TECHNIQUE ASSESSMENTS

Fiducial Point Placement and the Accuracy of Point-based, Rigid Body Registration

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OBJECTIVE: To demonstrate that the shape of the configuration of fiducial points is an important factor governing target registration error (TRE) in point-based, rigid registration.

METHODS: We consider two clinical situations: cranial neurosurgery and pedicle screw placement. For cranial neurosurgery, we apply theoretical results concerning TRE prediction, which we have previously derived and validated, to three hypothetical fiducial marker configurations. We illustrate the profile of expected TRE for each configuration. For pedicle screw placement, we apply the same theory to a common anatomic landmark configuration (tips of spinous and transverse processes) used for pedicle screw placement, and we estimate the error rate expected in placement of the screw.

RESULTS: In the cranial neurosurgery example, we demonstrate that relatively small values of TRE may be achieved by using widely spread fiducial markers and/or placing the centroid of the markers near the target. We also demonstrate that near-collinear marker configurations far from the target may result in large TRE values. In the pedicle screw placement example, we demonstrate that the screw must be approximately 4 mm narrower than the pedicle in which it is implanted to minimize the chance of pedicle violation during placement.

CONCLUSION: The placement of fiducial points is an important factor in minimizing the error rate for point-based, rigid registration. By using as many points as possible, avoiding near-collinear configurations, and ensuring that the centroid of the fiducial points is as near as possible to the target, TREs can be minimized.

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Key words: Fiducial markers, Point-based registration, Target registration error

Stereotactic neurosurgery has evolved into an indispensable tool for the neurosurgeon. If we understand the limits of the systems used in surgery, we can maximize the tool's performance and enhance patient safety. Most commercially available frameless stereotactic systems rely on the point-based registration of preoperative images. The typical feedback these registration systems provide to the surgeon concerns only the expected degree of alignment of the points used for registration.

During patient registration, surgeons strive to minimize a number provided as feedback by the imaging system. Unfortunately, this "measure of error" is merely an estimate of the accuracy of the rigid body transformation. This estimate informs the operator only of the error in the geometric alignment of the fiducial markers registered. Reliance on this number as a proxy for the accuracy of computer-assisted navigation during surgery is naïve at best. At worst, the values may be misleading, especially with respect to the target registration error (TRE) figure, which is of paramount importance clinically. In this article, we introduce a new predictor of accuracy that is more appropriate, and we demonstrate the assistance it may provide surgeons in both cranial and spinal surgical navigation. We demonstrate that the feedback given by most commercially available frameless stereotactic navigational systems is imprecise, and we suggest ways to improve the accuracy of navigation when it counts for clinicians, i.e., in the accurate localization of the surgical target.

A multitude of errors impacts the accuracy of frameless stereotactic surgical procedures. Some of the errors occur independently of the surgical navigational system, but nonetheless they are within the control of the surgeon. In cranial neurosurgery, brain shift after dural opening, positioning, diuresis, and hyperventilation all can lead to errors in target localization (10). These errors may be minimized through optimization of positioning and the judicious use of diuresis and hyperventilation, but they cannot be eliminated entirely.

The type and placement of fiducials as well as the manner in which they are localized are more readily controlled by the surgeon. Two basic types of fiducial markers are used in frameless stereotactic neurosurgery: bone implantable markers (13) and skin surface fiducials (1). Skin surface fiducials are, by nature, more mobile on the scalp than bone implantable markers, and they may lead to an increase in fiducial localization errors (FLEs). It is imperative that the surgeon place these markers over less mobile areas of skin and avoid their placement over areas that may be deformed or shifted when the patient lies supine for magnetic resonance imaging or during positioning for the surgical procedure.

In this article, we discuss the importance of fiducial placement and the manner in which the result we reported previously (6) allows discovery of potentially dangerous fiducial configurations. Improvement in fiducial heuristics decreases the TRE rate and enables improved surgical decision management.

