CT to US Registration of the Lumbar Spine: A Clinical Feasibility Study

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Abstract. Spine needle injections are widely applied to alleviate pain and to remove nerve sensation through analgesia and anesthesia. Currently, spinal injections are performed using either no image guidance or modalities that expose the patient to ionizing radiation such as fluoroscopy or computed tomography (CT). Ultrasound (US) is being investigated as an alternative as it is a non-ionizing and more accessible image modality. An inherent challenge to US imaging of the spine is the acoustic shadows created by the bony structures of the vertebrae limiting visibility. It is possible to enhance the anatomical information in US through its fusion with a pre-operative CT. In this manuscript we propose a clinical feasibility study involving a novel registration pipeline to align CT and US images of the spine. This pipeline involves automatic global and multi-vertebrae registration. We evaluate the proposed methodology on five clinical data sets. The proposed method is able to register the data sets from initial misalignments of up to 25 mm, with a mean TRE of 1.17 mm, sufficient for many spine needle interventions.

Keywords: Registration, ultrasound, lumbar spine, multi-vertebrae.

1 Introduction

Spine needle injections are commonly used to deliver anesthesia and analgesia. Facet joint injections are an example of a common spinal intervention to treat chronic lower back pain [1]. Injections into this region are particularly challenging due to the deep location and the narrow space of the joint, and proximity to nerve tissue. These challenges make it difficult to provide accurate treatment to the target area when the procedure is performed without guidance. The current gold standard to guide the injection is fluoroscopy or intra-operative computed tomography (CT), exposing the patient and the clinician to ionizing radiation.

Intra-operative ultrasound (US) guidance for spine needle procedures is an attractive alternative as US is a non-ionizing and more accessible image modality compared to fluoroscopy or CT [2]. Using US guidance eliminates radiation

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associated with intra-operative CT or fluoroscopy. Additionally, US images can be taken in any location, as opposed to specialized facilities required for CT or fluoroscopy, improving the accessibility of spine needle interventions. US, however, has not become the standard-of-care for spine needle injections due to the difficulty associated with its interpretation of anatomy. Specifically, acoustic shadows from the bony structures of vertebrae limit the visibility of anatomical targets, such as facet joints in US images. To enhance the interpretation of US images and provide improved guidance, three dimensional (3D) anatomical information (e.g. from a pre-operative CT or a statistical shape model) can be integrated with the intra-operative US images through image registration.

Over the past decade, several point-based methods for registration of CT and US images of boney structures other than the spine have been presented in the literature [3, 4, 6]. A challenge of those techniques has been to reliably extract the bone surface from US images. Recently, local phase-based image processing of US has shown great promise in the automatic enhancement of the US bone surface [7]. To avoid US bone segmentation, intensity-based approaches to registration are also used [8–10]. Our group has also proposed several techniques for the registration of CT and US images [11, 12] based on a biomechanical model of the spine to constrain the possible space of solutions for registration.

Despite this surge of interest, to date, reliable registration of CT and US images of the spine for multiple vertebrae has not been effectively demonstrated, *in vivo*. The closest work is by Winter *et al.* [9] but only for a single vertebra; this approach does not consider the relative change in the pose of the vertebrae with respect to each other that naturally occurs between CT and US data acquisition. Since facet joints lay in the space between two adjacent vertebrae, a fast and robust registration approach of multiple vertebrae is clinically desirable.

In this paper, we present a clinical feasibility study involving a novel registration approach that aligns pre-operative diagnostic CT and intra-operative US images of multiple vertebrae. We validate the approach on data obtained from five patients who were scheduled for a spine injection. The registration approach involves both intensity and point based methods; it starts with global registration of the spine followed by a multi-vertebrae point-based registration.

