Optimal landmarks selection and fiducial marker placement for minimal target registration error in image-guided neurosurgery

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ABSTRACT

We describe a new framework and method for the optimal selection of anatomical landmarks and optimal placement of fiducial markers in image-guided neurosurgery. The method allows the surgeon to optimally plan the markers locations on routine diagnostic images before preoperative imaging and to intraoperatively select the fiducial markers and the anatomical landmarks that minimize the Target Registration Error (TRE). The optimal fiducial marker configuration selection is performed by the surgeon on the diagnostic image following the target selection based on a visual Estimated TRE (E-TRE) map. The E-TRE map is automatically updated when the surgeon interactively adds and deletes candidate markers and targets. The method takes the guesswork out of the registration process, provides a reliable localization uncertainty error for navigation, and can reduce the localization error without additional imaging and hardware. Our clinical experiments on five patients who underwent brain surgery with a navigation system show that optimizing one marker location and the anatomical landmarks configuration reduces the average TRE from 4.7mm to 3.2mm, with a maximum improvement of 4mm. The reduction of the target registration error has the potential to support safer and more accurate minimally invasive neurosurgical procedures.

Keywords: Rigid registration, Neurosurgical Procedure, Therapy Planning, Localization and Tracking Technologies

1. INTRODUCTION

Image-Guided Surgery (IGS) has become the standard of care for many neurosurgery procedures. A key step in IGS is the accurate intraoperative alignment, called registration, between preoperative MRI/CT images and the intraoperative physical anatomy. Fiducial-based registration is the method of choice in existing IGS systems [1, 2]. It calls for localizing predefined fiducials (implanted spheres, bone screws, adhesive skin markers, and anatomical landmarks) on the preoperative MRI/CT images and correlating them with their counterparts on the intraoperative physical anatomy. Quantifying the registration error is of great clinical importance, as it has direct implications for the treatment decisions and their risks assessment. However, since the targets locations usually cannot be measured directly, the Target Registration Error (TRE) is estimated with the Fiducial Registration Error (FRE), or with Fitzpatrick’s TRE formula [3].

The placement of fiducial markers and the selection of the anatomical landmarks have a direct influence on the TRE and on the navigation localization error. Poorly placed fiducial markers or anatomical landmarks selections with large localization errors can yield clinically unacceptable navigation and target localization errors [4, 5]. The TRE accuracy can be improved by the judicious placement of the fiducial markers before imaging and by the selection of the subset of anatomical landmarks that minimizes the localization error. Moreover, the registration error should be estimated at the target and not at the fiducials, as is customary in commercial systems.

Previous works show that the optimal placement of markers before point-based registration can significantly reduce the predicted TRE [5-8]. West et al. [5] report in a clinical study on cranial CT/MRI images that the fiducial locations significantly influence the TRE. They propose three guidelines for good anatomical landmark selection and fiducial markers placement: 1) use as many fiducials as possible; 2) ensure that the fiducials center of mass is as close as possible to the target location, and; 3) avoid nearly collinear fiducials. The guidelines assume identical Fiducial Localization Error (FLE) distribution and rely on Fitzpatrick’s TRE estimation method [9]. However, our clinical and theoretical studies [4, 10] reveal a significant difference in the localization error distributions of different anatomical landmarks and poor FRE-TRE correlation. These findings raise questions about the correctness of the first two guidelines.

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Recent works propose methods to optimize fiducials selection and placement. Liu et al. [8] introduce a genetic algorithm based on the Fitzpatrick TRE formula to approximate the optimal fiducials selection. The method was evaluated on abdominal and thoracic phantoms with a photogrammetry positioning system. The authors show that optimizing a set of randomly placed fiducials reduced the TRE from 1.9mm to 0.8mm. Riboldi et al. [7] propose a method that combines genetic algorithms and taboo search. Their simulation study on 10 images of prostate patients shows that optimizing a set of randomly placed fiducials with their method reduces the TRE by 26% vs. 19% with an ordinary genetic algorithm. Atuegwu et al. [6] incorporate a model of skin motion and approximate the optimal landmarks placement for a target region. They report a mean improvement of 1.5mm in their phantom and simulation studies.