The only feedback currently available to the surgeon from frameless stereotactic navigational systems is the error in fiducial alignment. This error may be measured directly by the registration system, and it results from inevitable errors in the localization of the exact geometrical position of the fiducials. These localization errors also cause errors in the localization of targets such as tumors, vascular malformations, or the ventricular system. Unfortunately, errors in the central task of target registration cannot be measured by the registration system. Instead, the surgeon must rely on statistical predictors of these errors on the basis of the known localization accuracy of the fiducials. Statistics on both fiducial registration error (FRE) and TRE have been studied for many years, and TRE has been of highest interest to the medical community. TREs can be expected to be related to the localization error of the fiducials, the fiducial configuration, and the position of the target. During the past several years, researchers have resorted to numerical simulations to gain a qualitative notion of the form of the expression governing this error (4, 9, 13). This simulation approach works to some extent, but it has serious shortcomings. Its limitations spring from the time required to perform a single simulation and the sparseness of the information contained in a set of simulations. We recently derived an analytical expression that allows a quantitative analysis of TRE by providing an excellent approximation of the expected squared value of the error at any given position and for any fiducial configuration (6). The expression is of particular value when fiducial markers are used. Unlike image registration procedures, which use information contained in the object to be registered to find a matching transformation, the accuracy of fiducial-based registration is largely independent of this object. This independence is achieved because the accuracy of the registration is determined not by any characteristics of the object to be registered but by the number, placement, and localization accuracy of the fiducial markers. Once the localization accuracy or FRE has been measured for the given imaging modality via experiments in phantoms or with previous patients, it will be possible to use this expression to determine the expected target registration accuracy for a patient. A thorough introduction to point-based registration and other registration methods can be found in the *Handbook of Medical Imaging* (5).

TYPES OF REGISTRATION ERRORS

Maurer et al. (12, 14) suggested three useful measures of error for analysis of the accuracy of point-based registration methods (*Fig. 1*): 1) FLE, which is the error in locating the fiducial points, 2) FRE, which is the distance between corresponding fiducial points after registration, and 3) TRE, which is the distance between corresponding points other than the fiducial points after registration. Although the FLE and FRE measured at each fiducial are vector quantities, as is the TRE measured at each target point, in general the FLE, FRE, and TRE are reported as scalar values that are the length of the vectors, i.e., the root mean square (RMS) of the vector components.

Some of the factors that contribute to FLE are the tracking system, the design of fiducials (such as infrared-emitting diodes [IREDs]) on the instrument being tracked in physical space, the digital nature of the images (voxel size is important to FLE), the signal-to-noise ratio of the images, the design of the imaging markers, and image distortion. In theory, FLE increases in quadrature between image and physical space; the square of the "total FLE" of the system may be thought of as statistically equivalent to the sum of the squares of the FLEs in image and physical space.

In TRE terminology, "target" is used to suggest that the points are directly associated with the reason for the registration. In medical applications they are typically points within, or on the boundary of, lesions to be resected during surgery or regions of functional activity to be examined for diagnostic purposes. It is difficult to measure TRE accurately with the registration system. Instead, the surgeon must rely on statistical predictors of these errors based on the known localization accuracy of the fiducials (RMS[FLE]), or the measured alignment error of the fiducials (RMS[FRE]).

METHODS

In the Appendix, we discuss the ways in which FRE and TRE vary according to the fiducial configuration and FLE. Perhaps the most pertinent point is that for a constant FLE and number of fiducials, FRE does not change according to the shape of the fiducial configuration. TRE, however, varies

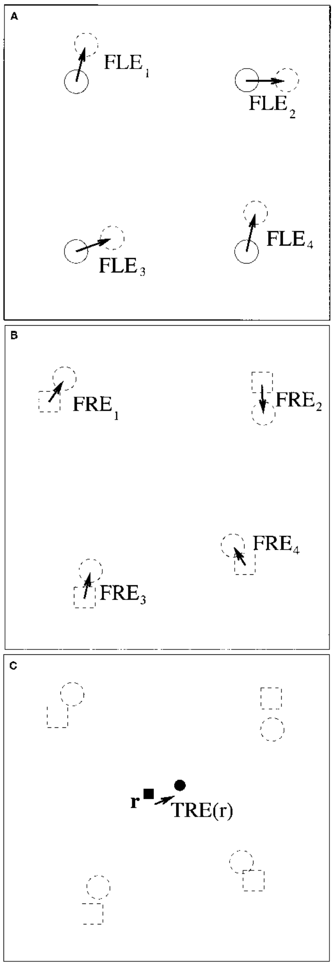

FIGURE 1. Various types of registration errors. *A*, the FLE measured at each fiducial is the distance between the true position (○) and the measured position (◌) of the fiducial. *B*, the FRE measured at each fiducial is the distance between the measured position of the fiducial in one space and its counterpart in the other space (◌ and ⬚) after registration. *C*, the TRE, measured at the point *r* relative to a given origin, is the distance after registration between the anatomic location (■) represented by *r* in one space and the corresponding anatomic point in the other space (●).

