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Chapter 5

Visualization of local changes in vessel wall morphology and plaque progression in serial carotid artery MRI

This chapter is in submission:

5.1 Introduction

Carotid atherosclerosis is an important cause of ischemic stroke. Assessment of plaque composition in addition to degree of luminal stenosis can be used to identify patients with increased risk of stroke and to assess disease progression. Magnetic resonance imaging (MRI) is an excellent non-invasive imaging technique to assess vessel wall morphology and plaque composition, with good accuracy and reproducibility [26]. Serial MRI of the carotid artery is used in several studies which focus on measuring the natural history of carotid artery plaques in symptomatic [26] and asymptomatic [29] patients and effects of lipid-lowering therapy using statins [27, 28]. Current standard to analyze serial MRI scans is to compare volume measurements based on manual segmentations of the vessel wall and plaque components. Before comparing the scans, the scans have to be aligned to each other on a slice level. Different approaches exist to align scans from different time points. One study aligns the scans by centering the image stack at each time point over the plaque [26], another study uses the baseline scan as a reference at the follow-up session to ensure targeting the same arterial segment [28]. Alternatively, post processing can be used to match the axial images from different time points according to their distance to the carotid bifurcation [27, 29]. Furthermore, comparison between time points is hindered by inconsistent repositioning of the artery from scan to scan in conjunction with thick image slices. Balu et al. studied the influence of subject repositioning on measurement precision in serial MRI and identified orientation variability as the most important factor that affected reproducibility [107]. Besides repositioning variability, the current comparison of time points is primarily based on volume measurements, which is a limited representation of the available image data, and no attention is given to local changes or visual presentation of differences between time points.

Therefore, we present a method for analyzing serial MRI scans which employs 3D image registration and visualization techniques to 1) decrease the measurement variability caused by inconsistent repositioning and 2) to enable detailed visual inspection of local differences between time points providing intuitive insight into the disease progression of an individual patient.

5.2 Methods

Patient

A 71 year old male was admitted to the hospital due to loss of strength and sensation of the left arm upon awakening. An MRI of the brain revealed several small cortical ischemic lesions in the region of the right middle cerebral artery. Carotid ultrasound showed an ipsilateral carotid artery plaque with approximately 30% luminal reduction. A minor stroke of the right hemisphere was diagnosed. The patient was included in a large prospective multicenter study to improve diagnosis of mild to moderate carotid plaques (Plaque At RISK study) [108]. The institutional Medical Ethical Committee approved the study and the patient gave written informed consent. The patient was followed up for 2 years, during which he did not experience new ischemic events.
Chapter 5. Improved analysis of serial carotid artery MRI

MRI

Carotid MRI examinations were performed 35 days after the event and after 2 years as previously described [108]. The high-resolution multi-sequence MRI protocol consisted of five MR sequences: 3D time of flight, 2D T1w turbo spin echo (TSE), 2D T2w TSE, 3D inversion recovery-turbo field echo (IR-TFE), and post-contrast 2D T1w TSE. Fifteen transverse adjoining slices of 2 mm each, with an in-plane reconstructed pixel size of 0.3 x 0.3 mm, covering the entire plaque were acquired.

Image analysis

The MR images at baseline and follow-up were manually segmented by delineating the lumen, outer wall, calcifications, lipid-rich necrotic core (LRNC) and intraplaque hemorrhage (IPH) according to previously published criteria [108]. Per definition, IPH was always located within the LRNC. Information from all MRI sequences was taken into account during the delineation process. The pre-contrast T1w images of both time points including segmentations are shown in Figure 5.1 and demonstrate a slice offset between time points at the bifurcation. The offset was manually corrected by applying a through plane translation of one slice to the follow-up image. To reduce the effect of the high anisotropy of the data on the measurements, the T1w images and segmented vessel wall boundaries were interpolated to a slice thickness of 0.5 mm. The vessel wall boundaries were visually inspected and corrected after interpolation. The interpolated vessel wall boundaries are used in the next section for the calculation of the vessel wall thickness and the creation of 3D meshes. The segmentations of the plaque components were not interpolated.
5.3 Results

Automated image registration

The baseline and follow-up T1w images were aligned to each other using an automated image registration framework which was optimized for carotid artery MRI scans [109]. After registration, point correspondence between the lumen of the baseline and the follow-up image was obtained, i.e. for each point on the lumen boundary in the baseline image, the corresponding point on the lumen boundary in the follow-up image is known.

