A Comparison of Ultrasound Intima Media Thickness Measurements of the Left and Right Common Carotid Artery

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***Abstract*—The intima–media thickness (IMT) of the common carotid artery (CCA) is an established indicator of cardiovascular disease (CVD). There have been reports about the difference between the left and the right sides of the CCA IMT and its importance when evaluated with various risk factors as well as their association with the risk of stroke. In this study, we use an automated system based on snakes, for segmenting the CCA and perform measurements of the IMT of the carotid artery and provide their differences between the left and right sides. The study was performed on 205 longitudinal-section ultrasound images acquired from 87 men and 118 women at a mean±SD age of 63±10.47 years, out of which 51 had cardiovascular symptoms. A cardiovascular expert manually measured the IMT on the left CCA side (mean±standard deviation = 0.79±0.21 mm) and the right CCA side (0.76±0.33 mm). The left and right IMT automated measurements were 0.70±0.15 mm and 0.66±0.15 mm, respectively. We found no statistical significant differences: 1) between the left and right IMT measurements, for both the manual and automated measurements, and 2) between the manual and automated measurements for both sides. These findings suggest that the measurement of the CCA IMT on one side only is enough (and this is in agreement with other studies), as well as automated measurements can be used.**

I. Introduction

Cardiovascular disease (CVD) is the largest cause of death worldwide [1]. Atherosclerosis is the main reason leading to CVD and can result to heart attack, and stroke [1], [2]. Carotid intima-media-thickness (IMT) is a measurement of the thickness of the innermost two layers of the arterial wall and provides the distance between the lumen-intima and the media-adventitia borders. The IMT can be observed and measured as the double line pattern on both walls of the longitudinal ultrasound images of the common carotid artery (CCA) [2] and it is well accepted as a validated surrogate marker for atherosclerosis disease.

It is a fact that the increase in the IMT of the CCA is directly associated with an increased risk of myocardial infarction and stroke, especially in elderly adults without any history of CVD [1]-[3]. Noninvasive B-mode ultrasound imaging is used to estimate the IMT of the human carotid. Thus, the IMT may be used for the screening of population as at least half of premature heart attacks and strokes, can, and should, be prevented. IMT is measured in both common CCA sides (left and right side of the CCA) and expressed as the mean value obtained from these measurements [4]-[6]. Yet it is not entirely clear whether the IMT is equal in both CCA arteries as several studies have shown a prediction for an increase of IMT in the left CCA [3]. A theoretical, not well investigated, explanation has been raised, namely that increased shear stress forces in the left CCA contribute to this inequality. However, most studies in the past were performed in individuals at the age of 50 years or more [7]-[10], thus excluding the possibility to reveal the differences at an earlier stage of the disease [7]. It was also shown [9], that the CCA IMT may be possibly used in the prediction of possible infract side, and in the prediction of potential risk of stroke by evaluating the IMT on both sides of the CCA. There have been very few studies regarding the effect of carotid IMT sidedness on the various risk factors associated with carotid IMT [11]. Because of the different anatomical origins of the left versus the right CCA, it was speculated that hemodynamics, age, gender, blood lipid level, blood glucose level, and other risk factors would have different effects depending on whether the left or right CCA was considered [11]. In [12], the side differences in CCA IMT measurements, and their prognostic values, among patients with stable coronary artery disease, were evaluated. The study in [12] showed that the left and right CCA may exhibit different prognostic values in the investigated population.

IMT can be measured through segmentation of the intima media complex (IMC), which corresponds to the intima and media layers of the arterial wall. There are a number of techniques that have been proposed for the segmentation of the IMC in ultrasound images of the CCA which were reviewed in [13]. In two recent studies performed by our group [4], [5] we presented a semi-automatic method for IMC segmentation [4], that incorporated the use of active contour models in a normalized rectangular region of interest where speckle removal had been applied [6]. In [5], we presented an extension of the integrated system proposed in [4], where also the intima- and media-layers of the CCA could be segmented. Finally, a fully automated method was recently proposed for the segmentation of the IMC from ultrasound images of the CCA [14].

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The objective of this study is to investigate the IMT measurement differences between the left and right CCA sides based on automated snake's segmentation. The findings may be relevant for the understanding of potential mechanisms that underlie the development of increase of carotid IMT at a relatively early stage of the disease.

