A multi-modal brain image registration framework for US-guided neuronavigation systems. Integrating MR and US for minimally invasive neuroimaging.

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Integrating MR and US for minimally invasive neuroimaging

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Keywords: Neuroimaging, US-based Neuronavigation, Multi-modal Image Registration, Image Processing, MR-US Image Integration.

Abstract: US-guided neuronavigation exploits the simplicity of use and minimal invasiveness of Ultrasound (US) imaging and the high tissue resolution and signal-to-noise ratio of Magnetic Resonance Imaging (MRI) to guide brain surgeries. More specifically, the intra-operative 3D US images are combined with pre-operative MR images to accurately localise the course of instruments in the operative field with minimal invasiveness. Multi-modal image registration of 3D US and MR images is an essential part of such system. In this paper, we present a complete software framework that enables the registration US and MR brain scans based on a multi resolution deformable transform, tackling elastic deformations (i.e. brain shifts) possibly occurring during the surgical procedure. The framework supports also simpler and faster registration techniques, based on rigid or affine transforms, and enables the interactive visualisation and rendering of the overlaid US and MRI volumes. The registration was experimentally validated on a public dataset of realistic brain phantom images, at different levels of artificially induced deformations.

1 INTRODUCTION

Neuronavigation consists in a comprehensive set of computer-assisted and neuroimaging technologies that help the neurosurgeons "navigating" within the skull to guide complex surgical interventions, such as brain biopsies or brain tumor resections.

Among the brain imaging modalities, Magnetic Resonance Imaging (MRI) provides the best discrimination between soft tissues inside the brain, and it is able to image tumors' borders with a good level of detail. Furthermore, differently from Computer Tomography (CT), it does not expose the tissues to dangerous ionising radiations, hence it is minimally invasive for the patient. This makes it the preferred imaging modality for planning brain surgical procedures.

On the other hand, planning a brain surgery based on pre-operative MR scans, which might have been acquired few days or even weeks before the surgery, raises many issues, especially in the practice of neurosurgical oncology. For example, in case of rapidly evolving neoplasms, the navigation might be extremely error prone because of the changing geometry and size of the lesion.

As a solution to this issue, modern neuronavigation systems integrate the information coming from pre-operative MRI with intra-operative MRI scans, possibly acquired several times after critical stages of the surgical procedure. Besides avoiding macroscopic errors due to the evolution of the lesion after the first set of scans, this setting allows to address brain shifts naturally occurring during the surgery. Brain shifts might alter the original position of critical cerebral structures, and include elastic deformations due to craniotomy, tissue resections, cyst decompressions, removal of cerebrospinal fluids or even haemorrhage or use of diuretics. Leveraging on the real-time anatomical information provided by intra-operative MRI, the surgical plan can be altered to account for such shifts.

In spite of its many advantages, using intra-operative MRI has also a number of critical logistic drawbacks. In fact, it requires specialised operating suites, costly and bulky instrumentations, as well as longer anaesthesia and operating room time.

To overcome these drawbacks, in the last few years ultrasound (US)-based techniques are becoming more and more attractive as a possible replacement of intra-operative MRI for neuronavigation purposes (C. Nikas et al., 2003).

Indeed, US-based neuronavigation has major advantages compared to traditional MRI-based systems. These advantages include its relatively low cost, simplicity of use and minimal invasiveness, both in terms of volume and complexity of equipment and of impact on the patient. On the other hand, US images

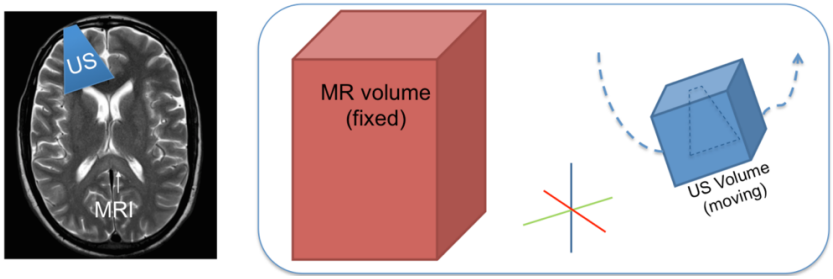

Figure 1: Scheme of principle of US-guided neurosurgery. A moving set of US volumes acquired during the surgical procedure are combined with a fixed set of pre-operative MR scans.

have well-known limitations, such as low signal-to-noise ratio and penetration depth. Moreover, they have much lower soft tissue discrimination capabilities compared to MR technology.