greatly according to this shape, with near-collinear configurations resulting in large TRE values at target locations removed from the line of the fiducials. *Figure 2* shows representations of several fiducial configurations, along with iso-error contours of TRE that are derived using *Equation 4*. In all the subfigures, we have assumed an RMS[FRE] value equal to 1.0 mm. Systems that use anatomic landmarks as fiducial points (7–9, 15) often have FRE values greater than 1.0 mm; RMS[FRE] values of 1.0 to 3.0 mm are typical, with the value of *N* ranging between 8 and 16. Systems that use skin-affixed markers (3, 17) may have FRE values less than 2.0 mm, although problems with marker movement in some clinical situations may result in FRE values greater than those obtained using phantom experiments; the value of *N* for these systems typically ranges from 6 to 10. For bone-implanted marker systems (11), the value of *N* is typically between 3 and 5, and the value of FRE is generally less than 1.0 mm. *Figure 2, A, E, I,* and *M* shows renderings of the left and right side of a head. *Figure 2, A–D* shows an approximately square marker configuration lying in the transverse plane; *Figure 2, E–H* shows a triangular configuration, again in the transverse plane; *Figure 2, I–L* shows a configuration consisting of a square patch of four markers on one side of the head, and *Figure 2, M–P* shows a near collinear configuration. Profiles of RMS[TRE] in a central coronal, sagittal, and transverse slice of the head are shown. As can be observed from *Equation 4*, for larger or smaller values of FRE, the TRE values in these figures will be increased or decreased proportionally. *Figure 3* shows a rendering of a vertebra and a transverse slice through the same vertebra. The tips of the transverse and spinous processes are used as anatomic landmarks that provide fiducial points; in the transverse slice, a planned position for a pedicle screw and contours of RMS[TRE] are shown.

The relationship between FRE and TRE described in *Equation 4* has several practical applications for point-based registration in frameless stereotaxy, some of which are illustrated in the given examples. The cranial illustrations represent a patient with a lesion in the right orbitofrontal lobe. The brain scans represented are T1-weighted magnetic resonance volume acquisitions similar to those used in data acquisition for frameless stereotactic craniotomy; in the vertebra, the scans are computed tomographic scans.

RESULTS

Figure 2, A–D shows the placement of four fiducial markers in a square lying in the plane of the lesion. The markers are well spread, near the level of the lesion, and similar to arrangements of markers often used in bone-implanted fiducial point-based registration systems. The contours in *Figure 2* show values of expected RMS[TRE] that are small (1–2 mm throughout the brain), with the smallest values centered at the middle of the fiducial marker arrangement. This array of fiducial markers provides a minimal RMS[TRE] for most areas within the brain and a near spherical character to the RMS[TRE] contour fields. However, fiducial placement could have been improved in this array through placement of one or both of the anterior markers in a more frontal position, so that the lesion lay within the square defined by the four fiducial markers. If these marker positions were more frontal, we might then expect the lesion to lie within the 1 mm RMS[TRE] contour line.

Figure 2, E–H shows a very similar fiducial placement; however, the two right-sided markers have been replaced by a single fiducial. Simply removing one marker nearly doubles the RMS[TRE] throughout most of the brain volume. The contours of the field are more elliptical in shape, and the ellipse is wider on the side of the two fiducials. The RMS[TRE] near the lesion is almost 2 mm; it would have been somewhat lower if the left anterior fiducial had been chosen for removal. The factors that minimized the RMS[TRE] in this example are the well-spaced, non-linear arrangements of these few markers located near the plane of the lesion.