II. MATERIAL & METHODS

A. Recording of Ultrasound Images

A total of 205 B-mode longitudinal ultrasound images of the CCA which display the vascular wall as a regular pattern (see Fig. 1a) that correlates with anatomical layers were recorded. The images were acquired by the ATL HDI-5000 ultrasound scanner (Advanced Technology Laboratories, Seattle, USA) [15] with a resolution of 576X768 pixels with 256 gray levels. For the recordings, a linear probe (L74) at a recording frequency of 7MHz was used. Assuming a sound velocity propagation of 1550 m/s and 1 cycle per pulse, we thus have an effective spatial pulse width of 0.22 mm with an axial system resolution of 0.11 mm [15]. We use bicubic spline interpolation to resize all images to a standard pixel density of 16.66 pixels/mm (with a resulting pixel width of 0.06 mm). The images were recorded at a cohort study in a Cyprus mountain village from asymptomatic, apparently healthy subjects, and symptomatic subjects, which have already developed CVD events. A written informed consent was obtained according to the instructions of the local ethics committee.

B. Ultrasound Image Normalization

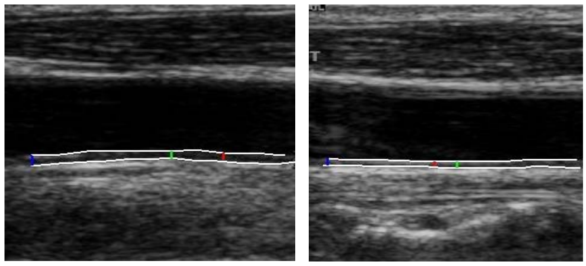
Brightness adjustments of ultrasound images (see also Fig. 1b) were carried out in this study based on the method introduced in [16]. This method improves image compatibility by reducing the variability introduced by different gain settings, different operators, different equipment, and facilitates ultrasound tissue comparability. Algebraic (linear) scaling of the images were manually performed by linearly adjusting the image so that the median gray level value of the blood was 0-5, and the median gray level of the adventitia (artery wall) was 180-190 [16]. The scale of the gray level of the images ranged from 0-255.

C. Speckle Reduction Filtering (DsFlsmv)

In this study the filter linear scaling (despeckle filter-DsFlsmv) [6], utilizing the mean and the variance of a pixel neighborhood was used to filter the ultrasound images. It was proposed in [17] and evaluated in [6] on 440 ultrasound images of the CCA. The filter may be described by a weighted average calculation using sub region statistics to estimate statistical measurements over a 5x5 pixel windows applied for three iterations [4]-[6] (see also Fig. 1 b).

D. Manual Measurements

The IMT measurements were performed by the cardiovascular expert between 1 and 2 cm proximal to the bifurcation of the CCA on the far wall [4] over a distance of 1.5 cm starting at a point 0.5 cm and ending at a point 2.0 cm proximal to the carotid bifurcation.



(a) Left CCA IMC (b) Right CCA IMC

Fig. 1. Automated IMC segmentation of the a) left side (IMT_{mean}=0.71 mm, IMT_{max}=0.9 mm, IMT_{min}=0.55 mm, IMT_{median}=0.65 mm), and b) right side (IMT_{mean}=0.45 mm, IMT_{max}=0.52 mm, IMT_{min}=0.11 mm, IMT_{median}=0.21 mm), respectively.

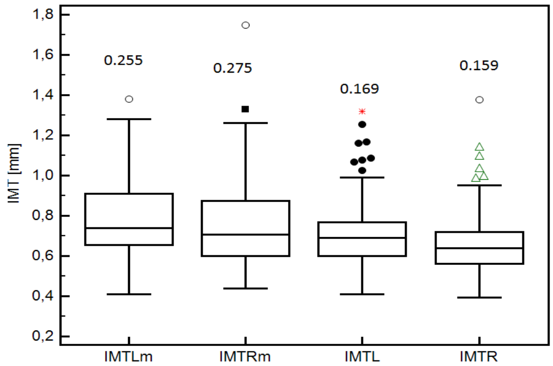


Fig. 2. Box plots for the left and right sides CCA IMT manual measuremnets (IMTLm, IMTRm) and IMT left and right sides automated measurements (IMTL, IMTR). Inter-quartile rage values are shown above the box plots. Straight lines connect the nearest observations with 1.5 of the inter-quartile range (IQR) of the lower and upper quartiles. Unfilled rectangles indicate possible outliers with values beyond the ends of the 1.5xIQR.