Visualization using 3D surface meshes

The interpolated lumen and outer wall segmentation were converted into 3D surface meshes. For each point on the lumen mesh, the distance to the nearest point on the outer wall mesh was calculated resulting in a local vessel wall thickness (VWT) measure. The VWT is color-coded on the lumen mesh to provide a 3D visualization. The VWT analysis was repeated for the follow-up segmentation.

By using the point correspondence between the baseline and follow-up lumen, differences in measurements between baseline and follow-up can be visualized by color coding this difference on the baseline luminal surface mesh. Similarly, increase or decrease of plaque components can be visualized by color coding the lumen surface. Presence of a plaque component was indicated on a lumen mesh point when a plaque component was present between that lumen mesh point and its closest point on the outer vessel wall. Nearest neighbor interpolation was used to extract this information from the manual segmentations.

5.3 Results

First, volume and area-based comparison between baseline and follow-up was performed. Lumen volume at baseline was 1.525 ml and 1.507 ml at follow-up, vessel wall volume 1.634 ml versus 1.577 ml, calcification volume 0.017 ml versus 0.015 ml, and LRNC 0.378 ml versus 0.444 ml. The external carotid artery was excluded from the volume and area-based measurements. Figure 5.2 shows the slice-based area measurements of the lumen, outer vessel wall, calcifications and LRNC. The volume and area measurements demonstrate a mixed result; a consistent increase in LRNC was observed, the other components showed a small decrease and little variation between baseline and follow-up.

Figure 5.3 shows the 3D visualization of VWT at baseline and follow-up, change in VWT and progression or regression of LRNC with or without IPH over time. All metrics were color-coded on the lumen surface and appropriate color maps were chosen. A bipolar color map was chosen for Figure 5.3, in which gray corresponds to no change, blue to a decrease and red to an increase in VWT. The strong red regions indicate a clear increase in VWT. The absence of strong blue regions suggests accurate registration between baseline and follow-up. The increase in VWT is positively correlated with the presence of LRNC (Figure 5.3d). The 3D visualizations are interactive which allows the clinician to explore the results using zoom and rotation.

The change in VWT was quantified for locations inside the vessel wall which were thickened (VWT > 1 mm) and grouped into locations without and with LRNC (with or without IPH) (Figure 5.4). The mean change and standard deviation in VWT was -0.02 ± 0.41 mm for thickened vessel wall and 0.36 ± 0.52 mm for the LRNC locations. Wilcoxon
Figure 5.2: slice-based area measurements for baseline (solid line) and 2 years follow-up (dashed line) showing lumen area (red), vessel wall area (green), calcifications (orange) and lipid-rich necrotic core (LRNC) (yellow).

Figure 5.3: a-b) 3D surface meshes showing local vessel wall thickness at baseline and follow-up, respectively; c) difference in vessel wall thickness over time, d) progression or regression of lipid-rich necrotic core (LNRC) with or without intraplaque hemorrhage over time.
5.4 Discussion

A new method was introduced to analyze and present serial MRI data of the carotid artery vessel wall. 3D image registration was used to obtain point correspondence between images from different time points which enables assessment of local changes in plaque morphology. 3D visualization techniques were applied to present changes in vessel wall morphology using difference maps which were color-coded on a mesh of the lumen segmentation of the baseline image and related to the presence of different atherosclerotic plaque components in the vessel wall. The bipolar color map of the difference map in Figure 5.3 allows the clinician to differentiate between small and substantial changes in VWT between time points. Moreover, the tool can be used to demonstrate a significant increase in VWT over time for locations with LRNC with or without IPH. Both observations could not be deducted from the traditional volume or area measurements.

The 3D visualizations provide an interactive and intuitive way to represent measurements extracted from the original image data. In this work visualizations were generated providing insight in the change in VWT and progression or regression of different plaque components. Other measurements, e.g. changes in degree of stenosis, can be visualized using the same methodology. These new visual data analysis tools provide clinicians with a detailed view of atherosclerotic disease progression of individual patients and can potentially improve understanding of the effect of changes in plaque components on local plaque progression/regression.

5.5 Conclusion

The presented method to analyze and visualize changes over time for carotid artery MRI is an improvement over the traditional volume-based analysis as it provides a detailed view
of local differences between baseline and follow-up scans and increased insight into the
disease progression of an individual patient.

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