2 Materials and Methods

2.1 Data Acquisition

Human data sets of the lumbar spine are used to validate the proposed registration method. Following Institutional Research Ethics Board approval, subjects provide informed consent to participate. Data is collected at St. Paul's Hospital in Vancouver, B.C., Canada. Only subjects with previous CT scans are recruited. The population of subjects include female and male patients with ages between 28 and 49 years, and weights between 135 and 202 lbs. The anonymized CT images of patients in supine position, the standard–of–care positioning for spinal CT, are provided as DICOM files by the hospital.

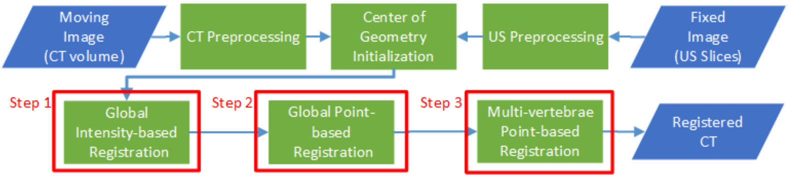

Fig. 1. General overview of the CT to US registration workflow

An imaging protocol is created for freehand US data acquisition that minimizes variability between subjects, and operators, and ensures setup time adheres to clinical practice. A SonixTouch US scanner (Ultrasonix, Richmond, B.C.) equipped with a magnetic tracker (Ascension DriveBay EM tracker, Burlington, VT) and a C5-2 curvilinear transducer are used for US data acquisition. An Ascension 800 EM tracking sensor, affixed to the patient's skin above the T12 vertebra is used as the patient coordinate reference. PLUS, an open-source toolkit [13] is used for US and tracking data recording; US calibration is performed using the N-wire method available in this toolkit as well. Subjects are set in the prone position, with a pillow under their stomach. An experienced sonographer scans the subjects and makes minor adjustments to preset US imaging parameters including depth; the parameters are preset earlier using a population of volunteers. The sonographer places marks on the skin surface corresponding to the T12-L1 and L5-S1 intervertebral spaces to delineate the US scanning region. Data is acquired by moving the US transducer slowly and smoothly in a downward zigzag pattern while holding the imaging plane sagittal, and maintaining contact with the subject's skin. Scanning starts at the left L1 transverse process, moving across to the right L1 transverse process. It then moves down to display the right L2 transverse process and across in the opposite direction, and continues in this zigzag manner to acquire US images of the entire lumbar spine. An US volume is reconstructed using the PLUS toolkit, where the pixel size in each dimension is taken into account. Only the portion of the lumbar spine visible in pre-operative CT, is included in the final US volume.

2.2 Registration

Our proposed method involves intensity- and point-based registration of the bone surfaces to harness the advantages of each method. The general overview of the registration pipeline is illustrated in Fig. 1. In our workflow, pre-operatively, CT volumes are automatically segmented [17]; in addition, points between adjacent vertebrae are manually selected to constrain an intra-operative multi-body registration step. Intra-operatively, registration is performed without any manual intervention. The registration is initialized given the transformation of the center of geometry of the preprocessed CT volume (see below) to the center of geometry of the preprocessed US volume, and assuming that this centre represents similar structures in both image modalities. The method has the following major steps:

Global Intensity-Based Registration: The General Registration (BRAINS) module, within the open source software 3D Slicer (version 4.2), that employs a rigid BRAINSFit algorithm with default parameters, is used to automatically align preprocessed CT and preprocessed US [14] volumes. To enhance the CT bone surface, images are filtered in the frequency domain using local phase image processing [7]. Subsequently, a simple ray-casting is done in the posterior to anterior direction such that the first bone pixel encountered for each column is saved as bone and anything below that pixel is saved as background. The ray-casting helps to remove the bright intensity values that exist in CT, but do not exist in US, since US signals cannot propagate through the bone surface. A sagittal CT slice from one patient overlaid with the enhanced bone surface is seen in Fig. 2, left. The inverse Euclidean distance map is calculated on the enhanced bone surface CT image by computing the distance between each pixel and the nearest non-zero pixel of the image, in physical coordinates (mm). In this map, the intensity values at the bone surface are maximized, and as the distance increases from the CT bone surface, the intensity values decrease.