E. Automatic IMC Segmentation

The IMC was automatically segmented after normalization and despeckle filtering (see sections II.B, II.C), using the automated snakes segmentation system proposed and evaluated in 100 ultrasound images of the CCA in [4] and [5], which is based on the Williams & Shah [18] snake segmentation method. The IMC was segmented using a Matlab® software, developed by our group, where the upper CCA wall boundaries (lumen-intima interface) and the lower CCA wall boundaries (media-adventitia interface) were extracted.

An IMC initialization procedure was carried out for positioning the initial snake contour as close as possible to the area of interest followed by the snakes segmentation. The segmentation procedure is described as follows [4], [5]: 1) Load the B-mode image (see Fig. 1a), perform image normalization (see section II.B) and despeckle filtering (see Section II.C). 2) Binarize the image in order to extract edges more easily. 3) Erode the binary image (from point 2) above) by applying an erode morphological operation that eliminates smaller not connected binary image areas. 4) Perform edge detection on the binary eroded image and extract the contour matrix of the image. Extract the contour matrix of the above area by locating points and their coordinates on the borders (contour) and construct three interpolating B-splines. Sample the interpolating B-splines in 30 equal segments, in order to define 30 snake points on the contour. Connect the first and the last snake points on the initial contour to form a closed contour. 5) Map the detected adventitia contour points from 4), on the image to form the initial snake contour for the adventitia border. 6) Deform the initial contour by the snake to accurately locate the adventitia borders and save the final adventitia contour. Perform steps 5) and 6) for all three initially detected contours and identify the final ones. Save and display the detected contours (i.e. far wall adventitia and intima and near wall adventitia) on the B-mode image (see Fig. 1a and b).

For the Williams & Shah snake, the strength, tension and stiffness parameters were equal to $\alpha_s = 0.6$, $\beta_s = 0.4$, and $\gamma_s = 0.2$ respectively. The extracted final snake contours (see Fig. 1a and 1b), correspond to the adventitia and intima borders of the IMC. The distance is computed between the two boundaries, at all points along the arterial wall segment of interest moving perpendicularly between pixel pairs, and then averaged to obtain the mean IMT (IMT_{mean}). Figure 1 shows the detected IMT_{mean} for the left and right ultrasound images of the CCA.

III. Results

We have evaluated 205 volunteers (100 women and 105 men) having a mean±SD age of 63±10.47 years (87 men and 118 women), out of which 51 had CVD symptoms. The mean±SD lying systolic blood pressure was 85±9.43 and the lying diastolic blood pressure was 144±16.58 mmHg.

Figure 1a) illustrates an example of automated IMT segmentations of the left CCA (IMT_{mean} = 0.71 mm, IMT_{max} = 0.9 mm, IMT_{min} = 0.55 mm, IMT_{median} = 0.65 mm), and the right CCA) (IMT_{mean} = 0.45 mm, IMT_{max} = 0.52 mm, IMT_{min} = 0.11 mm, IMT_{median} = 0.21 mm) in Fig. 1b) respectively. It is shown that for this example left and right IMT measurements of the CCA are different.

Table I illustrates the automated segmentation results for the mean, maximum, minimum, and median IMT values in mm performed on the normalized despeckled images of the left and right CCA and the corresponding manual IMT left and right measurements performed by the vascular expert. The mean±standard deviation left and right IMT manual measurements were 0.79±0.21 mm and 0.76±0.33 mm, whereas the corresponding mean±standard deviation left and right IMT automated measurements were 0.70±0.15 mm and 0.66±0.15 mm, respectively.

Table II presents the results after performing the non-parametric Wilcoxon rank sum test between the left and right CCA as well as between manual and automated segmentation measurements. We found no statistical significant differences between the left and right CCA sides IMT measurements (for both the manual and automated measurements), as well as between the manual and the automated IMT measurements. The Spearman correlation coefficient, ρ, between the left and right automated IMT measurements was ρ=0.54 and between the left and right sides automated versus manual IMT measurements was ρ=0.67 and ρ=0.31 respectively.

