Relation of arterial stiffness and axial motion of the carotid artery wall –a pilot study to test our motion tracking algorithm in practice

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Abstract— **Recently researchers have shown growing interest in axial motion of common carotid artery wall. The amplitude of the axial motion of the wall has been initially linked to arterial stiffness and the direction of the axial stretch has been noted to vary, although not highlighted in the studies. In this study, an enhanced block matching algorithm, developed in our earlier study, was used to measure 2D-motion of the human carotid artery wall. A total of 19 healthy subjects were imaged and divided into two groups based on whether their axial motion of intima-media in left common carotid artery was primarily oriented along or against the direction of the blood flow. Statistically significant differences in two independent indices of arterial stiffness, as well as in the size of the artery, were found between the groups, suggesting that retrograde motion of intima-media is associated with smaller carotid arteries and is a possible sign of arterial stiffness.**

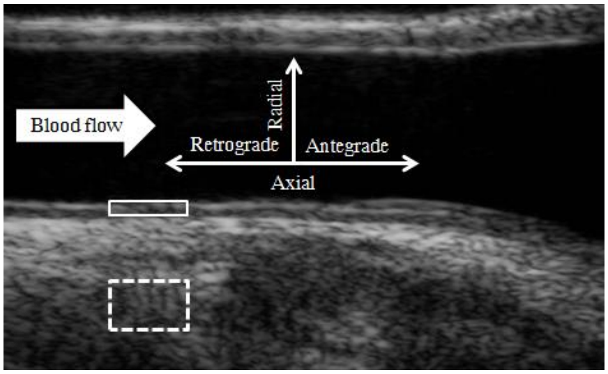

Figure 1. B-mode ultrasound image of a common carotid artery. Retrograde and antegrade directions have been marked on the axial plane. Solid rectangle displays the region of interest (ROI) used in the motion tracking of intima-media and dashed rectangle displays the ROI used as a reference point for the motion estimation.

I. INTRODUCTION

The development of high-resolution ultrasound scanners has made it possible to noninvasively measure the axial motion of the intima-media layer in the common carotid artery (CCA). Although it is possible, the measurement of the axial motion of the CCA wall is challenging and the clinical understanding of the influence of the axial motion to hemodynamics is incomplete. However, it has been shown that the current measurements are reproducible [1, 2] and that axial waveforms preserve their forms over a 4-month-long period [3].

Biphasic waveform of the axial motion of the CCA wall has been reported in multiple studies, where the wall stirs back and forth in the axial direction during a heartbeat [1, 2]. In addition, it has been reported that in some subjects the retrograde amplitude of the motion, i.e. in the opposite direction of the blood flow (See Fig. 1), is greater than the antegrade amplitude, i.e. in the direction of the blood flow [2, 3].

In this paper, the possible relation between the main direction of the axial motion and arterial stiffness was studied, for the first time. The axial wall motion was measured using our previously published motion tracking algorithm and applanation tonometry was used for the referential arterial stiffness measurements.

II. METHODS

A. Study protocol

The left CCA of 19 healthy volunteers was imaged with an ultrasound scanner (Acuson Sequoia 512, Siemens, Mountain View, CA, USA) equipped with a 14 MHz linear array transducer (Acuson 15L8-S, Siemens, Mountain View, CA, USA). The recorded ultrasound video was analyzed using customized software in Matlab for signal analysis. A cross-correlation based motion tracking algorithm, introduced in our earlier study [2], was used to detect the 2D-motion of the carotid wall.

Alongside with the ultrasound study, the aortic pressure waveform was measured from the radial artery noninvasively with applanation tonometry system (SphygmoCor system version 9, AtCor Medical Inc., Itasca, IL, USA). Diastolic and systolic blood pressures of the subjects were measured from the upper arm with an automatic blood pressure monitor (Omron, M4-I, Matsusaka, Japan). A total of 3 blood pressure measurements were conducted: just before and after the ultrasound study and just before the applanation

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tonometry measurement. This study protocol enabled to measure the axial motion of the CCA and to compute multiple known indices of arterial stiffness from the CCA dilatation graph and from the aortic pressure curve.

