis includes potential errors caused by using the CBCT image to register. This retrospective analysis was performed in 31 consecutive DBS leads that had postoperative MRI images and final intraoperative CBCT images. In this workflow a targeting 3 T MRI and preoperative stereotactic CT (without halo) was performed in an outpatient setting within a week of surgery. The typical radiation exposure in this CT scan was 73.2 ± 3.4 mGy. On the day of surgery, a CRW halo was placed in the operating room under propofol anesthesia, and an CBCT registration study was obtained. The typical radiation exposure per O-arm2 image using large field of view mode was 14.7 ± 1.6 mGy. The MRI, CT, and CBCT registration studies were fused in targeting software using the CT as reference. Direct targeting was performed on MRI, and registration was performed on the CBCT registration study, yielding the stereotactic coordinates. DBS surgery was performed using microelectrode mapping and macrostimulation in an awake fashion. [1] The “final surgical target” was defined as the expected position of the DBS lead, modified with neurophysiological techniques including microelectrode recording and macrostimulation trials. The surgical target was adjusted by microelectrode recording in 6 of 31 leads based on neurophysiology. The anatomical position of the lead was confirmed at the conclusion of surgery using the CBCT, using standard mode (17.1 ± 2.0 mGy). [1]. The total radiation exposure for the registration CBCT study and intraoperative lead confirmation study was 31.8 ± 3.4 mGy. This image was fused to the preoperative CT and MRI, and the position of the lead was measured from the surgical target, termed the CBCT end-to-end accuracy

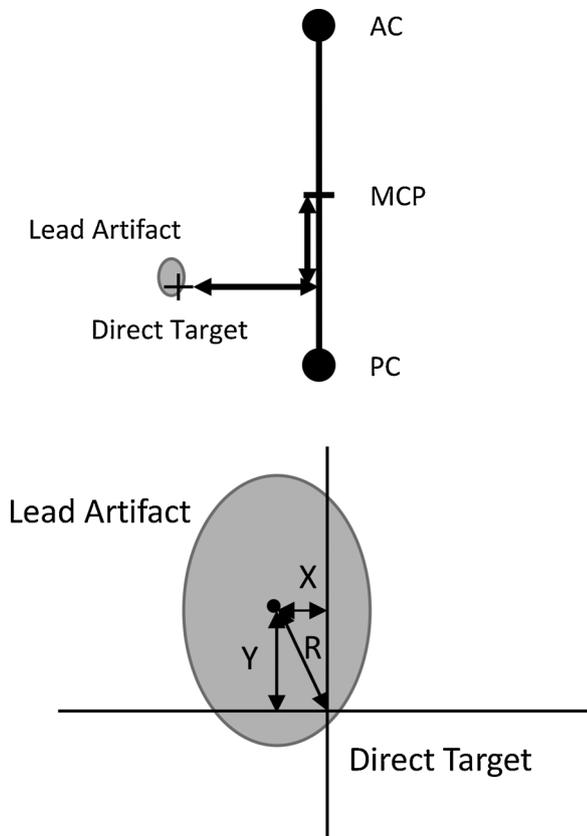
Then a postoperative MRI was obtained within a week of implantation (1.5 T, T1 FSPGR, 320 × 320 matrix, 2 mm thick). This was loaded into the targeting software in the usual fashion to confirm lead location (Fig. 1). The position of the center of the DBS lead at target was measured from the final surgical target. In this fashion the end-to-end accuracy and precision based on postoperative MRI was determined (Fig. 2). It should be noted that these methods of determination of lead location are routinely performed in all DBS patients, both as part of internal quality control, and for clinical programming and management.

Accuracy is defined as how close the expected lead locations are to the actual location for the group. Precision is defined as how variable the lead locations are from the expected lead location, i.e how tightly packed the leads are around the expected lead location. In the first analysis the accuracy and precision in the X, Y, Z, coordinates of the surgical target were compared between the preoperative registration CT and the intraoperative registration CBCT studies. Radial coordinate was calculated as:  $(X^2 + Y^2 + Z^2)^{0.5}$ . Predicted error and maximal rod error were compared between the CT and CBCT registration studies.

In the second analysis, the precision was calculated by measuring the average of the absolute value of the difference between expected and actual location of the lead in the X and Y direction. The precision was measured by calculating the average radial distance between the expected and actual lead position (radial coordinate =  $(X^2 + Y^2)$



**Fig. 1.** Appearance of the DBS lead position on postoperative MRI relative to the initial stereotactic coordinate. The cross hairs were set at the initial direct target coordinates chosen on the preoperative MRI direct targeting. The end-to-end error was measured from the center of the dark artifact of the DBS lead to the direct target in the lateral (X) and anterior-posterior (Y) coordinate.



**Fig. 2.** Schematic of the end-to-end accuracy measurement. The anterior commissure (AC) posterior commissure (PC) line and midpoint (MCP) was drawn on postoperative MRI. The direct target coordinates were re-entered into the software based on ACPC coordinates. The center of the DBS lead artifact was identified. Then at the vertical level of the surgical target the distance between the direct target and center of the DBS lead was measured in the lateral (X) and anterior-posterior (Y) coordinates. This difference is defined as the “end-to-end” accuracy. The radial (R) difference was calculated:  $(X^2 + Y^2)^{0.5}$ .