Hence, the latest trend in neuronavigation is the use of hybrid surgical planning techniques, integrating pre-operative MRI scans with intra-operative US. In this case, the procedure is guided by a fixed set of pre-operative MRI scans and a moving set of US volumes acquired during the surgery (see the scheme of Figure 1). The pre-operative MR scans are used to construct a structural model of the patient's head, and provide a detailed anatomical 3D map of the brain and of the targeted lesions. The position of the US probe with respect to the patient's coordinate system is obtained real-time using a probe tracking system. Then, the pre-operative MR scans are registered and overlaid on the US images acquired in the Operating Room, updating the structural model of the brain's patient based on the new anatomical information provided by US.

In such US-guided hybrid system, the accurate automated registration of MR and US scans plays a fundamental role. Nonetheless, while multi-modal brain image registration has a very consolidated tradition in other imaging technologies such as MR and CT (Sarkar et al., 2005), the registration of US and MR images is still a research topic in development, with a number of challenges that need to be tackled:

(i) low signal-to-noise conditions typical of US imaging. (ii) absence of highly contrasted anatomical structures (e.g. bones, high-density tissues) driving the registration algorithm. (iii) possible non-linear brain shifts induced by the surgical procedure.

Most of the currently available solutions do not explicitly deal with non-rigid brain shifts (Coupé et al., 2012), or are user-dependent, in that they rely either on the interactive delineation of markers or surfaces (Lunn et al., 2001; Liu et al., 2014), which is not feasible in the context of real-time neuronavigation. In this paper, we present an automated framework tackling these issues. It takes as input MR and US scans and probe positioning information, as provided by a tracking system, and allows a fully-automated registration and overlay of the two volumes, without requiring any interaction from the user.

Our methodology is based on a non-rigid registration algorithm, in order to tackle possible non-linear deformations, with a self-adjusting parameters search. Nonetheless, the tool supports also other simpler registration techniques, which can be selected when to tackle stages of the procedure not implying elastic warping between US and MR scans.

The registration accuracy is experimentally validated using a publicly available set of MR and US scans from an anatomically realistic human brain phantom, even in presence of extensive elastic deformations.

The rest of the paper is organised as follows. In Section 2, we describe the main modules of the proposed framework. In Section 3, we discuss the multi-modal image registration technique. In Section 4, we provide few implementation details. In Section 5, we present and discuss the experimental results. In Section 6 we conclude the paper.

2 SOFTWARE FRAMEWORK

The software was implemented in python and C++, making use of ITK and VTK libraries (Yoo et al., 2002; Schroeder et al., 2003). In the following, we briefly describe the main modules, as shown in Figure 2.

2.1 Volumes acquisition

Through this module, the software receives as input:
(i) the pre-operative 3D MRI scans of the patient.
(ii) the intra-operative US scans (reconstructed volumes).

The two volumes are in their own reference space and Field of View (FOV). Hence, the 2D slices composing the two different input volumes do not match.