For statistical analysis, the study population was divided into two groups according to the main direction of the axial motion of the intima-media layer. A nonparametric Mann-Whitney U-test was used to identify the significant differences in the arterial stiffness indices between the two groups.

B. *Motion tracking algorithm*

The base of the motion tracking algorithm is a conventional block matching, where the user selects a ROI from the ultrasound video and computer calculates 2D-cross-correlation between the selected ROI and the template obtained from the next frame. The size of the template is chosen to be as small as possible, but still covering the largest possible movement that the CCA wall can make in the time between two subsequent frames. Thus the size of the template is a function of the estimated velocity of motion and the frame rate of the recorded ultrasound video.

A bicubic interpolation is used to virtually improve the spatial resolution of the ultrasound video. This is a very time consuming procedure but it must be done to verify adequate motion tracking. With an online use of a smaller imaging window, the offline interpolation could have been avoided, but in this study we used a large field-of-view, to be able to simultaneously track the motion of the near wall and far wall of the carotid, and of the surrounding tissues. Surrounding tissues were tracked to eliminate the artifacts caused by the motion of the ultrasound probe during the imaging sequence.

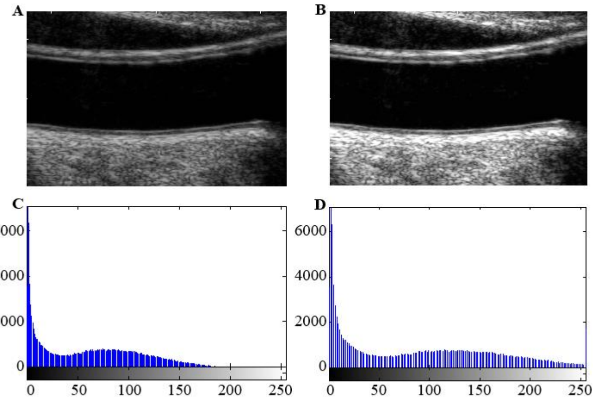

Figure 2. Contrast optimization performed for a ROI that is the size of a full video frame. A; original ultrasound image. B; contrast optimized ultrasound image. C; histogram of the original ultrasound image. Original ultrasound has 8-bit intensity coding and thus the values on x-axis are from 0 to 255. D; histogram of the contrast optimized video frame.

As an addition to the conventional block matching, we have introduced a contrast optimization technique. After the ROI selection, the program detects intensity values within the ROI and modifies the histogram of the template to match those values (See Fig. 2). This procedure intentionally over or under saturates areas in the template that are darker or lighter than the intensity values inside the ROI. The reason for doing this is to prevent false detection of the ROI in the template.

C. *Indices of arterial stiffness*

Three different indices of arterial stiffness were used in this study. From the radial distension curve of the CCA we measured the maximum cross-sectional lumen area change during the systole (ΔA) and the cross-sectional distensibility coefficient (DC). ΔA is a simple measure of arterial elasticity, since it only measures how much artery stretches during the systole and gives smaller values when artery is stiffer. DC takes into account the stretching blood pressure [4]:

$$DC = \Delta A \,/\, (A_{diastole} * PP), \tag{1}$$

where $A_{diastole}$ is diastolic lumen area of the CCA and PP is pulse pressure.

From the aortic pressure curve, measured with applanation tonometry system, we obtained aortic augmentation index adjusted for the heart rate of 75 (*Aix@75*). Augmentation index compares the proceeding pulse pressure wave, originating from the heart, and the reflected pressure wave from the periphery. In multiple studies, augmentation index has been shown to be associated with cardiovascular risk [7-9]:

$$Aix = (SBP - P1) \,/\, PP, \tag{2}$$

where SBP is systolic blood pressure and $P1$ is the first notch on aortic pressure curve.