~0.5). Because the accuracy and precision were measured at the vertical position of the target the Z coordinate was zero. This analysis could be considered an estimation of trajectory error at the level of the target. The time from the start of the halo placement till incision which includes acquisition of the registration study, registration, and direct targeting was compared between the first analysis and the second using independent t-test. Statistical tests were conducted in Excel v.15 (Microsoft, Redmond, WA). Significance was set at  $P < 0.05$ . Data are reported as mean  $\pm$  standard deviation (SD).

### 3. Results

#### 3.1. Comparison of CT vs. CBCT registration accuracy

The accuracy and precision of stereotactic coordinates produced by the CBCT registration study were not statistically significantly different from those produced by the CT registration study. The coordinates were on average nearly identical. However, there was some slight variability, as measured by the precision, in stereotactic coordinates between CBCT and CT registration studies that did not exceed 0.5 mm (Table 1). The difference in the radial coordinate was likewise small  $0.46 \pm 0.17$  mm (max 0.81), and arguably not clinically significant. Thus, the CBCT registration images yielded stereotactic coordinates clinically similar to CT registration images.

When an image is registered the software reports a registration error, called the predicted error. The predicted error for the CBCT registration study was  $0.69 \pm 0.09$  mm (max 0.9), similar to that for the CT registration study  $0.73 \pm 0.34$  mm (max 1.2) (Table 2). Maximum rod error from expected geometric arrangement is displayed in the software screen, and was recorded at the target level by inspection. The maximum rod error on the CBCT registration study was  $0.50 \pm 0.12$  mm (max 0.7), significantly less than the CT registration study  $1.02 \pm 0.63$  mm (max 1.8) ( $P = 0.018$ ). This demonstrates that the CBCT image was not distorted and fiducial rod detection was highly accurate.

**Table 1**  
Differences in stereotactic coordinates generated by CT registration study and CBCT registration study.

	X (Lateral)	Y (Anterior)	Z (Vertical)	Radial Coordinate
Precision	0.16 ± 0.10 mm (max 0.30)	0.23 ± 0.24 mm (max 0.80)	0.26 ± 0.17 mm (max 0.60)	0.46 ± 0.17 mm (max 0.81)
Accuracy	0.04 ± 0.19 mm (max 0.30)	0.11 ± 0.32 mm (max 0.80)	-0.14 ± 0.29 mm (max -0.60)	

Registration studies using CT and the cone-beam computed tomography (CBCT) yielded nearly identical stereotactic coordinates (n = 10). Precision was measured as the average of the absolute value of the paired difference in each coordinate. Accuracy was measured as the average paired difference in coordinates. The differences in these coordinates are arguably not clinically significant.

**Table 2**  
Registration accuracy.

	CT	CBCT
Predicted Error	0.73 ± 0.34 mm (max 1.2)	0.69 ± 0.09 mm (max 0.9)
Max Rod Error at Target	1.02 ± 0.63 mm (max 1.8)	0.50 ± 0.12 mm (max 0.7)*

Comparison of the predicted error and maximum rod error measured at the level of the direct target for a CT registration study and an CBCT registration study (n = 10). Data are presented as mean ± SD, and maximum. \*P < 0.05.

**3.2. End-to-end surgical accuracy using CBCT registration**

The end-to-end precision and accuracy was evaluated first by comparing the surgical target to the final intraoperative CBCT image of the lead at the conclusion of surgery, and second by comparing the final surgical target to a postoperative MRI image of the lead, in a retrospective fashion. Using the CBCT to register saved an average of 26 min from start of the procedure till incision (P < 0.001, independent t-test), compared to obtaining a stereotactic registration CT in the first analysis. The precision of the surgical workflow was excellent, with average radial error was less than 1.1 mm (Table 3). End-to-end precision using the CBCT image of the DBS lead was just as accurate as the postoperative MRI, less than 0.9 mm. Thus, registration with the CBCT images yielded accurate surgical lead placement (see Fig. 3).

