A Neuronavigation Toolkit for 3D Visualization, Spatial Registration and Segmentation of Brain Vessels from MR Angiography Images

Nguyen Thanh Duc and Boreom Lee

Abstract Neuronavigations are real-time approaches implemented to help neurosurgeons precisely localize different intracerebral pathologies by using multiple neuroimaging modalities. However, current systems suffer from several shortcomings including time-consuming, 3D registration and segmentation accuracies as well as difficulties transferring 3D vessel imaging to the neuronavigation systems. In this work, we introduce a standalone platform for image-fusion, and semantic segmentation of MR angiography images supported for neurovascular interventions. The full-stack toolkit consists of two parts: back-end and front-end. At back-end, Tensorflow library and Ajax for application programming interface server request-response interactions are embedded. As to front-end, we implement C++_based Qt platform for GUI (Graphic User Interface) in Visual Studio integrated development environment. The toolkit provides 3D volume and slice-based visualizations of brain multimodal images. All medical images are archived in DICOM standard, then converted into NIfTI formats. Visualization Toolkit was used to render 3D MR images. The implemented volume-rendering techniques allow the direct visualization of vascular structures, thus reveal vessel abnormalities more faithfully. We provide GUI interface of the modality brain image registration and segmentation functionality. There are two machine-learning based automatic registration categories: (1) intensity-based, (2) geometry-based. The registration error in mm is computed by using Hausdorff Distance metric. As for cerebrovascular segmentation, a method that utilizes an enhanced vesselness filter which bases on multiscale Hessian eigenvalues is performed to extract neurovascular trees. The introduced toolkit is expected to be a validated platform that allows researchers to apply insightful results into the operating room for clinical evaluations.

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1 Introduction

Neuronavigation systems, or image-guided neurosurgery tools, have become a standard practice and are used to allow preoperative phase of surgical trajectories to aid surgical procedures. Neuronavigation systems also allow objective real-time acquired neuroimaging in three-dimensional (3D) volumes, thus significantly reducing uncertainties throughout the surgical operation [1]. It is widely reported that the navigation systems help to guarantee the safeness of the surgery, reduce risks and provides tools for the inexperienced surgeons to self-practice and gain experiences. Several typical commercial neuronavigations including SonoWand system, Medtronic, and Brain Lab, have normally been manipulated in the surgery operations for multiple neuro-interventional purposes [2]. However, such neuronavigation systems experience several drawbacks regarding to visualization functions, registration, and segmentation accuracy. Furthermore, the recent developments in image-guided neurosurgery have moderately impact on the cerebrovascular surgery due to practical challenges moving 3D vessel volumes to the systems [3].

Advanced developments of 3D Computed Tomography Angiography (CTA) and Time-of-Flight (TOF) Magnetic Resonant Angiography (MRA) images have open the way for visualization and curing cerebral vascular diseases i.e., aneurysm, arteriovenous malformation (AVM), and brain tumor surgery [4]. Bringing the 3D MRA to image-guided neuronavigation to the real-time neurosurgical operation is a current state-of-the-art evolution to offer the surgeons to robustly localize brain vessels [5]. Particularly, it is crucial to determine correctly 3D interactions of an aneurysm with nearly vasculatures and penetrating arteries during the surgery of aneurysm, or correct drainage features of an arteriovenous malformation, or precise associations of a brain tumor with closed brain vessels and degree of vascular invasion [3].

There are several critical limitations of the current neuronavigation systems assisted for cerebrovascular interventions [6]. The most critical limitation is the low accuracy when segmenting small brain vessels using angiographic neuroimaging. Second limitation relates to the registration procedure that is still time-consuming especially when registering the rotated 3D angiographic images to the within-subject anatomical MRI. Giving the gaps in the exist literature, in this paper we introduce a preliminary version of our navigation toolkit that is specifically designed for neurovascular surgical interventions. Specifically, we describe several important techniques for visualization purposes of magnetic resonant angiography images, MRI-MRA image registrations of the same subjects as well as cerebral vascular structure segmentations, which are expected to be essential in the neurovascular interventions.