The last two examples demonstrate the manner in which poor fiducial placement may add considerable (≥2 mm) error within the volume of the head. In *Figure 2, I–L*, the fiducials are placed in a small square on the head opposite the side of the lesion. In this situation, the RMS[TRE] contours are concentric ellipsoids. If the target is near the center of these ellipsoids, the TRE will be small, but if it lies on the opposite side, the RMS[TRE] may be as large as 3 to 4 mm. Spreading the four fiducial markers apart would have expanded the

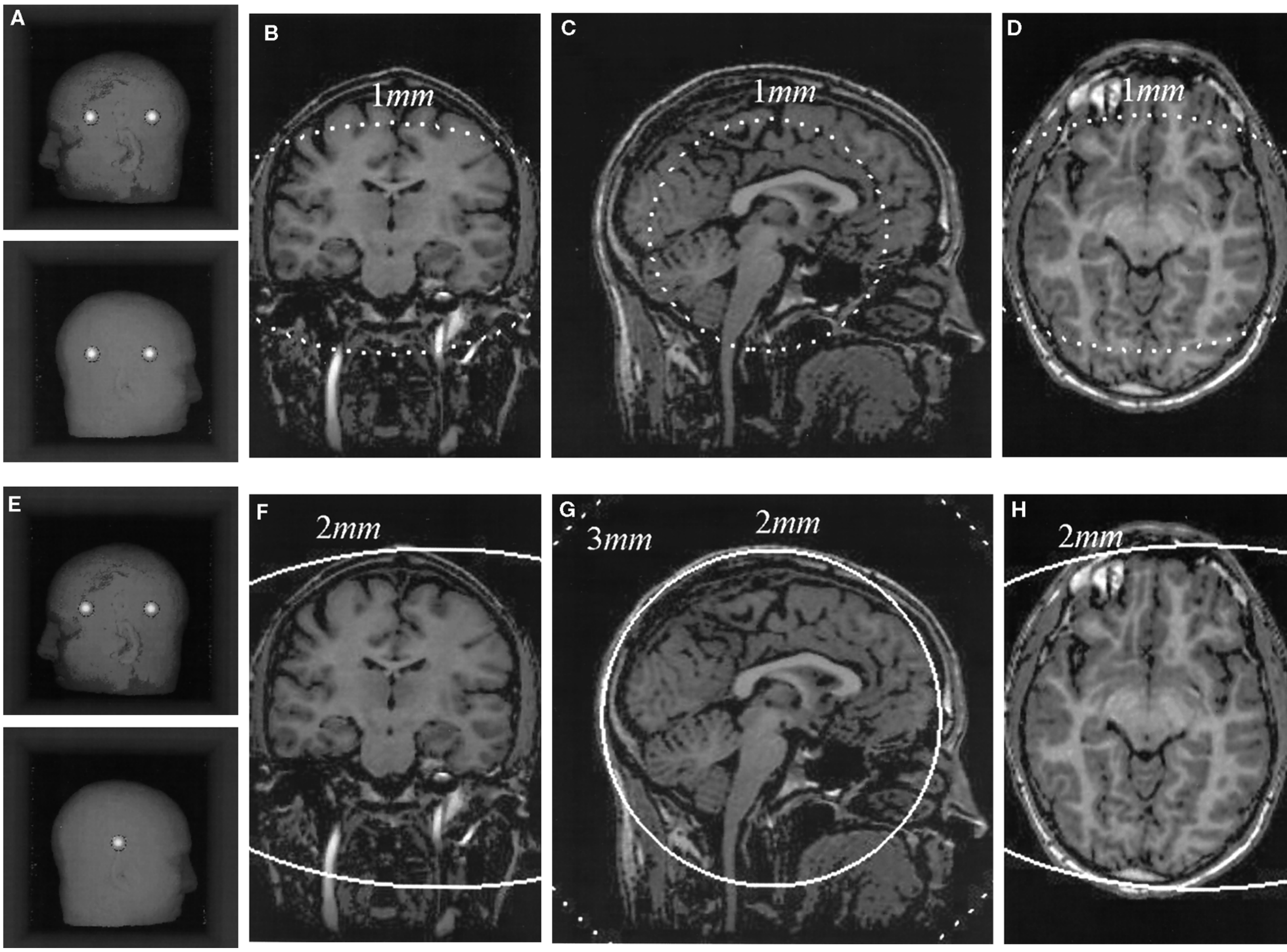

FIGURE 2. ***A–H*, views of a large square and large triangular fiducial configurations and their corresponding TRE profiles. Missing iso-error contours indicate that the TRE value was either consistently above or below that isocontour value for the entire displayed slice. *A*, left and right view; *B*, coronal view; *C*, sagittal view; *D*, axial view; *E*, left and right view; *F*, coronal view; *G*, sagittal view; *H*, axial view.**

contours and reduced the TRE at the lesion. Placement of the markers surrounding or nearer to the lesion also would have helped reduce the TRE. *Figure 2, M–P* demonstrates the danger of a near-collinear configuration. In the midsagittal slice, the RMS[TRE] is greater than 10 mm throughout.