The existing studies and solutions have the following limitations. 1) the methods were tested on a phantom or with a simulation study, and thus do not reflect all the error factors; 2) no user interaction and error visualization is provided; 3) solutions are locally optimal and depend on the initialization seed, and; 4) the methods are applicable only to fiducial markers and not to anatomical landmarks since they assume identical FLE distribution, which is not realistic [4].

We describe in this paper a new framework and method for the optimal anatomical landmarks selection and fiducial markers placement in image-guided neurosurgery. Our method computes a globally optimal solution which does not require any initialization. It provides surgeons with intuitive visual feedback of the expected TRE and allows them to interactively change the fiducial markers locations and anatomical landmarks selection based on clinical considerations. The method takes the guesswork out of the registration process, provides a reliable localization uncertainty error for navigation, and can reduce the localization error without additional imaging and hardware. Our clinical experiments on five patients who underwent brain surgery with a navigation system show that optimizing one marker location and the anatomical landmarks configuration reduces the average TRE from 4.7mm to 3.2mm, with a maximum improvement of 4mm. The TRE reduction has the potential to support safer, more accurate minimally invasive neurosurgical procedures.

The rest of this paper is organized as follows. In section 2 we present the mathematical framework of the point-based rigid registration problem and define the optimal landmarks selection and optimal fiducials placement problems and suggested solutions. In section 3 we describe the clinical experiment setup where we quantify the impact of optimal selection and fiducial marker placement and anatomical landmarks selection on the targeting accuracy. In section 4 we present our experiments results. In sections 5, we discuss the implications of our results.

2. METHODS

2.1 Problem definition

Fiducial-based registration consists of computing the rigid-body transformation that best matches the preoperative fiducials locations to the intraoperative ones. The inputs are the preoperative and intraoperative fiducials datasets. The output is the rigid transformation that brings the datasets as close as possible according to a similarity measure.

Let \( A = \{a_1, a_2, \ldots, a_n\} \) and \( B = \{b_1, b_2, \ldots, b_n\} \) be two sets of \( n \) paired points, each representing a fiducial location in the preoperative and intraoperative dataset in their respective coordinate systems. Let \( T_a^b \) be the rigid transformation (rotation and translation) that best aligns the fiducial pairs \((a_i, b_i)\). The transformation minimizes a similarity measure:

\[
T_a^b = \arg \min_T \{SIMILARITY(A, B, T)\}
\]

where \( T \) is a rigid transformation. The most commonly used similarity measure is the Root Mean Square (RMS) distance between the two point sets, which corresponds to the FRE. Since fiducial locations cannot be determined precisely, a Fiducial Localization Error (FLE) is associated to each fiducial to model the locations uncertainty.

Let \( A_{\text{target}} = \{a_{1, \text{target}}, a_{2, \text{target}}, \ldots, a_{m, \text{target}}\} \) and \( B_{\text{target}} = \{b_{1, \text{target}}, b_{2, \text{target}}, \ldots, b_{m, \text{target}}\} \) be two sets of \( m \) paired points, each representing a target location in the preoperative and intraoperative datasets. The TRE after registration is defined as:

\[
TRE(A_{\text{target}}, B_{\text{target}}, T_a^b) = \sqrt{\frac{\sum_{i=1}^{m} (T_a^b a_{i, \text{target}} - b_{i, \text{target}})^2}{m}}
\]
Note that this measure gives equal weight to all targets. A weighted error may also be defined, and various models of the landmarks and targets localization errors can be also incorporated.

Since the TRE cannot be obtained directly in most cases, it must be estimated. A variety of Estimated TRE (E-TRE) methods have been proposed [1, 9, 11-18]. They all assume that the landmarks have the same FLE distribution model. However, our clinical study [4] showed that the FLE of anatomical landmarks varies for both the image and the physical space. Thus, none of these methods provides a clinically reliable TRE estimator. The alternative method which we used in our experiments is to randomly draw samples of fiducial locations from a predefined empirical error model, compute the TRE for each scenario, and average the results. This E-TRE method empirically accounts for different anisotropic FLE distributions for landmarks, patients, and surgeons.