**4. Discussion**

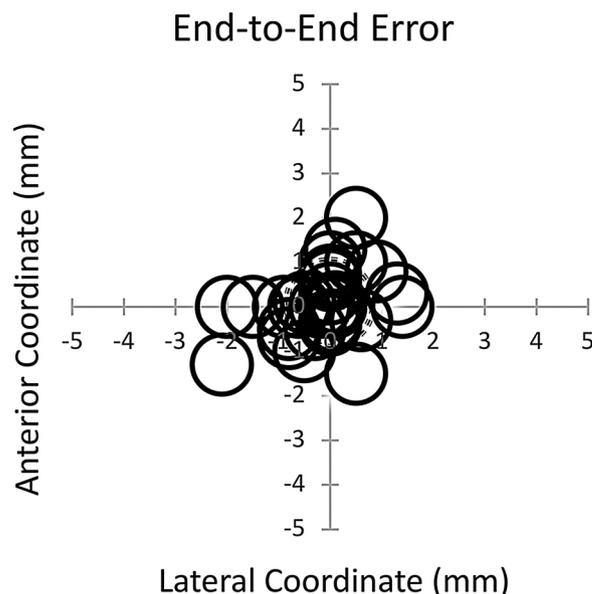
This study demonstrates that frame-based registration using a CBCT image is accurate, and utilizing the described workflow, yields accurate and precise DBS lead placement. Registration studies using the CBCT images produced stereotactic coordinates on average less than 0.5 mm different from those generated by CT registration studies. Software reported registration errors were not substantially different between the CBCT and stereotactic CT.

End-to-end analysis confirmed that both the CBCT registration study and the image fusion process were sufficiently accurate and precise, as measured by DBS lead placement within 1.1 mm of the surgical target based on postoperative MRI, and within 0.9 mm based on intraoperative CBCT images. Others have reported end-to-end errors using CBCT, intraoperative CT, and intraoperative MRI in similar range of less than 2 mm [5,8–10]. This study again demonstrates that the

**Table 3**  
End-to-end accuracy. Distance between the surgical target and lead location following DBS surgery using the cone beam computed tomography (CBCT) for registration.

	X (Lateral) Difference	Y (Anterior) Difference	Radial Difference
CBCT Precision	0.55 ± 0.60 mm (max 2.1)	0.49 ± 0.54 mm (max 2.0)	0.88 ± 0.64 mm (max 2.4)
CBCT Accuracy	-0.13 ± 0.81 mm (max -2.1)	0.06 ± 0.73 mm (max 2.0)	
MRI Precision	0.65 ± 0.49 mm (max 1.6)	0.70 ± 0.66 mm (max 2.4)	1.07 ± 0.67 mm (max 2.4)
MRI Accuracy	0.54 ± 0.62 mm (max 1.6)	0.36 ± 0.90 mm (max 2.4)	

The position of the center of the DBS lead on final intraoperative CBCT image and postoperative MRI was measured from the surgical target. Precision was measured as the average of the absolute value of the paired difference in each coordinate. Accuracy was measured as the average paired difference in coordinates. Data are presented as mean ± SD, and maximum (n = 31 leads).



**Fig. 3.** Axial representation of the final lead locations compared to final surgical target measured on final cone-beam CT. On average the leads were near the expected target (accurate). Most of the leads were close to the target, and thus the precision was high. The leads diameter is to scale. The radial precision for MRI was 0.88 ± 0.64 mm represented as the dotted circle.

CBCT representation of lead location is as precise as postoperative MRI [1].

The end-to-end error in this study includes many possible sources such as image fusion, brain shift, MRI image distortion, and surgical errors. We have previously published that microelectrode mapping revised the target in 14% of cases (n = 23 of 135 leads). [1] The surgical technique is very similar to the present study except this the current study uses the CBCT to register rather than stereotactic CT obtained on the day of surgery with fiducials. This study found a similar rate of target adjustment based on microelectrode mapping (19%, 6 of 31 leads), which indirectly demonstrates a similar degree of registration accuracy. Taken together, these data suggest that CBCT registration studies can guide precise DBS lead placement.

The use of a CBCT for intraoperative registration improves surgical workflow and saves time (an average of 26 min in this study). This

allows for the registration study to be obtained in the operating room, without transport of the patient around the hospital to CT or MRI scanners. General anesthesia, if so desired, can be performed only in the operating room, not down hallways. Frame placement can be performed in the operating room under anesthesia allowing for a more comfortable patient experience.

The radiation exposure for the patient from the intraoperative O-arm O2 registration and intraoperative lead confirmation was  $31.8 \pm 3.4$  mGy. This is less than a standard stereotactic CT scan which was  $73.2 \pm 3.4$  mGy, performed typically a week prior to DBS surgery in this workflow. If a stereotactic registration CT scan, and a post-operative stereotactic registration study were both performed on the same day, the radiation exposure would have been 146 mGy. Thus, registration and lead confirmation with the O-arm O2 in this work flow substantially reduced the radiation exposure by 80%.

The end-to-end precision of the workflow in this study is specific to this software (Cranial 3.0) and hardware (O-arm O2 and CRW stereotactic frame). This workflow is illustrative of ways other software, intraoperative imaging platforms, and stereotactic hardware including frameless techniques may be incorporated into intraoperative registration and lead confirmation workflows. The image-based methods of fusion evaluation and the end-to-end analysis techniques described in this study can be applied to any workflow combination of other equipment.

## 5. Conclusions

The CBCT can be used to acquire registration studies which are as accurate as a CT registration study. End-to-end accuracy of DBS surgery using the CBCT for registration and lead confirmation validated this workflow. These data indicate that the CBCT can be relied upon for registration and lead confirmation in frame-based DBS surgery.

## Conflicts of interest

The author is a consultant for Medtronic.

## Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

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