III. RESULTS

The axial motion of the CCA wall was successfully measured from all 19 subjects, using our motion tracking algorithm. Eight of the subjects had the largest axial amplitude in the antegrade direction and 11 subjects had the largest amplitude in the retrograde direction. Examples of the antegrade and retrograde motion curves have been displayed in Figure 3 and the clinical characteristic of the two populations have been presented in Table 1. In addition to the Figure 3, multiple cases showed bidirectional axial motion, where the artery moves back and forth around the baseline. These cases were differentiated into retrograde and antegrade groups simply by measuring in which direction the largest amplitude was oriented. In the whole study population, the peak-to-peak amplitudes of the axial wall motion varied in range 0.26-0.59 mm and there was no

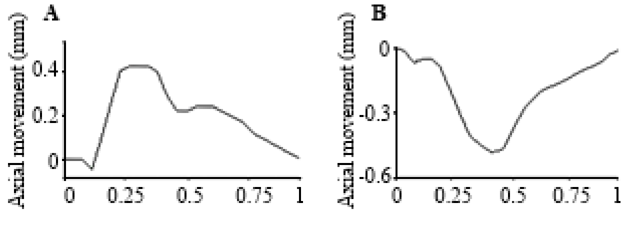

Figure 3. A heartbeat long axial motion curve recorded from two subjects. A; antegrade oriented axial motion. B; retrograde oriented axial motion.

statistically significant difference in the peak-to-peak amplitudes between the groups since the p-value was 0.15.

In the retrograde group, ΔA and $A_{diastole}$ were smaller (median values 3.6 mm^2 vs. 5.3 mm^2 and 22.1 mm^2 vs. 24.9 mm^2, respectively) while *Aix@75* was bigger (median values 14 % vs. 7 %) compared to the antegrade group (see Fig. 4). ΔA and $A_{diastole}$ displayed statistically significant difference between the two groups while *Aix@75* merely missed the 95 % confidence criteria. *DC* did not differ between the study groups.

TABLE I. CLINICAL CHARASTERISTICS OF THE STUDY POPULATION

Variables	**Study populations**		
	Antegrade (n = 8)	***Retrograde (n = 11)***	***p-value***
Age (years)	35 ± 10	45 ± 16	0.15
BMI (kg/m^2)	23 ± 2	23 ± 2	0.97
PP (mmHg)	49 ± 6	46 ± 15	0.17
Female/male	3/5	8/3	0.21

Above values have been presented in form: mean ± standard deviation

IV. DISCUSSION

The good reproducibility and feasibility of our algorithm for tracking the axial movement of the carotid intima-media has been published earlier [2]. This was our first experiment to observe how well-functioning our program is in clinical practice. All radial and axial motion tracking and computation of the arterial stiffness indices were performed with our software. The results are preliminary, but the differences in the ΔA and *Aix@75* values indicate that the prominent retrograde component of the axial motion curve is associated to higher arterial stiffness. In addition, the retrograde axial motion seems to be dominant in smaller carotid arteries.

Peak-to-peak amplitudes of the axial motion of the carotid wall have been previously connected to cardiovascular risk indices and plaque burden [10-12]. In addition, the retrograde dominance in the axial motion has been reported in some subjects, although not highlighted in the publications [2, 3, 13]. This is the first study to focus on the relevance of the retrograde motion. The results imply that the direction of the axial motion might reveal something new about arterial stiffness, compared to the axial amplitudes, since there was no significant difference in the peak-to-peak amplitudes but still the stiffness related indices ΔA and *Aix@75* differed between the two study populations. *DC* did not differ between the study populations, but on the other hand the distensibility coefficient and augmentation index are independent stiffness indices i.e. they do not correlate with each other [14].

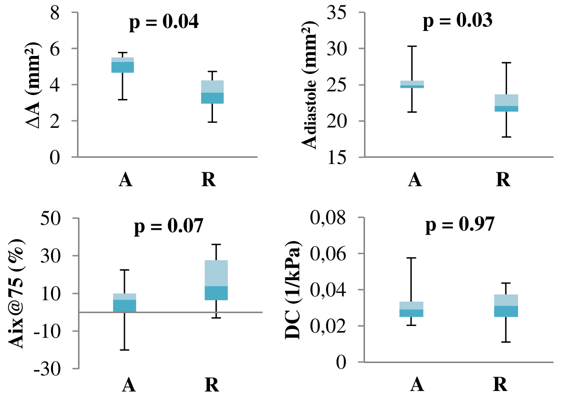

Figure 4. Arterial size and indices of arterial stiffness between the two groups. The left bars display the data from the antegrade group (A) and the right bars display the data from the retrograde group (R). The bottom and top of the box are the first and third quartiles, and the band inside the box is the median. The ends of the whiskers represent the minimum and maximum. Abbreviations: ΔA, lumen area change during systole; $A_{diastole}$, diastolic lumen area; *DC*, cross-sectional distensibility coefficient; *Aix@75*, augmentation index.