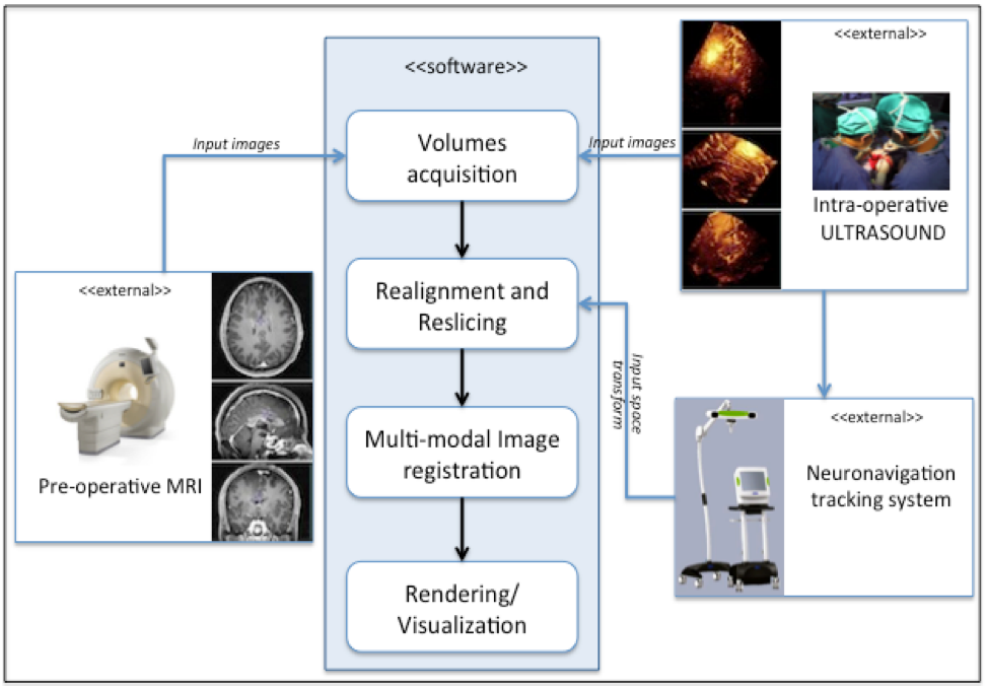

Figure 2: Diagram of software architecture, with main modules.

The module supports either DICOM, NIfTI or vtk image formats.

2.2 Realignment and Reslicing

Through this module, the coordinate spaces of the pre-operative MR images and the intra-operative US volumes remapped to a common patient's reference space and FOV and resliced for voxels' coherency. This way, the 2D orthogonal slices of the two image volumes are coherently reconstructed for both image modalities.

To match the reference systems of US and MRI, the software communicates with an external optical motion tracking system, that is able to record the position and orientation of the US probe during image acquisition. The tracking system processes this information and provides a transformation matrix to our software, in the form of a $4X4$ matrix T:

$$x' = T \cdot x \tag{1}$$

which in matricial form is:

$$\begin{bmatrix} x'_1 \\ x'_2 \\ x'_3 \\ 1 \end{bmatrix} = \begin{bmatrix} q_{1,1} & q_{1,2} & q_{1,3} & q_{1,4} \\ q_{2,1} & q_{2,2} & q_{2,3} & q_{2,4} \\ q_{3,1} & q_{3,2} & q_{3,3} & q_{3,4} \\ 0 & 0 & 0 & 1 \end{bmatrix} \cdot \begin{bmatrix} x_1 \\ x_2 \\ x_3 \\ 1 \end{bmatrix} \tag{2}$$

2.3 Multi-modal Image Registration

Through this module, the two realigned volumes are co-registered.

More in detail, the MR volume containing the pre-operative structural information of the patient's brain is deformed in order to match the intra-operative US scans. Hence, brain shift deformations occurring during the surgery can be compensated.

As mentioned in Section 1, this molule supports three different registration methods, which will be described in more details later.

These methods are:

(i) Multi-resolution rigid transform. Simplest solution consisting in rotation and translation, which ensures best computational time.

(ii) Multi-resolution affine transform. Consisting in rotation, translation, scaling and shearing, which was found to be the best option when elastic deformations are negligible (e.g. at stages not requiring brain resections).

(iii) Multi-resolution non-rigid transform. Consisting in a non-linear deformable transform, where local deformations at the voxel-level, including local warping, are defined by a Free Form Deformation (FFD) model as a mesh of control points. This approach was found to be the best for the correction of extensive elastic brain-shift deformations.