Local phase filtering of the US volume is performed to automatically enhance the US bone surface relative to the soft tissue. In this approach the US images are filtered with a Gradient Energy Tensor filter. The US local phase filtering differs from the CT phase filtering in that multiple edge features (step edge, line, corner, junction) have to be extracted due to the complex shape of the vertebrae's appearance in US. This method is intensity invariant; a detailed description of its implementation along with robustness studies to noise are available in [7]. The filter parameters are chosen empirically using a small subset of in vivo images to produce a good bone surface localization in the presence of speckle. The parameters are then held fixed all throughout registration. A sagittal US slice of a patient with enhanced bone surface overlaid is shown in Fig. 2, centre.

Global Point-Based Registration: We use the Coherent Point Drift (CPD)[15] to further adjust the result of registration in the previous step. CPD uses probability density estimation to find corresponding points between the CT and US and has a closed-form solution. Myronenko, *et al.* have performed a comparison of the performance of CPD with Iterative Closets Point (ICP) in the presence of outliers and noise, and have demonstrated the robustness of CPD [15]. For each vertebrae in CT data , the vertebrae are automatically labeled pre-operatively using [17]. We automatically extract a single pixel thick bone surface from phase filtered US images by modifying an algorithm originally presented in [16]. In the original algorithm, the US images are smoothed using Gaussian filtering; the bone surface pixels are then enhanced by a combination of two main bone features: high acoustic impedance and acoustic shadowing. Continuity and smoothness of the bone surface are established by minimizing a cost function using dynamic programming [16]. Our modification makes this approach applicable to clinical patient data. Instead of using the intensity values from the smoothed US image, intensity values from a phase filtered US image are used. This results in less noise in the segmented bone surfaces, critical for an accurate point-based registration (Fig. 2, right).

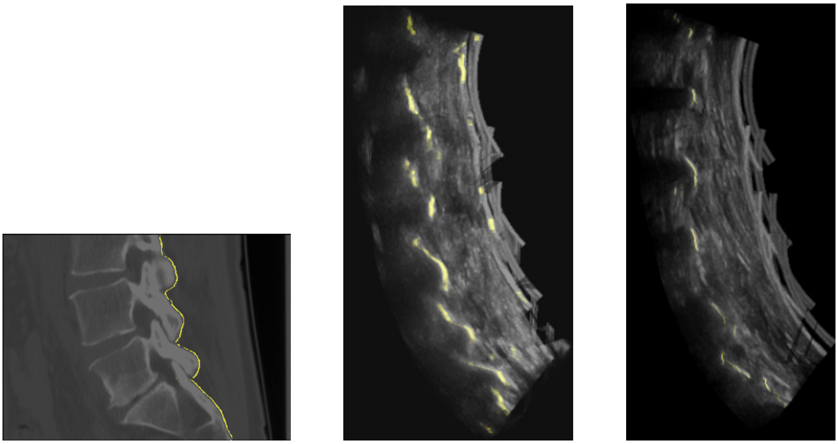

Fig. 2. (left) A sagittal CT slice with the phase filtered and raycasted bone surface overlaid in yellow; (centre) Sagittal US slices with the phase filtered and raycasted bone surface overlaid in yellow (centre) and with the single pixel bone surface (right)