Figure 3 shows that anatomic landmarks, if arranged in a noncollinear configuration surrounding the target area, may be sufficient to perform a reasonably accurate registration if the FLE for the landmarks is sufficiently small. (In *Figure 3*, we assume that the RMS[FRE] is 1.0 mm, implying that the RMS[FLE] is approximately 1.73 mm). The RMS[TRE] in the pedicle is approximately 2 mm. This means that typically the component of TRE in the mediolateral direction will be approximately $2 \div \sqrt{3} = 1.2$ mm. This error level means that the screw must be approximately 2.5 mm narrower than the pedicle to allow implantation of the screw with a small chance of pedicle violation through inaccurate placement. It should be noted, however, that this value of 2.5 mm does not necessarily apply to all vertebrae. As a result of the changes in shape and relative position of the processes used for registration, the shape of the fiducial configuration and the localization accuracy of the fiducial points tend to vary according to the region of the spine in which surgery is performed.

DISCUSSION

Further applications of the results discussed above include adding error bounds along trajectories in surgical navigation systems and providing bounds to radiation therapy and radiosurgery isodose contours in radiotherapy planning software. These results also may be useful for improving the design of probes that rely on fiducial markers (such as IREDs) for physical space tracking. Consideration of *Equation 4* in the Appendix will allow IREDs to be placed on the probe to optimize tip position accuracy (equivalent to TRE).

Assumptions were made to derive this equation, and examples of circumstances in which these assumptions may be violated are available. First, we assumed that the localization