2.4 Rendering/Visualization

Through this module, the realigned and co-registered volumes can be visualised and overlaid. Two different options of visualisation are supported:

(i) Volume rendering, with clipping box. When this option is selected, the overlaid MR and US images are visualised using 3D volume rendering based on a ray casting and 3D texture mapping technique. Two different sets of colours are applied to render the two imaging modalities. The user can interactively rotate the volumes to obtain a better view of the anatomical details in each modality. The visualisation supports cropping, clipping and blending modes. Thanks to these features, the user can clip away the volume at any point, allowing a better view of the internal structures.

(ii) Interactive 3D slider. When this option is selected, the user can interactively switch from volume rendering to a 2D visualisation of single slices. The user can navigate along either coronal, sagittal or transverse directions using a sliding bar or simply scrolling the mouse, select a plane of interest on the rendered volume and then visualise the 2D image (either MR, US, or a superposition of the two) obtained cutting the volume through the selected plane.

3 REGISTRATION TECHNIQUE

The US-MR registration technique is implemented as an iterative optimisation problem, where the search for the optimal transform matching US and MR volumes is driven by the maximisation of a fitness value quantifying the similarity between the two input images. This can be schematically represented by the components reported in Figure 3.

3.1 Similarity metric

Of the large number of image registration similarity measures that have been proposed over the years (among the most relevant: cross-correlation, sum of squared intensity differences, ratio image uniformity, etc.), Mutual Information (MI) is widely acknowledged as the best choice for the registration of multi-modality images. Indeed, this metric is best suited to measure the matching degree of images having different characteristics in terms of range of image intensities, because it does not assume a linear relationship among the two sets of intensity values. On top of that, MI is an automatic intensity-based metric that does not require the preventive segmentation of anatomical parts, surfaces or landmarks on the images, nor the definition of specific features to drive the registration process.

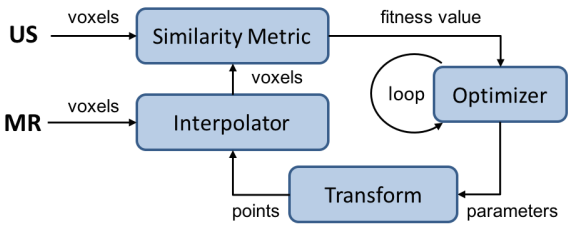

Figure 3: Diagram of the multi-modal registration module.

MI applies the joint probability distribution of pixels from the two images to measure the certainty that the values of the first image pixels map to similar values in the other image, which is a reliable quantitative measure of how similar the images are. Higher values of MI imply a large reduction in the uncertainty (i.e. entropy) between the two distributions of pixels' values, which is a clear indication that the two images are better aligned.

More specifically, if U and V are the two image volumes, their Mutual Information is defined as:

$$MI = H(U) + H(V) - H(U,V), \tag{3}$$

where $H(U)$ and $H(V)$ are the individual marginal entropies of U and V, respectively, and $H(U,V)$ is the joint entropy.

On the other hand, the individual and joint entropies are defined as:

$$H(U) = -\sum_i P_U(u_i) \cdot logP_U(u_i), \tag{4}$$

$$H(V) = -\sum_j P_V(v_j) \cdot logP_V(v_j), \tag{5}$$

$$H(U,V) = -\sum_{i,j} P_{UV}(u_i,v_j) \cdot logP_{UV}(u_i,v_j), \tag{6}$$

where P is the marginal probability density distribution of the intensities in the image, estimated based on the method by (Mattes et al., 2001) using Parzen histograms (Xu et al., 2008).

3.2 Optimizer

In order to reduce computational cost of the algorithm, the optimization problem is implemented as multi-resolution strategy, schematically represented in Figure 4. The rationale of this approach is the following:

- First, the optimal transform parameters are searched applying at a rough scale in terms of image resolution (i.e. the input images are resampled so that only a fraction of the available voxels are used for the optimization)

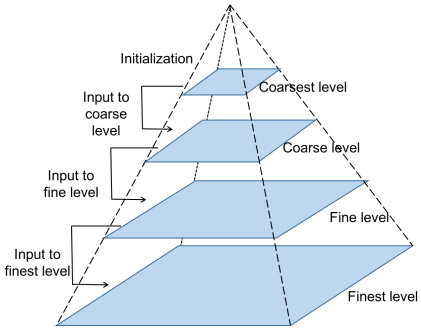

Figure 4: Scheme of the multi-resolution optimization approach.