Multi-vertebrae Point-Based Registration: Although vertebrae are rigid bodies, the intervertebral discs are deformable. To account for possible curvature changes of each vertebra along the lumbar spine, we present a novel multi-body rigid CPD registration. At every iteration of the algorithm, each vertebra is transformed individually. As a result, it is possible that they can be transformed into a pose of the lumbar spine that is not physically possible. To overcome this challenge, ten points are chosen pre-operatively on two adjacent vertebra in the CT. Five points on the sagittal slices on the left of the spinous process and five points on the right of the spinous process. Henceforward, these point sets are referred to as springs, since although they are not mechanical springs, they act to constrain the registration similarly to mechanical springs. The points are placed at the midpoint of either the space between the vertebral bodies or the space between the facet joint. Each point is then duplicated to act as a spring, where one point belongs to the superior vertebrae's side and the other point belongs to the inferior vertebrae's side. At each iteration, the springs points are transformed according to the vertebrae they belong to. An example sagittal slice where three points are chosen is shown in Fig. 3. The cost function for CPD, $E(t)$ (where t represents the transformation), has the form of a likelihood function of point correspondences between CT and US data, described as weighted sum of distances [15]. Myronenko *et al.* have provided a closed form solution to $E(t)$; for multi-vertebrae registration, we add a regularization term, $R(t)$ representing springs, to the cost function to achieve the form: $E(t) + \alpha * R(t)$. Here α determines the contribution of the springs. It can be shown that $\alpha * R(t)$ can be combined into $E(t)$, and the closed form solution can be used to minimize the new cost function. As such, in our registration algorithm, springs are integrated into the existing probability density estimations and the cost function is not

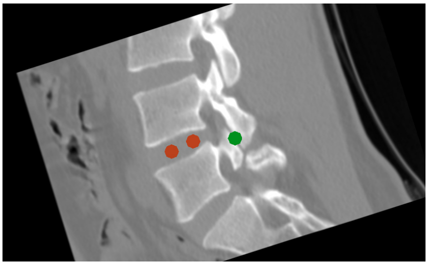

Fig. 3. Sagittal slice of a CT demonstrating three spring points between two vertebrae. Two are at midpoint between vertebral bodies (red) and one is in the facet joint (green).

modified from CPD. Values of α between 2^{-3} to 2^7 were tested; a value of 2^5 provided the most accurate registration for all clinical data sets and was chosen.

2.3 Experiments

Since the CT scans are previously acquired, fiducial markers that are visible in both CT and US cannot be used for gold standard evaluation. Instead, anatomical landmarks on the lamina of each vertebra are placed on the US images. Two clinicians with spine anatomy expertise choose these anatomical landmarks and we pool the data. We assume the CT and US to have optimal alignment following registration. To determine the accuracy and precision of the registration method, the CT and the points representing the lamina landmarks are perturbed by a transformation selected randomly from a uniform distribution of 5° rotation about each axis and 5 mm translation along each axis. The transformation is applied to the entire lumbar spine that is visible in the CT. The initial misalignment is determined by calculating the target registration error (TRE) between the original position of the lamina landmark points and the position of the landmarks after the initial perturbation. To determine the capture range for the registration pipeline, 20 tests are performed with misalignment errors randomly generated within the range 0 - 25 mm. Registration is then performed and the final TRE is calculated as the root mean square between the transformed lamina landmark points and their original positions. A qualitative clinical validation is also performed. Here, a point is added on the posterior dura between two adjacent vertebra in the US images by both operators. This is where the clinician aims their needle for spinal anaesthesia and thus provides a clinically relevant validation. If the points selected are in the correct region after registering the CT to the US, the registration is potentially suitable for spinal injection.

3 Results and Discussion

For three patient data sets L3, L4 and L5 vertebrae were available in the CT volume for registration, while for the other two patients only L4 and L5 vertebrae were available and used for registration. The mean TRE, maximum point