In the following sections, the core blocks, i.e., functionalities, architectures, methodologies, and interfaces of the proposed toolkit are presented. In section Materials and Methods, we first report various registration approaches implemented in our software and graphic user interface implementation for users to choose favored methods. Neuroimaging registration includes intensity-based methods that compare the intensity values of the assessed pixels, and geometry-based methods that use handcrafted feature descriptors. In addition, we describe a statistical method that employs an enhancement vesselness filter, which is based on the multiscale Hessian eigenvalues to extract cerebrovascular trees. In the Results section, we present the full-stack architecture of the toolkit. We also detail the Graphical User Interface (GUI) for 3D volume and slice-based visualization as well as volume-rendering of the vessels, spatial registration, and vascular-tree segmentation in which the users are able to select the preferred methods based on their prior-knowledge to perform the task. Finally, we discuss on the paper' limitations as well as several future works which should be done to improve the toolkit performance in order to move a step forward to the clinical application.

2 Materials and Methods

2.1 Neuroimaging Registration in Neuronavigation Systems

The registration of images is a growing research topic and forms an integral part in many medical image analysis tasks, and is a vital important task in neurosurgery interventions. Spatial registration refers to a process of finding corresponding structures within different images. Areas of clinical applications include alignments of datasets from multiple neuroimaging modalities, within-subject follow-up and baseline scans comparisons, pre-operative and post-operative within-subject examinations, therapeutic selections for radiotherapy, segmentation and parcellation based on template atlas, aligning training images for disease classification and clinical variable regression [7].

Various neuroimaging modalities are deployed in multiple phases of the neurosurgical interventions; for instance, several common types are CT brain images, T1- and T2-weighted anatomical MRI, metabolic screening using nuclear Positron Emission Tomography (PET), estimating the white matter structure using Diffusion Tensor Imaging (DTI), and angiographic images CTA, MRA for brain vessel diagnosis. Spatially aligning of multiple brain images of the same subject to a standard coordination is of importance to provide additional information of the patients and robust interpretations to the neurosurgeons throughout the interventions. Furthermore, spatial registration is needed for neuro-related clinical applications, for example, examining the clinical progression of a patient's health condition by using within-subject follow-up scans, and radiotherapy operations as well as image-guided neurosurgery [8].

2.2 Registration Methods

Medical image registration is a time-consuming process that spatial remodels coordinates of different medical images acquired from different acquisition sites into one standard coordinates while keeping the clinical contents unchanged. The primary task is basically to transform a so-called moving image, $\boldsymbol{I}_M(\boldsymbol{x})$, to make it aligned to the fixed image $\boldsymbol{I}_F(\boldsymbol{x})$. Specifically, registration procedure requires the finding of a transformed coordinate $\boldsymbol{T}(\boldsymbol{x})$ that allows $\boldsymbol{I}_M(\boldsymbol{x})$ spatially fit to $\boldsymbol{I}_F(\boldsymbol{x})$. The registration performance is assessed through a measure of match or cost function $\mathbb{C}(\boldsymbol{T}; \boldsymbol{I}_F(\boldsymbol{x}), \boldsymbol{I}_M(\boldsymbol{x}))$ that measures the differences or similarity between the transformed images and its reference. The transformation of coordinate can be predicted using an optimization method of the cost function based on $\boldsymbol{T}(\boldsymbol{x})$. The optimization algorithm is usually performed by iteratively updating the parameters of the transformation matrix such that the differences between these images are minimized.

There are multiple factors that should be borne in mind when selecting a precise registration method. For instance, these considered factors include models for coordinate transformation, optimization algorithms, multiresolution analyses, interpolation methods to evaluate $\boldsymbol{I}_M(\boldsymbol{T}(\boldsymbol{x}))$, and last but not least, a robust cost function. Regarding the coordinate transformation models, the degrees-of-freedom parameter, $\boldsymbol{T}(\boldsymbol{x})$, determine the deformations methods that can be used. There are several transformation models in the current literature covering from a very simple linear translation to more sophisticated linear rigid transforms and non-linear non-rigid or elastic models. Illustrations of various transformation models used for neuroimaging registrations are provided in Fig. 1.