Additional requirements such as a minimum distance requirement of a trajectory from a critical structure or a lower bound on the localization error of an individual target are common and should be taken into account when computing the registration. We collectively account for these constraints with a set of inequalities, which we denote as CONSTRAINTS.

2.1 Optimal fiducials selection

The optimal fiducials selection is the task of selecting a subset of fiducials from a given initial set such that the TRE is minimized. It is applicable for pre-imaging anatomical landmarks selection, or for intra-operative refinement of the previously chosen landmarks and the fiducial markers.

Let $A$ and $B$ be two sets of preoperative and intraoperative fiducials, and $A_{\text{target}}$ the targets set. The goal is to find the optimal fiducials subset pairing that minimizes the E-TRE:

$$
(A^*, B^*) = \arg \min_{A' \subseteq A, B' \subseteq B} E\text{-TRE}(A_{\text{target}}, A', B', A_{\text{target}}', \text{FLE})
$$

s. t. CONSTRAINTS are satisfied.

The most direct method to find the optimal pairing and transformation is to enumerate all possible pairings $A' \subseteq A$ and $B' \subseteq B$, compute for each its E-TRE, and select the pairings which yield the smallest value and satisfy the constraints. This exhaustive enumeration is feasible when both $A$ and $B$ are of small size, or when the total number of fiducials pairings can be restricted, as is the case in current commercial systems.

2.2 Optimal fiducials placement

The optimal landmarks placement is the task of defining fiducial markers locations on the patient such that the TRE is minimized. In current practice, fiducials are placed according to the surgeon's experience and often at the discretion of the imaging technician. This can lead to larger than desired TRE errors. Optimal fiducials placement is applicable for pre-imaging planning of skin/skull mounted markers. Since this planning is performed on the available diagnostic images routinely available before surgery, no additional imaging is necessary.

Let $A$ be a set of preoperative fiducials and $A_{\text{target}}$ a set of targets. The goal is to find the locations of one or more fiducial markers, $A_{\text{complement}}$ such that the augmented set of fiducials minimizes the E-TRE:

$$
A_{\text{complement}} = \arg \min_{A \subseteq S} E\text{-TRE}(A_{\text{target}}, A \cup A', \text{FLE})
$$

s. t. CONSTRAINTS are satisfied.

where $A'$ is a set of points on the anatomy surface $S$ (in image coordinates).
The most direct method to find the optimal fiducial markers placement is as follows. First, we evenly sample points on the cranial surface $S$ extracted from the MRI/CT to obtain a set of potential fiducial markers locations $P$. Then, we compute the E-TRE value for each possible small subset of $P$, and select the one with the minimum E-TRE value. The result is the set $A_{\text{complement}}$ of $3 \leq k \leq |P|$ fiducial markers locations with the smallest E-TRE value. Since there are $O(2^{|P|})$ possible fiducial markers subsets, this approach is only practical when $|P|$ is small ($\leq 10$) or when the number of fiducial markers $|A_{\text{complement}}| \leq 3$ and their possible locations are restricted.

Alternatively, the following heuristic method can be used. First, compute the optimal landmarks set $A_{\text{complement}}$ on a small set of potential fiducial markers locations $P$ sparsely sampled on $S$. Then, for each fiducial in $A_{\text{complement}}$, define a neighborhood on $S$ and build a hierarchical spatial data structure, such as a quad-tree rooted at the landmark location. For each fiducial marker, find its four descendants on the quad-tree, compute the E-TRE of all possible combinations, and select the one with the smallest E-TRE. This refinement strategy relies on the fact that E-TRE values are locally continuous and have small variability for small location changes [4].