Figure 2 presents box plots for the left and right CCA sides IMT manual ($IMTL_m$, $IMTR_m$) as well as for the IMT left and right automated (IMTL, IMTR) measurements.

TABLE I
MEAN, MAXIMUM, AND MINIMUM (STANDARD DEVIATION) AND MEDIAN (INTER QUARTILE RANGE, IQR) VALUES FOR THE MANUAL AND AUTOMATED IMT MEASUREMENTS FOR THE LEFT AND RIGHT CCA.

	Mean (mm)	Maximum (mm)	Minimum (mm)	Median (mm)
Left side CCA				
IMT_{manual}	0.79(0.21)	0.85(0.22)	0.41(0.24)	0.74(0.20)
$IMT_{automatedd}$	0.70(0.15)	0.84(0.19)	0.55(0.14)	0.70(0.17)
Right side CCA				
IMT_{manual}	0.76(0.33)	0.85(0.22)	0.44(0.19)	0.71(0.21)
$IMT_{automated}$	0.66(0.15)	0.79(0.18)	0.52(0.13)	0.66(0.16)

TABLE II
IMT LEFT AND RIGHT MANUAL AND AUTOMATED SEGMENTATION COMPARISONS BASED ON THE WILCOXON RANK SUM TEST AT P<0.05

Left vs Right	
Manual	NS(0.44)
Automated	NS(0.82)
Manual vs Automated	
Left CCA	NS(0.19)
Right CCA	NS(0.23)

p-values are given in parentheses. NS indicates Non-Significant difference.

IV. Discussion

The results of this study showed that the left CCA IMT is thicker than the right CCA IMT. However, no statistical significant differences were found between the left and the right IMT sides of the CCA and between the automated and the manual measurements for both CCA sides. The study showed that is enough to measure only one side of the CCA. Our IMT automated measurement results performed in this study are consistent with the studies in [7] and [11], where also similar findings were reported.

More specifically, in [7], 98 healthy adults with a mean age of 28 years underwent blood tests to evaluate various CVD risk factors as well as automated ultrasonic measurements of their CCA IMT on both sides. No significant difference was noted between the IMT on both sides. (left IMT: 0.625±0.078 mm, right IMT: 0.626±0.075 mm). In other studies [8]-[11], as well as in the present study (left IMT=0.70±0.15 mm, right IMT=0.66±0.15 mm) an increase of IMT on the left CCA in older individuals was found. This was not the case in [7], where a group of young and relatively healthy adults were investigated.

In [11], 447 people were assigned into six age groups and their left and right IMT as well as other hemodynamic parameters were measured. It was shown that the left CCA IMT was thicker than the right between the ages of 35 and 65 years old. In [12], correlations between the left and right CCA side were investigated in 149 patients with coronary artery disease. It was also shown that the left and right CCA IMT exhibited different predictive values on CVD events, suggesting differential correlations between the two different sides with CVD risk factors and clinical outcomes.

Furthermore, in [19] the presence of vascular risk factors and correlates of the IMT with the degree of the distal internal carotid stenosis and the proximal CCA resistive index were investigated in 1655 patients. Significant side differences were found with higher IMT on the left side (0.97±0.21 mm) versus the right side (0.95±0.19 mm). The results in [19], confirmed the relation of vascular risk factors with age being the most relevant. Additionally increased wall shear stress was noted in the left side of the CCA. It is documented in [20] that the IMT progression accelerates in the elderly and therefore could account for the difference in IMT seen at older ages that are non-existent in younger patients.

Some limitations of the proposed method include the presence of acoustic shadowing together with strong speckle noise, which hinders the visual and automatic analysis in ultrasound images. Such images, with bad visual perception, were neither included in this study nor were they delineated by the experts [4]-[7], [13], [14], [16]. We have also excluded from our segmentation experiments images with extensive echolucency and calcification. Furthermore, the estimation and positioning of the initial snake contour may sometimes result to segmentation errors. This should be placed as close as possible to the area of interest otherwise it may be trapped into local minima or false edges and converge to a wrong location. In the present study in less than 3% of the cases the positioning of the initial snake contour was not calculated correctly. Furthermore, only vessels without atherosclerotic plaques were segmented in this study.

Additionally, the study should be further applied on a larger sample, a task which is currently undertaken by our group. Additional variables, such as age, sex, weight, blood pressure and others should be taken into account for predicting future cardiovascular outcomes.

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