The ordinary image registration approaches include intensity-based methods that compare the values of intensity at all pixels that represent the images, and geometry-based methods that use handcrafted image feature descriptors. In the existing literature, multiple cost functions $\mathbb{C}(\boldsymbol{T}; \boldsymbol{I}_F(\boldsymbol{x}), \boldsymbol{I}_M(\boldsymbol{x}))$ for intensity-based registration are commonly used including the mean squared difference (MSD, Equal. 1), or normalized correlation coefficience [5], and mutual information (MI). On the other hand, the regular geometrical descriptor for 3D brain volume registrations is a well-known

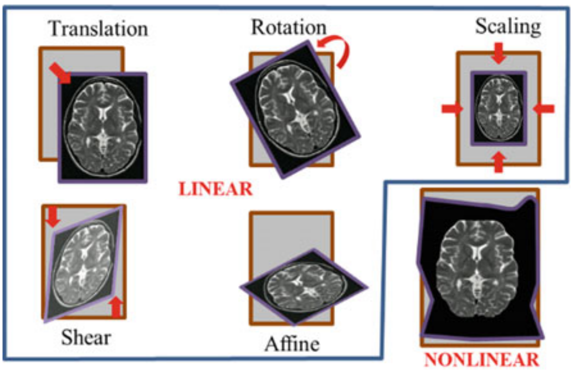

Fig. 1 Transformation methods for spatial neuroimaging registrations

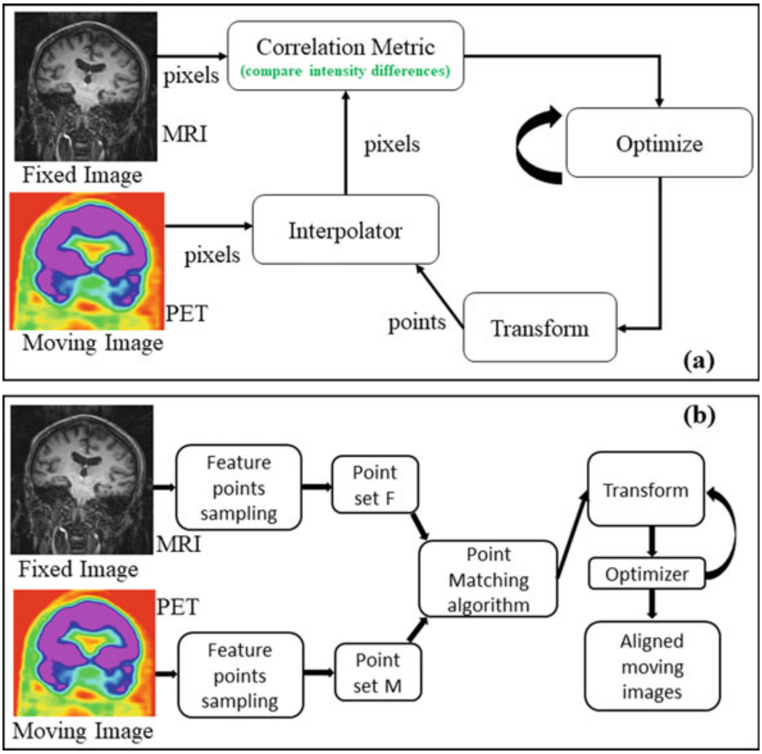

Fig. 2 Traditional neuroimaging (example of MRI and PET aligning) registration methods. **a** Intensity-based, **b** geometry-based pipelines

Iterative Closest Point (ICP) while Fast Point Feature Histogram (FPFH) is applied by several available researches. Figure 2a illustrates the intensity-based registrations while geometry-based neuroimaging registrations can be seen in Fig. 2b, respectively. Further details of iterative machine learning-based spatial registrations in neuroimaging applications can be seen in review papers.

$$\mathrm{MSD}(\boldsymbol{T}; \boldsymbol{I}_F(\boldsymbol{x}), \boldsymbol{I}_F(\boldsymbol{x})) = \frac{1}{N} \sum_{x \in \Omega_F} (\boldsymbol{I}_F(\boldsymbol{x}) - \boldsymbol{I}_M(\boldsymbol{T}(\boldsymbol{x})))^2 \tag{1}$$