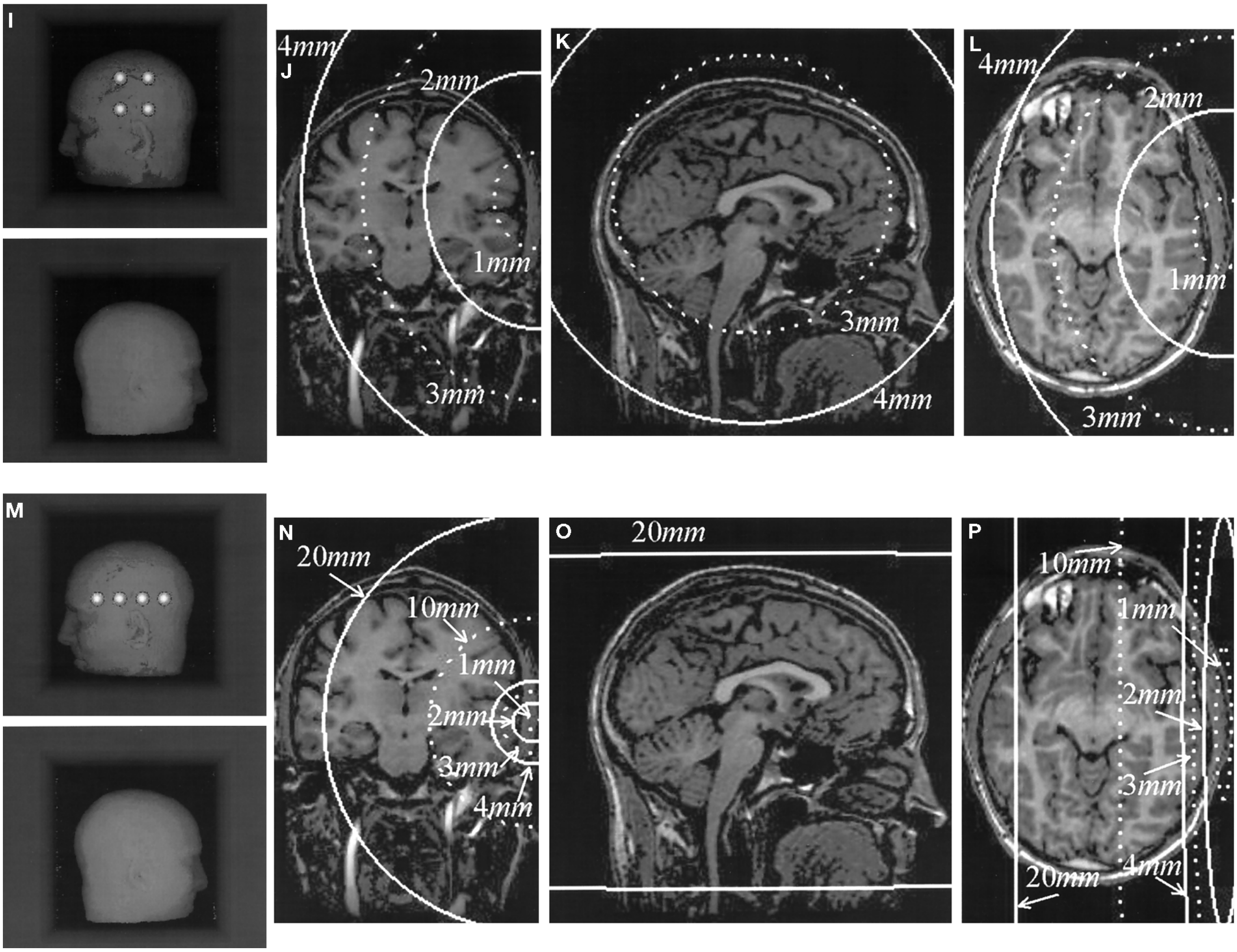

FIGURE 2. ***I–P*, views of small square and near-collinear fiducial configurations and their corresponding TRE profiles. Missing iso-error contours indicate that the TRE value was either consistently above or below that isocontour value for the entire displayed slice. *I*, left and right view; *J*, coronal view; *K*, sagittal view; *L*, axial view; *M*, left and right view; *N*, coronal view; *O*, sagittal view; *P*, axial view.**

errors at each fiducial are identically distributed and uncorrelated. In the case of skin-affixed markers, for example, large-scale motion of the skin may cause correlated localization errors in the markers. We also assumed that the two spaces being registered are related by a rigid body transformation. Problems such as tissue deformation, magnetic resonance image and scale distortion, patient motion during computed tomographic scan acquisition, and patient movement with respect to the intraoperative coordinate system (such as the reference emitter, dynamic frame of reference) may invalidate the assumption of rigid body motion. The effect of FLE correlation on the relationship among FLE, FRE, and TRE depends critically on the type of correlation. For example, for a large-scale motion of the skin, in which the skin-affixed markers were all to have a constant component added to their FLE in addition to random error, FRE would be unchanged but TRE would be increased. This is because the constant component would be added to the translational part of the registration transform, and it would "cancel out" of FRE. Because the markers in this example would move relative to a target within the head, however, TRE would be increased. In this situation, *Equation 4* would underestimate the potential target error.

As long as these assumptions hold true, we know that our TRE isocontours are close to correct, as they are in excellent agreement with numerical simulations that we have performed (6). To investigate how well this theory may be applied in practice, we performed another study (18), in which we compared predicted and observed values of TRE on a database of 86 patient image volumes. Although the agreement is not as close as with the numerical simulations, it is still sufficiently close that our theory is useful for predicting TRE in practice.

We have applied a formula for registration to several fiducial point (fiducial marker or anatomic landmark) configurations. We have demonstrated that marker placement influ-

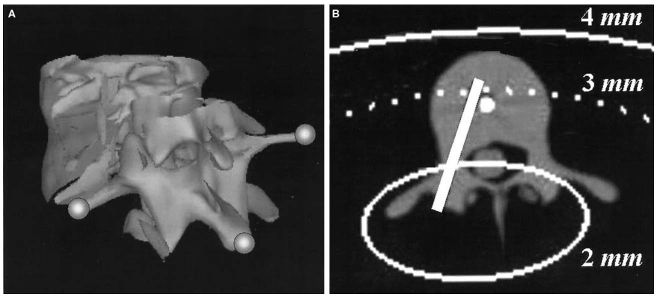

FIGURE 3. View of the vertebra from a plastic phantom, showing the tips of the transverse and spinous processes used as the three fiducial points (*spheres*). *A*, fiducial positions; *B*, transverse view. The transverse view shows a pedicle screw approximately 4 mm wide and the expected TRE values. An alternative illustration that might be more useful to the surgeon would show the pedicle screw in one color surrounded by an expected error box in a different color.

ences TRE considerably, and it may affect the accuracy of navigation in frameless stereotactic surgery. The conclusions may be summarized in four simple guidelines for the placement of fiducial markers in rigid body, point-based registration: 1) avoid linear, or almost linear marker configurations, 2) arrange the markers so that the center of their configuration is as close as possible to the regions that are most critical during surgery, 3) keep the markers as far from each other as possible, and 4) use as many markers as feasible (although for this rule, the return diminishes rapidly after five or six markers are used).