Current noninvasive methods to measure arterial stiffness have their advantages and disadvantages. Dynamic angiography is a promising new MRI-based measurement but too expensive and time consuming to be used for screening larger populations [15]. On the other hand, determination of the widely used carotid *IMT* is a fast and cheap measurement, but tells more about plague burden than actual stiffness of the artery. Quantifying arterial stiffness by measuring the carotid diameter change and comparing the value with measured blood pressure is not without problems either: the blood pressure is usually measured from the upper arm, and in a slightly different time window than the carotid ultrasound video. Hence the obtained pulse pressure is not the driving force for the measured carotid stretch and causes discrepancy to the result (*DC*). In addition, measuring aortic pressure curve via transfer function, using applanation tonometry data from the radial artery and combining it to the upper arm blood pressure, produces multiple error sources to the measurement. In addition, *Aix@75* has been shown to saturate in older population [16]. Thus new indices of arterial stiffness are needed to differentiate the artery wall elasticity in the elderly, but also generally, a better risk assessment for arterial stiffness is needed [17]. The aforementioned unconformities and general saturation problems in the *Aix@75* measurements might be the reason why the augmentation index merely missed the statistically significant difference between the two study groups. Furthermore, the current shortcoming of noninvasive methods to detect preclinical atherosclerosis was the motivation to investigate and to develop better tools for measuring the axial motion of the carotid wall. Referring to our results and to other publications on the subject [10-12], the axial motion of the CCA wall might provide new information on studying the well-being of the vascular system.

Despite the potential that quantifying axial motion provides, measuring the wall movements is challenging due to the fast rate of the motion and heterogeneous structure of the intima-media in the axial direction of the ultrasound image. The fast motion of the carotid wall can cause motion blur and thus errors in motion tracking. In addition, the motion blur makes the intima-media layer even more heterogeneous than it is in sharp images, which makes the pattern recognition based motion tracking more difficult. Our contrast optimization method tries to take the most out of the spatial resolution that is currently available for carotid imaging. In the future, the frame acquisition time in ultrasound imaging is likely to get faster and thus decrease the amount of visible motion blur in the images. Further, modern medical ultrasound devices allow the user to access the acquired raw image data without heavy post-processing. In our experience, generally post-processing, done by the ultrasound device, makes the axial motion tracking harder.

The clinical limitation of this pilot study is that the study population was small and without a proper baseline control. None of the participants had a history of major cardiovascular diseases and they all were at normal weight, but the study population included men and women with a wide age span. Gender of the subjects should not considerably affect the results, since there was no significant difference in the proportion of men and women, between the two groups. We chose to have a wide age span, since aging is associated with arterial changes, which lead to arterial stiffening. A certain degree of variation in such a small population was useful, in order to determine whether the direction of the axial CCA wall motion had any connection to arterial stiffness. For clinical validation of the results, the measurements must be conducted on a bigger population with a proper baseline control.

V. CONCLUSION

Our contrast optimized motion tracking algorithm was successfully applied for measurements of axial motion of the carotid wall. Eleven subjects out of 19 had the main axial motion of the wall against the direction of blood flow. Three known indices of arterial stiffness were computed and two indices, ΔA and $Aix@75$, displayed that subjects, whose axial motion was against the blood stream, had stiffer arteries. The third index DC could not differentiate the two study groups. While the preliminary correlation to arterial stiffness was found, the causality remains unclear. The results also raise the question: what causes the carotid wall to stretch against the direction of blood flow. According to the results, the size of the artery and the amplitude of the radial stretch seem to be associated to the phenomenon more than the pulse pressure. More studies are needed to understand the biomechanics of the wall motion, but our method is shown to be adequate to measure the phenomenon.

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