2.3 Error visualization and user interaction

For practical and clinical reasons, the surgeon may need to modify the computed optimal fiducials configuration. For this purpose, we have developed a module that allows the surgeon to add and/or remove the selected fiducial markers and anatomical landmarks with a visual error feedback. The expected TRE map is superimposed on the patient's cranial surface. The map colors show the resulting predicted TRE after the addition/deletion/location change of fiducials (Figure 1). With this module, the surgeon can incorporate clinical information into the fiducials planning and avoid anatomical landmarks that are difficult to locate or areas known for large skin deformations. Although this does not guarantee optimality, it keeps the surgeon in control and allows the incorporation of additional personal and experience-based considerations.
3. EXPERIMENTAL SETUP

To quantify the impact of optimal selection and placement of fiducials on the targeting accuracy, we conducted the following clinical experiment. Five patients whom underwent a brain surgery with a commercial navigation system were randomly selected. For each patient, the surgeon defined one simulated target location and nine anatomical landmarks on the diagnostic MRI image. Then, the cranial surface was automatically segmented and modeled with a set of points representing possible fiducial markers location. The E-TRE was computed for each possible marker location with isotropic, identically distributed FLE, and an E-TRE map was generated. The surgeon selected two fiducial markers locations on the map: one with a low E-TRE value (good) and with a high E-TRE value (bad).

Prior to pre-operative imaging, three fiducial markers were affixed to the patient’s head according to the previous selection: two at the good and bad locations, and one at the target location. After MRI imaging with the standard navigation protocol, the surgeon localized the corresponding anatomical landmarks and the three fiducial markers on the patient’s preoperative image. Each MRI dataset had 512×512×160 voxels, each of size 0.47×0.47×1.0mm³.

In the operating room, two surgeons correlated the predefined anatomical landmarks and the three fiducial markers with their physical locations by touching them with a tracked pointer. Each fiducial was repeatedly selected 3–6 times on both the preoperative image and on the physical anatomy.

In the laboratory, we ran our program to automatically select the optimal anatomical landmarks. The E-TRE values of all the possible subsets of the anatomical landmarks were computed and the subset with the smallest E-TRE value was considered optimal. The anatomical landmarks were modeled with the FLE distributions that we obtained empirically in the same setup [4]. E-TRE values were computed by Monte-Carlo statistical simulation with these FLEs distributions.

Three fiducials configurations were generated and their TRE was compared to their actual TRE: 1) original predefined anatomical landmarks and a bad fiducial placement; 2) original predefined anatomical landmarks and a good fiducial placement, and; 3) selected optimal anatomical landmarks and a good fiducial placement. Overall, 324 different landmarks pairings were generated and analyzed from the three different landmarks configurations, the 3-6 repetitive selections of the same landmarks on 5 patients’ MRI images and physical anatomy by the two surgeons.
Table 1. Three fiducials configurations are compared with respect to their measured TRE on 5 patients: 1) all predefined anatomical landmarks and the ‘bad’ fiducial marker; 2) all predefined anatomical landmarks and the ‘good’ fiducial marker, and; 3) selected optimal anatomical landmarks and ‘good’ fiducial marker. A total of 324 different fiducials pairings were analyzed from the three different fiducials configurations, the 3-6 repetitive selections of the same fiducials on 5 patients’ MRI images, and physical anatomy selection by two surgeons. All measured TRE values are reported in mm.

<table>
<thead>
<tr>
<th>Fiducials setup</th>
<th>Patient 1</th>
<th>Patient 2</th>
<th>Patient 3</th>
<th>Patient 4</th>
<th>Patient 5</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Bad marker +</td>
<td>mean</td>
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<td>5.2</td>
<td>4.3</td>
<td>3.4</td>
</tr>
<tr>
<td>all anatomical</td>
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<td>6.9</td>
<td>6.8</td>
<td>5.5</td>
<td>5.4</td>
</tr>
<tr>
<td>2. Good marker +</td>
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<td>5.3</td>
<td>4.0</td>
<td>4.0</td>
<td>1.8</td>
</tr>
<tr>
<td>all anatomical</td>
<td>std</td>
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<td>0.5</td>
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<tr>
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<tr>
<td>3. Good marker +</td>
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<tr>
<td>landmarks</td>
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<td>4.7</td>
<td>5.12</td>
<td>5.1</td>
<td>2.8</td>
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</tbody>
</table>