The first guideline is necessary because almost linear marker configurations lead to a small value of one of the f_k in the denominator of *Equation 4*, which could therefore result in a large value of TRE. The second guideline is intended to minimize the values of d_1, d_2, and d_3 in the numerator of the last term in *Equation 4*. By ensuring that the target is kept close to the center of the fiducial configuration, the rotational part of TRE (represented in *Equation 4* by the term multiplied by ⅓) may be minimized. By keeping the markers as far apart as possible, as suggested in the third guideline, we maximize the f_k in the denominator of the rotational part of TRE. By obeying the fourth guideline and using as many markers as feasible, the value of N in *Equation 4* is increased, thus TRE is decreased.

These guidelines must be balanced, of course, with the physical restrictions governing feasible marker placement for a particular patient. For example, occasionally skin markers are placed only on the forehead to keep them out of the hair; in other cases, all markers may be placed on the side of the head contralateral to the lesion to ensure they do not interfere with surgery. When an intraoperative microscope is used, it may be tempting to cluster the markers closely together to facilitate their localization with the microscope. Each of these practices tends to increase TRE. It is our hope that the mathematical results presented here will be used in conjunction with these practical considerations to achieve the maximum feasible registration accuracy.

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APPENDIX

We demonstrated previously (6) the calculation of expected squared TRE^2 at a point r (measured relative to the fiducials' centroid) in terms of the expected squared FLE (FLE^2) and the number and positions of the fiducial points. This relationship may be written as

$$\langle \mathrm{TRE}^2(\mathbf{r})\rangle \approx \frac{\langle \mathrm{FLE}^2\rangle}{N}\left(1+\frac{1}{3}\sum_{k=1}^{3}\frac{d_k^2}{f_k^2}\right), \qquad (1)$$

where f_k is the RMS distance of the fiducials, and d_k is the distance of the target from principal axis k of the fiducial configuration. We note that f_k is analogous to the radius of gyration of the fiducial configuration. The constant inside the parentheses in *Equation 1* represents the translational component of TRE; the summation term represents the rotational component. The iso-error contours generated by *Equation 1* are ellipsoidal: this is in agreement with the observations of Maurer et al. (13) and Darabi et al. (2). From *Equation 1* we can observe that if, for any value of k, f_k is small relative to d_k, a large value of TRE can be expected. Expressed another way, a fiducial configuration that is close to collinear will tend to cause large TRE values at target positions removed from the line to which the fiducials are close. In 1979, Sibson (16) demonstrated that the FRE is, to a good approximation, independent of the shape of the fiducial configuration, and it depends only on the FLE and number (N) of fiducials. If it is assumed that the coordinate components of the FLEs at each fiducial are independent, identically distributed, zero-mean normal variables, Sibson (16) demonstrated that

$$\sum_{i=1}^{N} \mathrm{FRE}_i^2 \sim \sigma^2\chi^2_{3N-6}, \qquad (2)$$

where σ^2, the variance of the coordinate components of FLE, equals $(FLE^2)/3$, and FRE$_i$ is the magnitude of the alignment error at fiducial i. *Equation 2* means that, for a given FLE, there will be a range of possible FRE values for which probabilities are given by the χ^2 distribution with $3N-6$ degrees of freedom. For the surgeon to interpret a given FRE for a registration task, consideration of *Equation 2* should permit discrimination between an FRE value that lies within acceptable bounds and a value that is improbably large. Such a large value would indicate with high probability a failure of the registration system (such as the inability to localize accurately one or more of the fiducial points in one or both of the spaces).