- The transform determined at the starting level is used to initialize image registration at the next stage, at a finer scale (i.e. a higher number of voxels is used for the optimization).

- This process is repeated until the finest scale possible (full image resolution) is reached.

3.3 Transform

As brain shifts might easily imply elastic deformations of the brain, the proposed method is a **non-rigid registration** technique, that leverages on a deformable transform of points from one N-dimensional space to another N-dimensional space. This deformation is defined at the voxel-level in terms of a Free Form Deformation (FFD) model, where a set of deformation vectors $\vec{g}$ is applied to a sparse regular grid of control points, one deformation vector per control point (see Figure 5).

As mentioned in Section 2, in order to provide the user with less computationally intensive solutions in stages of the procedure not involving elastic brain deformations, the framework supports also the use of affine transforms (applying a linear combination of translation, rotation, scaling and shearing, i.e. non-uniform scaling in some directions), or of even simpler rigid transforms (applying only translation and rotation). In this case, the transforms can be expressed geometrically in terms of transform matrices, as in Equation 1.

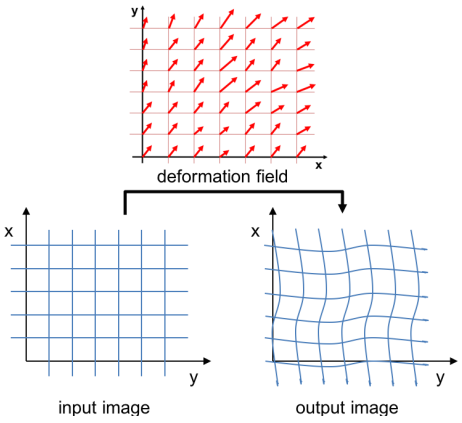

Figure 5: Non-rigid registration.

3.4 Interpolator

The interpolator is applied to compute the voxel-wise intensities of the transformed image at non-grid positions. The interpolation method affects the smoothness of the optimisation search space as well as the overall computation time. As a compromise between accuracy and computational costs, our system implements B-spline interpolation for non-rigid transform and linear interpolation for either rigid body or affine transform models.

4 ALGORITHM SET-UP

Summarising, the registration algorithm works towards the maximisation of MI similarity between US and MR scans. This metric is embedded into an objective function and optimized numerically. As reported in Equation 3, this requires an estimation of the probability density functions (PDFs) associated with the US and MR images, as well as their joint intensities. Such PDFs are not known a priori, hence they have to be estimated from intensity samples, treated as independent and identically distributed random measures. In our implementation, a set of intensity samples is randomly selected on the input image. Then, the PDF is estimated at discrete bins uniformly spread within the dynamic range. Entropy values are then computed by summing over such bins. Hence, an accurate choice of the number of bins is crucial for registration accuracy.

Besides sample bins, the main parameters that need a careful set-up are the number of samples used for the calculation (the higher this number, the higher the significance of the estimation), as well as the size of the mesh associated with the deformation field (the higher the size, the higher the variety of deformations that can be modelled by the system).

As all these parameters can dramatically impact on the computational time, the set-up needs to find a reasonable trade-off between number of iterations of the optimisation problem and registration accuracy. In our system, this trade-off can be automatically adjusted based on a training pair of US and MR scans. A simple heuristic algorithm is implemented, that starts

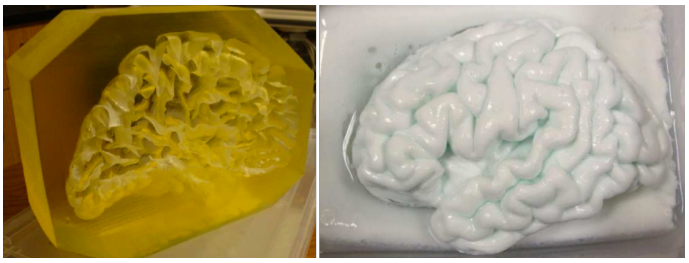

Figure 6: PVA brain phantom (`http://pvabrain.inria.fr/`.)

with a very coarse grid of parameters. Then, increasingly finer search grids are applied around the optimal parameters determined at each stage of the heuristics.

