AUTOMATED CAROTID ARTERY DISTENSIBILITY MEASUREMENTS FROM CTA USING NONRIGID REGISTRATION

K. Hameeteman¹, S. Rozie², C.T. Metz¹, S. Klein¹, T. van Walsum ¹, A. van der Lugt², W.J. Niessen¹,³

¹Biomedical Imaging Group Rotterdam, Departments of Radiology & Medical Informatics Erasmus MC, Rotterdam, The Netherlands
²Department of Radiology, Erasmus MC, Rotterdam, The Netherlands
³Imaging Science and Technology, Faculty of Applied Sciences, Delft University of Technology, Delft, The Netherlands

ABSTRACT

The distensibility of a blood vessel is a marker of atherosclerotic disease. Manual measurement of the distensibility on CTA images is a difficult task. In this paper we describe a method to automatically determine the distensibility of the carotid artery by locally analyzing the deformation field of a nonrigid registration of a series of ECG-gated CTA images. We evaluate two variants of the method, and compare the results with manually measured distensibilities.

Index Terms— distensibility, cta, carotid, registration

1. INTRODUCTION

Distensibility is a measure of the local compliance of a blood vessel and therefore a measure of the stiffness of that vessel with respect to pressure changes. Measuring the distensibility is clinically relevant as the elasticity of the arterial vessel wall decreases with the accumulation of atherosclerotic plaque [1, 2]. Increasing stiffness of the vessel is thus a marker for atherosclerotic disease.

Traditionally the arterial stiffness is assessed with ultrasound techniques [3, 4]. Using ultrasound, a 2D image parallel to the centerline of the carotid artery is acquired and subsequently the minimum and maximum distance between the imaged vessel walls during one or more heart cycles is measured. Assuming a circular cross-section, the area is then calculated. Recently, several studies have demonstrated the feasibility of semi automated measurement of the distensibility of large vessels (aortic arch, abdominal aorta) using ECG-gated CTA [5, 6, 7]. An advantage of CTA over ultrasound is that the true cross-sectional area can be measured, and thus non-circular cross-sections can be accounted for. These studies all used an Multi Planar Reformatted (MPR) image containing the cross-section of the investigated vessel. On these MPR images the lumen was segmentation on each time frame and voxel counting was used to get the lumen area. In this paper we investigate the feasibility of automated distensibility measurement on the carotid artery, a vessel much smaller than the aorta. Also the expected area changes are much smaller. The main methodological difference with the above mentioned methods is the way the area change is measured.

The distensibility of a vessel is defined as the maximum change in cross-sectional area, \( \Delta A \), relative to the change in pressure, \( \Delta p \), scaled by the minimal area, \( A_{\text{min}} \):

\[
D = \frac{\Delta A}{A_{\text{min}} \Delta p} \quad (1)
\]

Distensibility measurements therefore require imaging data over the complete cardiac cycle, and measuring the cross-sectional area of the vessel over this cardiac cycle.

2. METHOD

The method to automatically measure the distensibility uses a registration step which is performed using either a 3D or 4D method. To calculate the distensibility of the carotid artery at a given position, first a cross-sectional contour of the vessel in the first time point is extracted. Currently this is done manually, but this step could be automated using lumen segmentation [8] and centerline detection [9]. In a second step the imaging data at all other time points in the ECG-gated time series is registered to the first time point. This step yields a deformation field \( T_{0t} \), between the first time point (0) and each other time point \( t \) within the RR-interval. We use Gauss’s theorem to calculate the change in cross sectional area of the vessel at a certain vessel position:

\[
\Delta A = \int \int_S \nabla \cdot T_{0t} \, dA = \int \int_{\partial S} T_{0t} \cdot \mathbf{n} \, dS \quad (2)
\]

where \( \partial S \) is the contour around the lumen area \( A \) and \( \mathbf{n} \) is the normal to the contour and the contour plane. Using this approach, the area changes within the plane of the contour are calculated for all time points with respect to the first time point. The resulting area time curve together with Equation (1) leads to the distensibility. Registration of the images at different time points was achieved using the ITK based registration toolbox elastix [10]. A B-spline model was used to parameterize the deformation field. The spacing between control points was set to 20 mm. This is comparable to the size of the diameter of the carotid. Mutual information was used as a similarity metric and for the optimization we used an adaptive stochastic gradient descent optimizer [11]. The registration was performed in a multi-resolution framework with 3 resolution levels. For each dataset we performed both a set of 3D registrations, in which all time points were independently registered to the first time point and a 4D registration [12] in which all time points were registered simultaneously to the first time point. The 4D registration method enforces smooth deformations in the time dimension and uses a similarity metric based on the variance of the image intensities along the time dimension. Because we expect smooth area changes during the cardiac cycle, the 4D registration method is expected to perform better as it is more robust against the noise in the images.
In this section we subsequently describe the used datasets, the manual procedure and the experiments to test the proposed automatic method.

3.1. Data

We acquired 39 ECG-gated CTA datasets of patients with ischemic cerebrovascular symptoms who underwent CTA of the carotid arteries for clinical workup. The scan range was 40 mm and the field of view 12 cm. The 3D reconstructions were made at 8% steps of the cardiac RR interval (the interval between two R waves of the ECG signal), resulting in a 4D set with 13 time points of one heart beat. The in-plane resolution was 0.4 x 0.4 mm, the slice thickness 0.6 mm, and a B31f reconstruction kernel was used. Figure 1 shows an example slice. Blood pressure was measured using an arm cuff.