2.3 *Cerebrovascular Structure Extractions*

Many traditional methods for cerebrovascular segmentation have been proposed: deformable models; statistical models; and recently developed deep neural networks (DNN). In deformable models, a classic method is a geodesic active contour that fits structural topologies of cerebrovascular appeared on MRA images. However, there are several critical limitations reported by using deformable models for brain vessel segmentation and one of them is leaking detection found around the edge of the vessels. During iteration process of the optimization, the leakage is wrongly detected in the nearly area which is right outside of brain vessels, which leads to poor performance. Statistical models perform cerebral vascular structure extraction by using statistical models such as Gaussian Mixture Models to fit the intensity distribution of multiple tissue types found the images. Particularly, Hidden Markov Random Field (HMRF) model integrated with Expectation–Maximization (EM) algorithm has been employed to separate brain White Matter with Gray Matter tissues and Cerebrospinal fluid in the anatomical MRI images. Their semantic segmentation performances are significantly contingent on the fitting between intensity histogram modelled in MRI and statistical models; therefore, the performances can be strongly limited by the intensity distortion in MRA data.

In this work, we apply a method, so-called vesselness filter proposed in [9, 10], to extract the vascular structure from MR angiography images. Vesselness filter employs multi-scale Hessian filter by implementing a newly enhanced function that overcomes the deficiencies of the currently well-developed ones and get properties close to a complete enhancement function. The proposed vesselness filter achieved the best evaluation scores compared to the existing methods in the literature and therefore it boosts a promising prospection and inspires the evolutions for better state-of-the-art approaches for separation and visualization of cerebral vasculature using MRA dataset. Further information and mathematic presentations of the method as well as proven assessment improvements of the vesselness filter over the current cutting-edge methods can be accessed in [9, 10].

2.4 Dataset

In this paper, we utilize a public available 3D time-of-flight angiography dataset of the TubeTK toolkit [11]. This dataset contains 100 (T1, MRA) image pairs acquired by a Siemens Allegra head-only 3 T MR system with voxel space of $0.53 \times 0.53 \times 0.83$ mm and 3D volume dimension of $448 \times 448 \times 128$ voxel for MRA images. The voxel spacing is 1 mm isotopic with a volume size of $176 \times 256 \times 176$ voxel for T1 images. The dataset has been collected with healthy subjects whom the ages are ranging from 18 to 74 years old, and without previous major cerebral vascular disease. This is the multimodality dataset in which our different neuroimaging scans are collected for each subjects, i.e., T1-weighted, T2-weighted MRI, MRA and DTI scans. However, for registration, we only utilize T1-weighted MRI and MRA in which the purpose is to align MRA image to corresponding MRI images of the same subject. For cerebrovascular segmentation, we utilize only MRA scans since MRA scans show the brain vascular structures.

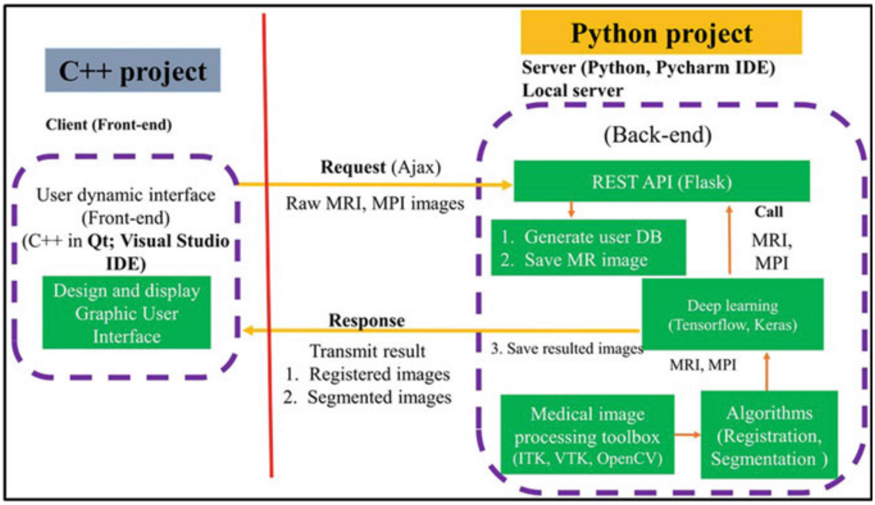

Fig. 3 An overview of the full-stack architecture of our toolkit. The toolkit consists of two parts: (i) Server-side (backend, right subfigure), and (ii) client-side (frontend, left subfigure)

3 Results

3.1 *A Toolkit Platform*

The objective of this sub-section is to implement a practical software for neuroimaging visualization and registration. The window form application consists of two parts: (i) Server-side (Backend), and (ii) Client-side (frontend). In case of the server-side, we used the Keras and Tensorflow for performing the deep neural network algorithms and Ajax for API server (Application programming Interface). All the registration methods including traditional machine-learning and deep convolutional neural network algorithms, which described in previous section, are implemented in this backend. In case of the client-side, we implemented C++_based Qt (https://www.qt.io/) platform for GUI (Graphic User Interface) in Visual Studio IDE (Integrated Development Environment) (https://visualstudio.microsoft.com/). Overall scheme for implementation of our software can be illustrated through Fig. 3.