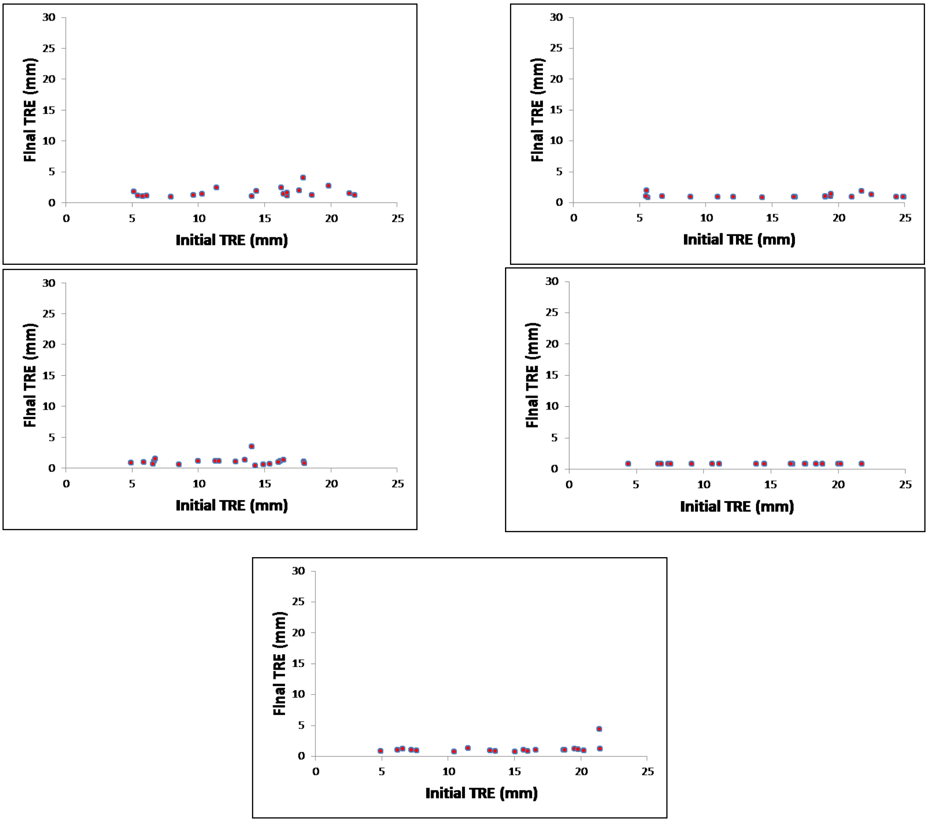

Fig. 4. Final mean TRE (mm) versus initial TRE (mm) for all vertebrae following random misalignment and CT to US registration. The subplots from top left to bottom right correspond to results from patients 1 to 5, respectively.

distance and total success rate for each patient, following the capture range experiments, is depicted in Table 1. The space within a facet joint is reported to be between 2 to 4 mm; previous literature also define 2 to 4 mm as a clinically acceptable accuracy for spinal injections [12]. In our manuscript, we set a more stringent criteria by defining registration success as achieving a mean TRE of 2 mm or less. This provides a conservative estimate for clinical acceptability of our proposed approach. Based on this definition and using Table 1, our average success rate is 97%. The final TRE after each run of the capture range experiment given the initial misalignment TRE for all patients is shown in Fig. 4. All reported values are the average TRE for each individual vertebra. The mean TRE is the average of the TRE values from the 20 runs of the capture experiments. From Table 1, it is evident that the mean TRE is well below 2 mm.

Registration was performed on a Lenovo ThinkCenter, with Intel i5-3570 quad-core CPU and 16 GB of RAM. The runtime for each of the main

