Visualization of Local Changes in Vessel Wall Morphology and Plaque Progression in Serial Carotid Artery Magnetic Resonance Imaging

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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 assess disease progression. Magnetic resonance imaging (MRI) is an excellent noninvasive imaging technique to assess vessel wall morphology and plaque composition, with good accuracy and reproducibility.1

Serial MRI of the carotid artery is used in several studies which focus on measuring the natural history of carotid artery plaques in symptomatic1 and asymptomatic2 patients and effects of lipid-lowering therapy using statins.3,4 The 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,1 and another study uses the baseline scan as a reference at the follow-up session to ensure targeting the same arterial segment.4 Alternatively, postprocessing can be used to match the axial images from different time points according to their distance to the carotid bifurcation.2,3 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 al5 studied the influence of subclinical arterial changes and plaque orientation variability as the most important factor that affected reproducibility. 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 uses 3-dimensional (3D) image registration and visualization techniques to enable detailed visual inspection of local differences between time points, providing intuitive insight into the disease progression of an individual patient.

Description of the Innovation

Patient

A 71-year-old man was admitted to the hospital because of loss of strength and sensation of the left arm on 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 ≈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).6 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.

Magnetic Resonance Imaging

Carotid MRI examinations were performed 35 days after the event and after 2 years as previously described.4 The high-resolution multisquence MRI protocol consisted of 5 magnetic resonance sequences: 3D time of flight, 2D T1-weighted (T1w) turbo spin echo, 2D T2w turbo spin echo, 3D inversion recovery–turbo field echo, and postcontrast 2D T1w turbo spin echo. Fifteen transverse adjoining slices of 2 mm each, with an in-plane reconstructed pixel size of 0.3×0.3 mm, covering the entire plaque were acquired.

Image Analysis

The magnetic resonance 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. Per definition, IPH was always located within the LRNC. Information from all MRI sequences was taken into account during the delineation process. The precontrast T1w images of both time points including segmentations are shown in Figure 1 and demonstrate a slice offset between time points at the bifurcation. The offset was manually corrected by applying a through-plane translation of 1 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 (VWT) and the creation of 3D meshes. The segmentations of the plaque components were not interpolated.

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. After registration, point correspondence between the lumen of the baseline and the follow-up image was obtained, that is, 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 segmentations 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 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.

Results of Pilot Testing
First, volume- and area-based comparison between baseline and follow-up was performed. Lumen volume at baseline was 1.525 and 1.507 mL at follow-up, vessel wall volume was 1.634 versus 1.577 mL, calcification volume was 0.017 versus 0.015 mL, and LRNC was 0.378 versus 0.444 mL. The external carotid artery was excluded from the volume- and area-based measurements. Figure 2 shows the slice-based area measurements of the lumen, outer vessel wall, calcifications, and LRNC of the manually aligned baseline and follow-up slices. The volume and area measurements demonstrate a mixed result; a consistent increase in LRNC was observed, whereas the other components showed a small decrease and little variation between baseline and follow-up.

Figure 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 are color coded on the lumen surface, and appropriate color maps are chosen. A bipolar color map was chosen for Figure 3C 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 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 4). The mean change and SD in VWT was $-0.02 \pm 0.41$ mm for thickened vessel wall and $0.36 \pm 0.52$ mm for the LRNC locations. Wilcoxon rank-sum test demonstrated a significant difference between both groups ($P < 0.001$).

**Conclusions**

We introduced a new method to analyze and present serial MRI data of the carotid artery vessel wall. Three-dimensional image registration is used to obtain point correspondence between images from different time points, which enables assessment of local changes in plaque morphology. Three-dimensional visualization techniques are applied to present changes in vessel wall morphology using difference maps which are 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 as shown in Figure 3C allows the clinician to differentiate between small and substantial changes in VWT between time points. Moreover, the presented 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. The visualizations as presented in this work provide insight in the change in VWT and progression or regression of different plaque components. Other measurements, for example, changes in degree of stenosis, can be visualized using a similar 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. Compared with conventional slice-wise comparison, which can only partly account for interscan misalignment, the presented approach based on 3D registration may potentially have a positive impact on measurement reproducibility. Further research on a larger cohort of patients and multiple readers is warranted to investigate this aspect.

To conclude, 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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**Disclosures**

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◼ magnetic resonance imaging ◼ stroke
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表5. FDA,HC和EMA药物标签中的药物相互作用比较

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* AUC指浓度曲线下面积; BID,每日2次; CrCl,肌酐清除率; MA,欧洲药品管理局; FDA,美国食品和药品管理局; HC,加拿大卫生部。
初步实验结果

首先，完成了基线和随访图像间基于体积和面积的比较。基线管腔体积是1.525ml，而随访图像体积是1.507ml，管壁体积分别是1.634ml和1.577ml，钙化体积分别是0.017ml和0.015ml，而LRNC是0.378ml和0.444ml。颈外动脉未做基于体积和面积的测量。图2示手工对齐基线和随访层面后，基于层面管腔、外壁、钙化、LRNC面积测量值比较结果。体积和面积测量结果是一个混杂的结果；在基线和随访图像中，LRNC可见一致增加，而其它成分少量减少或没有变化。图3示基线和随访图像中VWT的3D图像，VMT的改变，以及全程含或不含IPH的LRNC的进展或逆转。所有测量值在管腔表面用颜色编码，从而呈现适宜的颜色图。图3C用双极彩图标示，灰色代表VWT无变化，蓝色代表减少，红色代表增加，而黑色代表无变化。3D显像技术用不同的彩色图展示血管壁形态的变化，用颜色编码基线图像中管腔节段的热点区域，对应血管壁不同动脉粥样硬化斑块成分的存在。

3D显像提供了两个直观的方式展示原始影像数据中提取的测量图像间的错配，而现在基于3D显像的方法对测量具有很好的可重复性。有必要开展大型患者队列研究进行多个读取程序来观察这方面的价值。

总之，目前分析和可视化颈动脉MRI全程改变数据的方法是传统基于体积分析方法的一个改进，为观察基线和随访图像间的局部差异提供了详细的图景，可更好地理解每个患者的疾病进展情况。

参考文献