3.2 *3D Neuroimaging Visualization and Volume Rendering*

Visualization of 3D medical images has a crucial role in the current development of the healthcare technology. Especially, 3D volume rendering techniques of neuroimaging provide various advantages and deep information needed in image-guided surgery, which offers neurosurgeons to see further the tissue level and brain

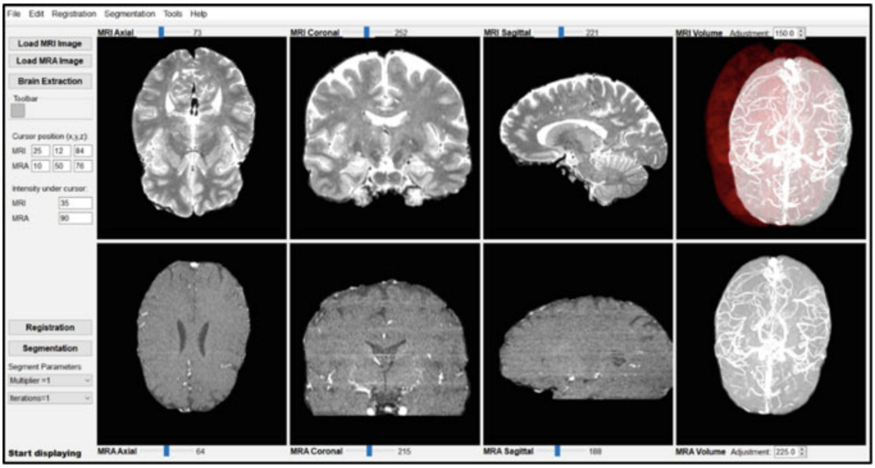

Fig. 4 3D volume-based and slice-based visualizations of multimodal brain images. The upper panel shows slice-based and 3D volume of MRI while the lower shows that of MRA images

vessels can be clearly seen by 3D visualization of multi-model MRI, MRA, CT and CTA, and Magnetic Particle Imaging (MPI) data. Visualizations of multimodal neuroimaging has significant role in brain surgical operation. In this study, we developed a software of 3D visualization of brain multimodal CTA, MRA and MRI images for optimal vascular neurosurgical planning. The input brain images are in DICOM format, then converted into NIfTI files. Visualization Toolkit (VTK) (https://vtk.org/) [12] is utilized to render MRA and MRI data. MRA images offer robust features of rigid structures and MRI provides better visualization of soft tissues. When volume rendering of MRA and MRI are performed, diverse information of the underlying features can be revealed respectively. Rendering implementation of 3D volumes unveils the straight view of the underlying contents which are hidden in the normal visualization, and help to disclose atypical vessels robustly.

In this software, we also implemented volume rendering functionality, which allows us to be able to divulge vascular structures. Figure 4 presents the GUI of the software, 3D MRI visualizations of brain images, and volume rendering with a focus on vessel visualization is depicted in Fig. 5.

3.3 Neuroimaging Registration Results

The Insight Segmentation and Registration Toolkit (ITK) which can be found at (https://itk.org/) [13, 14] is among the most common tools for researchers in the field of medical imaging analyses, and is already being implemented in various clinical applications. However, ITK is not designed for visualization and it does not have graphic user interface functionality for a dedicated development platform. Our

Fig. 5 Brain vascular tree visualization using volume-rendering technique implemented in our toolkit

software offers a visual programming interface with multiple necessary functionality of registration and visualization provide by VTK library. Figure 6 provides GUI interface of the modality brain image registration developed in our software package. There are three registration categories: (1) intensity-based, (2) geometry-based, and (3) landmark-based models. We compute and show the registration error in mm by using Hausdorff Distance metric. Figure 7a, b show the registration results, which have been performed by intensity-based and geometry-based registration algorithms, respectively. We are able to achieve a registration spatial error of 0.386 and 0.4266 mm by using intensity- and geometry-based algorithms, respectively. Figure 8 illustrates of the image differences before registration and after registration in which the robust alignments are achieved.