Brachial pulse pressure ($\Delta p$) was calculated as the difference between mean systolic and mean diastolic blood pressure.

3.2. Manual measurements

Using a custom made tool based on MeVisLab (MeVis Research, Bremen, Germany) a centerline through the Common Carotid Artery and Internal Carotid Artery was defined. Along this centerline MPR images perpendicular to the centerline were created, showing cross sections of the carotid artery at different positions along the centerline. The same centerline was used for all 13 cardiac phases. For every cardiac phase a contour of the lumen area was drawn at the same position along the centerline. Contrary to the studies on the aorta[5, 6, 7] where the area was calculated using voxel counting, the contours used in this study had subvoxel precision. Calculation of the cross sectional area from the drawn contours then leads to the area curve of the vessel during one heart cycle. Using Eq. 1 the distensibility can then easily be calculated. These manual measurements were performed on all 39 datasets.

To assess the interobserver variability of the manual measurements, two observers annotated the cross-sectional area in the first 10 subjects on both the left and the right Common Carotid Artery (CCA). As each dataset contains 13 time points, this results in 260 area pairs and 20 area change pairs. Both observers used the same centerline to generate the MPR images and drew the contour at the same position along the centerline. In this way the accuracy of the contour drawing can be estimated.

3.3. Automated measurements

To assess the accuracy of the automatic 3D and 4D algorithms, a synthetic deformation was applied to the clinical data. A 3D test set was created by using the first time point of a 4D data set and scaling this 3D dataset in the axial plane. In this way we approximate an expansion of the blood vessel. The scaling factor was set to $\frac{1}{1.4}$, which is comparable to the expected area change. The scaled data sets were registered to the original datasets. Because the true area change is known, the error can be calculated. We tested this on 39 datasets which were split into two sides, containing the left and right carotid artery respectively.

To construct a 4D test set (for the 4D registration method), the scaling was changed over the time points according to the following formula:

$$S = \frac{1}{1 - 0.1 \sin^2(\frac{t}{13})}$$

where $S$ is the scaling factor and $t \in [0, 12]$ is the time point number. So the first time point is not scaled and half way the cardiac cycle the scaling is the same as for the 3D test images. During the 4D registration the first time point was set as reference point. Because the 4D registration requires several hours computing time, this registration experiment was done using only 23 datasets that were randomly selected.

3.4. Comparison

As a final experiment, the area curves produced by the manual and automatic methods for all 39 clinical datasets were visually compared. To be able to visualize the area curves of different patients in one graph, we normalized all area curves by subtracting the area of the first time point and dividing by the absolute maximum area of the curve. This normalization leads to curves that are in the 0-1 interval and are independent of the size of the carotid artery and its change in cross-sectional area.

4. RESULTS

4.1. Interobserver variability

In Figure 2 the Bland-Altman plot of the manual area measurements for the two observers is shown. The limits of agreement are $-8.1 \text{mm}^2$ and $4.7 \text{mm}^2$ and the standard error is $0.21 \text{mm}^2$. The mean area difference is $-1.7 \text{mm}^2$ which means that on average observer 2 drew bigger cross-sectional areas than observer 1. The Bland-Altman plot of the area change $\Delta A$ for both observers is shown in Figure 3. Here the limits of agreement are $-4.1 \text{mm}^2$ and $2.2 \text{mm}^2$ and the standard error of the difference is $0.36 \text{mm}^2$. The average area change that was measured by Observer 1 was $5.2 \text{mm}^2$ and Observer 2 found an average change of $6.1 \text{mm}^2$. As can be seen from these graphs, the measured area change ($2 - 8 \text{mm}^2$) is within the range of the inter observer variability in measuring lumen area.

4.2. Automated measurements

Using the synthetic images and the 3D B-spline registration we calculated the difference between the expected area due to the applied...
4.3. Comparison

Figure 4, 5 and 6 show the normalized area curves for the manual measurements, the automatic method using 3D registration and the automatic method using 4D registration respectively.

5. DISCUSSION AND CONCLUSION

We presented an automated method for the measurement of distensibility in carotid arteries, based on 4D CTA data.

The experiments on synthetic data show that the automated measurements slightly underestimate the lumen area. This error is however well below the expected area change of 4.7mm²[13], which is an indication that this method can be used to estimate the area change. The 4D registration, the average difference between the expected area and the area calculated from the deformation field was $-0.71 \pm 0.32$mm². This error is slightly smaller than using the 3D registration. Using a paired t-test, the calculated p-value of the difference is 0.031.

Future work focuses on integration of automated lumen segmentation, and more extensive evaluation of the method to investigate the value of automated distensibility measurements in clinical practice.

In conclusion, we presented and evaluated a method for the automated measurement of the distensibility of the carotid artery and quantitatively showed its accuracy in experiments using simulated deformations. We furthermore demonstrated that the automated measurement of the distensibility is feasible.

6. REFERENCES


Fig. 4. Normalized area of the manual area measurements.

Fig. 5. Normalized area of the automatic method using 3D registration.

Fig. 6. Normalized area of the automatic method using 4D registration.