Table 4. RESULTS

Table 1 shows the mean, standard deviation, and maximum TRE values for each of the 324 different fiducials pairings on five patients. The mean observed TRE with the ‘bad’ marker and all the predefined anatomical landmarks was 4.7±1.3mm, with a 95% confidence interval of 6.7mm, and maximum error of 7.6mm. The mean TRE with the ‘good’ marker and all the predefined anatomical landmarks was 3.5±1.4mm, with a 95% confidence interval of 5.7mm, and maximum error of 6.0mm. The mean observed TRE with the ‘good’ marker and selected anatomical landmarks was 3.2±1.1mm, with a 95% confidence interval of 4.8mm, and maximum error of 5.2mm. The mean difference between the TRE of the ‘bad’ and ‘good’ markers was 1.2±1.0mm with a maximum improvement of 4.1mm. The mean difference between the TRE of the ‘bad’ and ‘good’ marker with optimal anatomical landmarks selection was 1.5±1.0mm with maximum improvement of 4.1mm.

These results show that optimizing the placement of a single fiducial marker location while keeping the others fixed reduces the TRE by 25% on average from 4.7mm to 3.5mm. Optimal anatomical landmarks selection reduced the mean TRE even further, to an average of 3.2mm that is reduction of 32%. For the most of the patients, the optimal anatomical landmarks selection algorithm selected all the predefined landmarks. However, in one case (Patient 1) a subset of the landmarks significantly reduced the TRE from 5.3mm to 3.6mm. These findings contrast with those of West et al. [5] and with the common belief that more fiducials reduce the TRE.

We also observe from the standard deviation and maximum TRE values that repetitive selections of the same fiducials for each patient results in TRE values that are near the average (<1.1mm). In 4 out of 5 patients, the maximum error of the "good marker + selected anatomical landmarks" scenario (Table 1, row 3) is smaller that the mean error of the "bad marker + all anatomical landmarks" scenario (Table 1, row 1). This indicates that the optimization can also provide a lower worst-case bound.

Another interesting observation is that the one fiducial marker results are similar those achieved in previous works by optimizing larger sets of fiducials [5-8]. This is somewhat unexpected, since it would seem that the TRE of multiple optimized fiducials will be lower (better) than the one of a single optimized fiducial marker. We see four possible reasons that may explain this: 1) We compared the TRE associated with the ‘worst’ and the ‘best’ fiducial marker locations, while others compared the random and ‘best’ configurations; 2) our optimization is global and independent of the initial seed configuration, which also determines their final result; 3) our solution allows to add or remove anatomical landmarks based on anisotropic FLE model, and; 4) our simulations use clinical data that includes all the actual localization errors that occur in the operating room – thus, there is more room for improvement.
5. CONCLUSIONS

We have presented new methods that allow surgeons to optimally plan fiducial markers locations prior to preoperative imaging, and to select the anatomical landmarks in the operating room that minimize the Target Registration Error. The improvement in accuracy is expected to reduce complications and may allow new procedures that could not be done because of the suboptimal targeting accuracy. It is expected to provide a new, principled pre-imaging method for landmarks placement, save preoperative and intraoperative time, and improve the reliability and accuracy of intraoperative target registration error.

The proposed method has several key advantages. Before preoperative image acquisition, it allows to automatically compute the optimal fiducial markers placement on the diagnostic MRI/CT. Since the diagnostic images are acquired routinely no additional scanning of the patient is required. The E-TRE map provides visual, intuitive feedback of the targeting error, and thus enables the surgeon to relocate fiducial markers and evaluate the expected targeting errors. It also provides a more realistic target localization error based on empirical localization error models. Intraoperatively, it can achieve the most accurate targeting localization in neurosurgical navigation without additional hardware. Since the landmarks selection process is fully automatic, it takes the guesswork out of the registration process and can thus shorten the intra-operative setup time. In a clinical experiment optimizing one marker placement and the anatomical landmarks selection we have observed an average improvement of 1.5mm in the TRE. The TRE improvement can allow safer and more accurate minimally invasive neurosurgical procedures.

REFERENCES