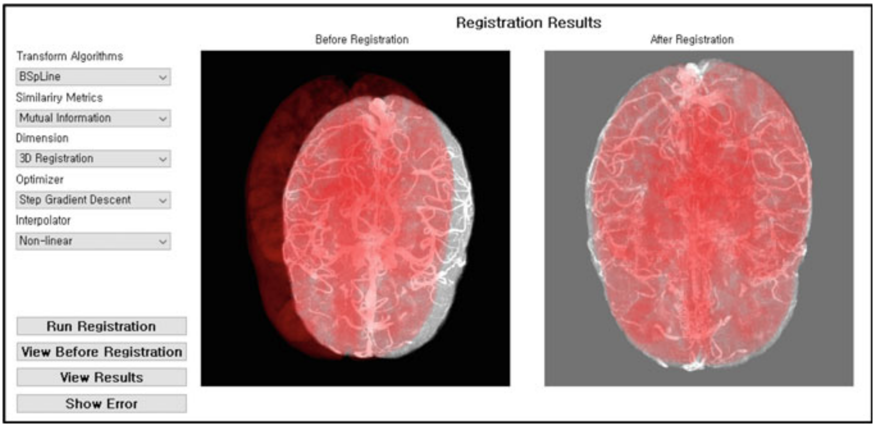

Fig. 6 GUI of 3D brain image registration implemented in our toolkit

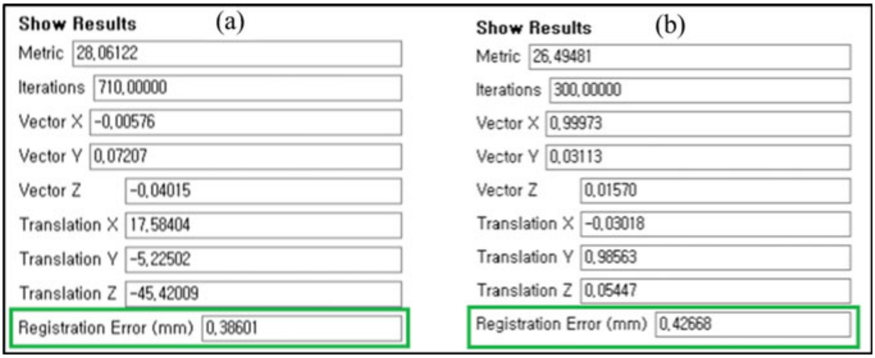

Fig. 7 3D registration errors using the intensity-based (**a**) and geometry-based (**b**) registrations

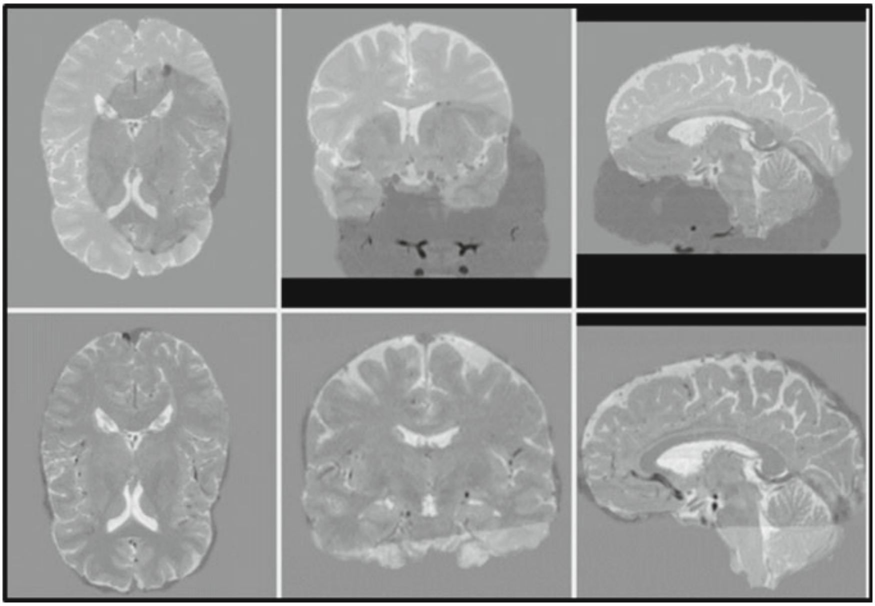

Fig. 8 Illustrative results of before (upper panel) and after (lower panel) registrations between in-subject MRI and MRA images