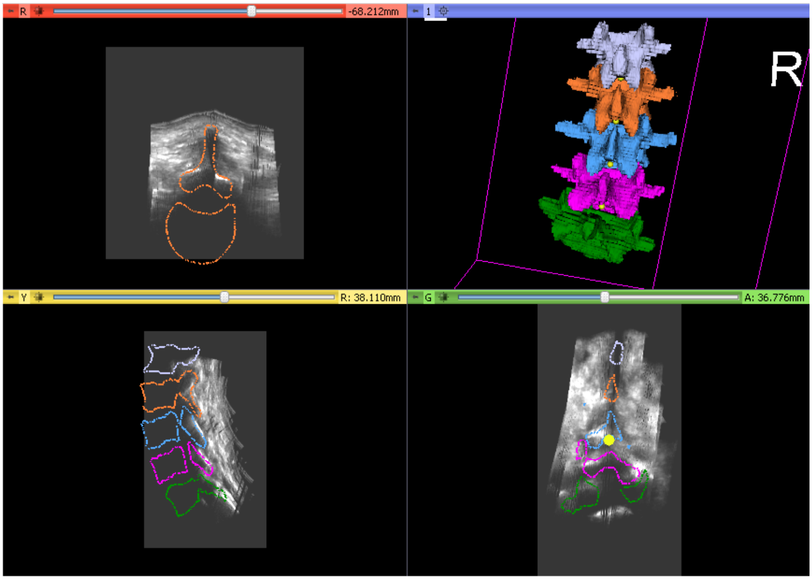

Fig. 5. 3D rendering of CT vertebrae with points on the posterior dura between two vertebrae in yellow (top right); transverse (top left), coronal (bottom right), and sagittal (bottom left) planes showing US slices with CT contours overlaid for one patient

Table 1. Mean TRE (mm), maximum point distance (mm) and total success rate from the CT to US registration for the five patients using the full registration pipeline

dataset	mean TRE ± std (mm)	max point distance (mm)	success rate
Patient 1	1.66 ± 0.77	4.61	16/20
Patient 2	1.09 ± 0.32	3.51	20/20
Patient 3	1.07 ± 0.64	3.76	19/20
Patient 4	0.85 ± 0.01	0.90	20/20
Patient 5	1.18 ± 0.77	4.64	19/20

registration components of the pipeline are as follows: intensity-based (step 1), 5–20 sec, point-based (step 2), 25–45 sec, and Multi-vertebrae (step 3), 20–120 sec.

To provide qualitative validation on successful registration runs, contours of the CT are overlaid on the sagittal, transverse and coronal planes of the US (an example illustrated in Fig. 5). A 3D rendering of the CT with a point on the posterior dura between each two adjacent vertebrae represents the target area for spinal injections. This is placed by our two operators, and provides a clinically relevant result to support quantitative validation. For all patients, the CT contours align in all three planes and the points on the posterior dura are all within the target area for spinal anesthesia (also seen in Fig. 5).

In preliminary analysis we evaluated the significance of the three major registration components. It was observed that both global intensity- and point-based registration steps are necessary for a robust registration especially in cases where there is limited US bone visibility in the data, or one approach does not provide a close initial alignment between the CT and US. We also studied the role of springs to constrain the multi-vertebrae point-based registration. As vertebrae are the rigid bodies transformed individually, registration can result in a pose of the lumbar spine that is not physically possible. This includes having two vertebrae intersect each other (collision). Indeed, our results show that, without the springs, registration of CT and US images resulted in collision in some patients. Capture range experiments when no springs are included to constrain registration, are performed. To determine if there is a significant difference in the TRE using the complete registration pipeline versus one without springs, we use the Wilcoxon Signed-Rank Test, where $p < 0.01$ is considered significant. TRE from all but one patient were statistically significantly worse without using springs.

4 Conclusion and Future Work

We presented a clinical feasibility study involving a novel registration pipeline for the lumbar spine that accurately aligns pre-operative CT to intra-operative US using five clinical data sets. By aligning the CT with the US, anatomical information that is not visible in US is provided to the clinician to guide spine needle interventions. This removes exposure of the physician or patient to radiation intra-operatively. To the best of our knowledge, this is the first work where multiple vertebrae are registered between CT and US using clinical data.

The proposed registration pipeline shows great promise for guiding percutaneous spine procedures, but further improvements are needed for its clinical use. The artificial springs are chosen manually pre-operatively; however, improvements can be made to automate the artificial spring selection for more practical use in the clinic. In addition, the spring parameter α value is set to a constant for all spring points, but could be adaptively adjusted based on the position of the springs on the vertebrae and their anatomical interpretation. Since the CPD registration of individual vertebrae can be parallelized, we can potentially use multi-CPU implementation with the Intel Math Kernel library to gain speed ups of several orders of magnitude. Finally, the registration pipeline includes multiple modules. For clinical applications, it is possible that a simpler pipeline could be selected with only a subsection of these modules, and further steps are only included when registration accuracy does not meet preset thresholds.

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