5 EXPERIMENTAL RESULTS

To experimentally validate our framework, we used the *PVA Brain 3D image dataset*, a publicly available dataset of multi-modal images acquired from a human brain phantom (Chen et al., 2010). The phantom, made of polyvinyl alcohol cryogel (PVA-C), was obtained using a shape mold 3D printed from ex-vivo human brain MR images, hence it is anatomically very accurate and realistic (see Figure 6). The phantom contains two inflatable catheters, allowing to artificially induce brain shift deformations of a priori known entity. The dataset contains corresponding MR and US scans at different stages of deformation. Per each stage, the dataset contains also the transformation matrices provided by an external neuronavigation probe tracking system, which can be used to remap US and MR scans into a common reference system, obtaining an initial rough alignment. Hence, the dataset can be used to test image registration and brain shift compensation techniques.

In order to obtain an objective measure of registration accuracy, we implemented the following validation procedure:

(i) With the help of a skilled neurologist, we interactively extracted a set of nine anatomical landmarks (i.e. points of interest) on the MR volume (see Figure 7).

(ii) We extracted the corresponding anatomical landmarks on the US volume.

(iii) We run our registration pipeline on the US and MR volumes.

We repeated steps (i) and (ii), independently, on the US and MR volumes obtained after registration. Then, we computed the Euclidean distance between homologous MR-US markers before and after registration. The same validation procedure was run on corresponding US and MR scans at three different deformation configurations, respectively with the two catheters inflated by 0 ml - 0 ml (i.e. absence of deformation), 0 ml - 5 ml and 5 ml - 10 ml.

The ideal target of a US-guided neurosurgical system is that MR and US volumes should be perfectly superimposed (see an example of US-MR overlay before and after registration in Figure 8), and that the homologous markers should coincide. Hence, we can establish a validation procedure based on the following:

- the Euclidean distance between homologous MR and US markers provides a measure of the initial spatial mismatch between the two sets of scans before registration (due to either imperfect probe tracking or to non-linear brain shift deformations occurring during the surgery).

- The same distance computed after registration provides a measure of the residual spatial mismatch (where some small mismatch, reasonably in the order of a mm, is possibly due to manual selection of the markers).

- The comparison of distances computed before and after registration provides a measure of registration quality, in terms of compensation of spatial mismatch between US and MR scans.

The obtained results are reported in the boxplots of Figure 9, respectively for registration based on rigid transform, affine transform and non-rigid deformable transform.

As it can be easily gathered from the boxplots, even after the initial realignment based on US probe tracking the US and MR scans have a consistent spatial mismatch (up-to 8 mm). This mismatch is hardly

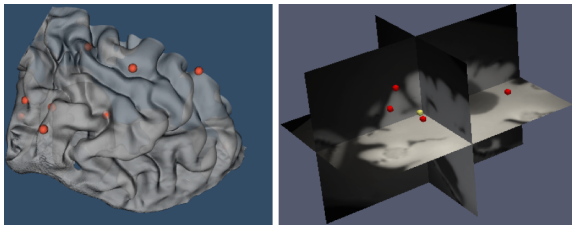

Figure 7: Anatomical landmarks on the PVA brain phantom images.

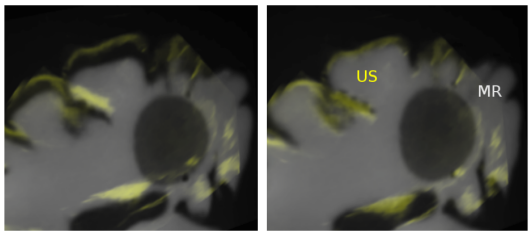

Figure 8: Example of registration outcome on PVA brain images. Overlay of MR and US scans before (left) and after (right) registration.

corrected by a simple rigid-body registration, because it is mainly due to elastic deformations induced by the inflatable catheters.