3.4 Cerebral Vascular Segmentation Results

Visualization and performance comparisons of the enhancement function for cerebral vascular trees using a 3D TOF-MRA data by applying the introduced vesselness filter, shown by maximum intensity projection (MIP) of the preprocessed image (left) and the MIP of the vesselness-based filtered image (right), is depicted in Fig. 9. As clearly seen in Fig. 9, the vesselness method results in high response values in all

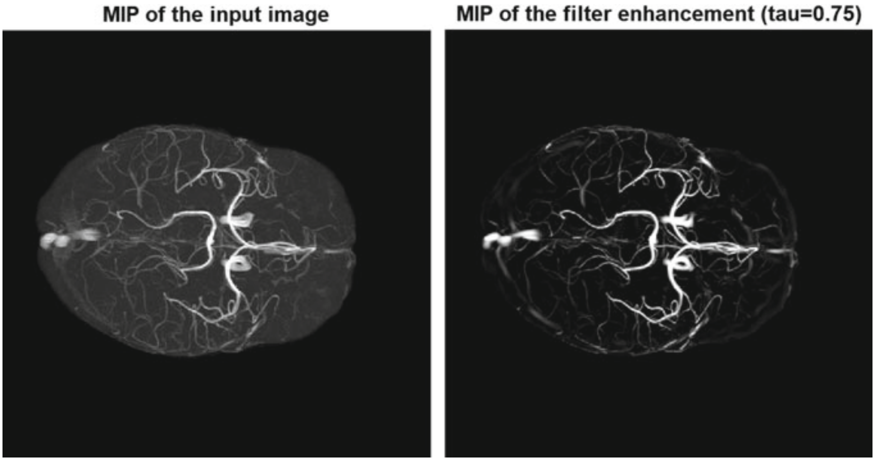

Fig. 9 Results of before (left) and after (right) segmentation using the vesselness filter

the cerebral vasculature including small and large vessels. Thus, the visualization of the segmented structures of the smallest brain vascular evidently proves with the effectiveness of the introduced method.

4 Discussion and Conclusion

In this work, we introduce a toolkit as an important feature that can be used to transform results of image-guided neurosurgery for neurovascular interventional research from the lab to the operation room. We have showed a full-stack toolkit, which includes several necessary components for implementation of an improved workflow for the image-guided neurovascular pathology. Our toolkit allows concurrent visualizations of 3D anatomical T1- and/or T2-weighted MRI images together with TOF MR Angiography image, which is spatially aligned to anatomical ones. Visualization features offer ones to view the 3D volumes and three slice-based (axial, sagittal, and coronal views) visualization functionalities. Moreover, we provide the volume rendering visualization, which allows researchers to visualize the 3D cerebrovascular structures from MRA images.

Our future works for improvements of the toolkit's performance focus on implementations of 3D deep learning approaches for registration and segmentation purposes. Whilst machine-learning approaches have long gained their reputations in implementation of registrations between within-subject pairwise images, recently proposed deep-learning-based frameworks directly estimate displacement fields without iterative optimisation for testing left-out images, using deep convolutional neural networks learned from a large amount of data [8, 15–20]. These recently developed deep learning methods are expected to solve various multiple critical drawbacks found in conventional pairwise machine learning based methods, i.e., time-consuming, robust generality [8, 17].

Methods using deep learning architectures are robustly appropriate for 3D high-dimension neuroimaging registration and segmentation, because these methods naturally learn to accumulate the information of diverse features that are applicable for the functionality. Moreover, deep learning approaches are expected to obtain high robust performance while reduce time processing. More importantly, deep learning architectures such as convolutional neural networks offer parallelism learning that boosts up implementation and learning mechanism using multiple GPUs fast and straightforward [15].

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Conflicts of Interest The authors have no conflict of interest to declare.

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