From *Equation 2*, the expected mean square FRE may be deduced:

$$\langle \mathrm{FRE}^2 \rangle \approx \frac{(N-2)\langle \mathrm{FLE}^2 \rangle}{N}. \qquad (3)$$

Because the right side of *Equation 3* is independent of the shape of the fiducial configuration, in cases of near-collinear configurations, FRE becomes a poor indicator of TRE. It should also be noted that *Equation 3* implies that decreasing the number of fiducials will also decrease FRE; from *Equation 1*, however, we observe that decreasing N tends to increase TRE, if the average distance of the fiducials from their centroid stays constant. By using the relationship between FLE and FRE given in *Equation 3*, we may rewrite *Equation 1* in terms of the expected FRE:

$$\langle \mathrm{TRE}^2(\mathbf{r}) \rangle \approx \frac{\langle \mathrm{FRE}^2 \rangle}{(N-2)}\left(1 + \frac{1}{3}\sum_{k=1}^{3}\frac{d_k^2}{f_k^2}\right). \qquad (4)$$

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COMMENTS

In this report, West et al. present a mathematical model that can be used to quantify the errors inherent to fiducial image-guided localization. The overall findings of this study are not surprising and are consistent with previous empirically derived clinical and phantom data. Although few neurosurgeons will understand the mathematics underlying the authors' hypothesis, the conclusions are relevant to neurosurgeons who use image guidance in their surgical practice. At the risk of stating the obvious, it is worth emphasizing that in a given patient, ultimately one of the best measures of targeting precision is the surgeon's qualitative assessment of how accurately known external landmarks can be localized with an image-guided system. Nevertheless, this article provides a valuable theoretical framework for optimizing the placement of fiducial arrays as part of image-guided procedures.

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There is something particularly seductive about the information (both graphic and numerical) presented on surgical navigational systems. The images and crosshairs are crisp. The registration error is displayed in millimeters and fractions (tenths, hundredths) thereof. It is little wonder that surgeons want to believe that what they see is what they get.

In this article, the authors show the true blur of error behind these slick facades and how the surgeon has substantial control over optimizing accuracy of registration in the area of interest. This article comes from a well-respected group in the area of defining the science of image-guided surgery and is another excellent example of their work. Although the results of their analyses are predictable, the authors present an elegant method of calculating average target registration error encountered when using different configurations of fiducials. The reader will likely get lost in the mathematical explanation, but the results are important for anyone who uses surgical navigation in operating on a patient's head or spine:

Avoid linear placement of fiducials,
More is better,
Keep them far apart,
And center them on your target.

Because this analysis assumes a rigid relationship of the fiducials to the target, to these principles I would add, "Keep scalp fiducials away from excessively mobile areas of the scalp" or "Use cranial fiducials." The authors also emphasize that the registration error presented by the navigation device does not necessarily predict the error of registration at the target.

Several years ago, we adopted a routine system of cranial fiducial placement (nine in all) that adheres to these principles: a pair just above the lateral aspect of the eyebrows, a pair on the lateral upper forehead, a pair on the asterions, one at the vertex, and a pair between the area just above the lateral aspect of the eyebrows and the vertex. Because this system is routine, the fiducials can be applied by a technician or by a nurse without regard to lesion placement. This pattern also minimizes the risk of displacement by fixation devices or imaging headholders, and because there is redundancy, displaced fiducials may be eliminated from the registration.

Although one might expect that the information in this article would be a routine part of training upon purchase of a surgical navigational system, these points are often overlooked, misrepresented, or not understood by purveyors of these systems. These systems, albeit complex, are just another tool, and the surgeon is obligated to understand how it does (and does not) work. This article should be required reading for all neurosurgeons.

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Who places fiducials before imaging for frameless stereotactic procedures? At many institutions, it is not the neurosurgeon but a nurse practitioner or a magnetic resonance imaging technician. Many paramedical personnel learn quickly and do a good job in applying a number of fiducials with adequate spacing between them. This article provides useful information on the proper placement of fiducials for the minimization of error in frameless stereotactic procedures. Many of the conclusions are intuitive. Nonetheless, the mathematical proof of their recommendations is reassuring. I suspect that copies of this article will be found in many magnetic resonance imaging suites in which frameless stereotactic database acquisitions are done.

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This article addresses the relationships among errors in fiducial localization, errors in registration of the fiducial array, and expected errors in localization of the target. It is relevant, refreshing, and provides substantive, practical information for the neurosurgeon who uses an image-guidance system. The authors are a highly experienced and talented group who have struck a good balance between demonstrating the derivation of their conclusions and orienting the focus of their article toward the interests of neurosurgeons. Their suggestions for fiducial arrays are sound.

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