Indeed, the most successful results are obtained by the non-rigid registration option (see third graph of Figure 9). This technique allows to obtain the best values in terms of residual distance between the homologous landmarks, of about 2.5 mm on average. On top of that, the obtained registration accuracy is reasonably stable at different stages of deformation. This confirms that a deformable transform is the preferable registration strategy.

As an additional analysis, we performed a paired-sample t-test on the obtained results, which revealed a significant difference between landmarks distance before and after the registration process (p = 7.091e-14). This confirms the qualitative observations drawn on the basis of Figure 9.

6 CONCLUSIONS

In this paper, we presented a software framework based on ITK and VTK that allows the automated registration and overlay of US and MR brain images, in the context of US-based neuronavigation.

The framework is a modular system that takes as input the pre-operative MR image and the intra-operative US image as well as the positioning information provided by an external probe tracking system, and provides as output the two volumes remapped in a common reference system and registered. Experimental results on a publicly available dataset of US and MR images of an anatomically realistic brain phantom demonstrate that the software is able to compensate non-linear deformations of the same order of surgical brain shifts with a good level of accuracy.

As future work, we plan to integrate our software with a custom US probe tracking system, in order to provide a complete US-based neuronavigation framework.

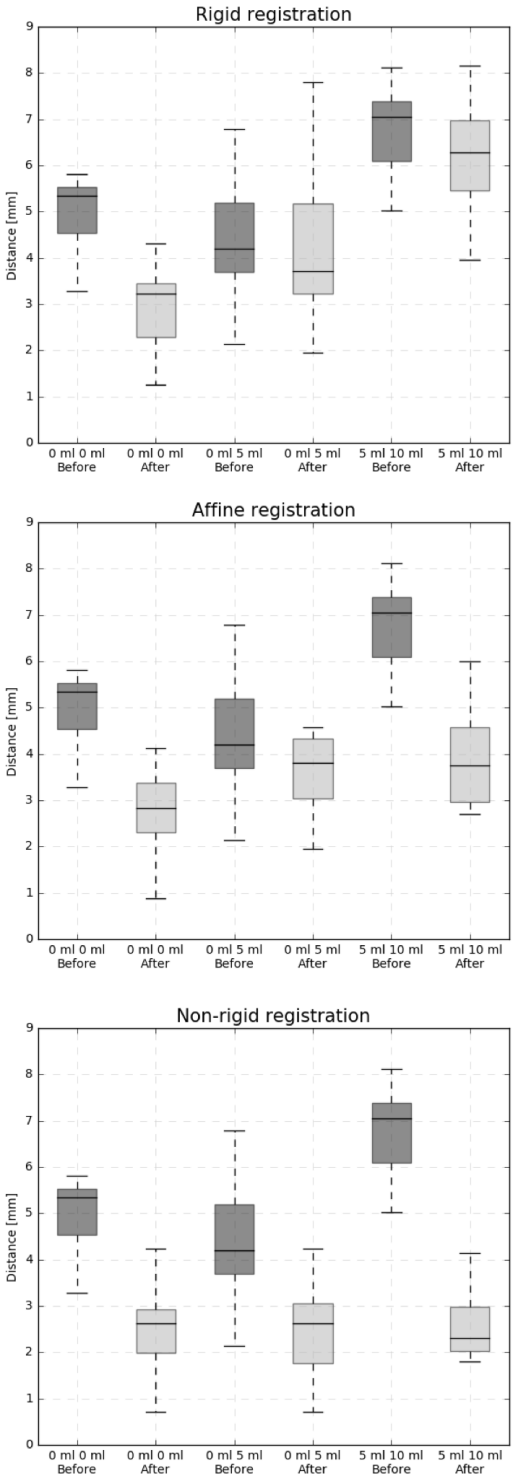

Figure 9: Distances of homologous landmarks in US and MR scans, before and after registration, for three different deformation stages (respectively, with the two catheters inflated by 0 ml - 0 ml, 0 ml - 5 ml, 5 ml - 10 ml).

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