ISSN 1392-2114 ULTRAGARSAS, Nr.2(43). 2002.

Ultrasonic measurements of human carotid artery wall *intima*-media thickness

D. Jegelevičius, A. Lukoševičius

Biomedical Engineering Institute of Kaunas University of Technology

Studentu str. 50, Kaunas, LT-3031

Introduction

Sclerotic and ageing changes in all cardiovascular system of human is well reflected by the status and structure of *arteria carotis* [1, 2]. This artery is well accessible by ultrasonic investigation and also is the main vessel supplying blood to the brain. Therefore ultrasonic investigation of *arteria carotis* (AC) has been the target of numerous attempts. Findings in the structure of AC walls are very actual in anticipating of possible changes of coronary arteries, especially when there are no other symptoms of coronary ischemia [3, 4]. AC wall structure and thickness are good indicators for estimation of risk for stroke and myocardial infarction [3]. There are many additional relations established between AC state from one side and diabetes, high blood pressure, early sclerosis, overweight and other pathologies from the other [5, 6].

The main changes in AC can be observed in the wall structure, which in its turn can be roughly divided into inner layer, contacting with blood (*intima*), middle layer of the wall (*media*) and outer layer (*adventitia*). *Intima* and media thickness (IMT) is recognised to be one of the most informative parameters for differential diagnosis.

Changes in thickness are observed well in advance of sclerotic plaque appearance, thus enabling early diagnosis of sclerosis [7]. Sclerotic damage of vascular system manifests itself by thickening of *intima* layer which is thin for young and healthy persons. *Media* of the AC wall consists mainly from spiral fibres of muscles and also is dependent on ability of arteria to support the blood flow and to react on stress factors.

Ultrasonography of AC including measurement of *intima* and media thickness is a good mean for ischemic disease prediction, diagnosis and treatment control [8, 9].

The main problem in diagnostics of the state of AC is insufficient precision of *intima* and media thickness measurements, since this defines all diagnostic reliability. Two layers are to be clearly separated because high blood pressure causes thickening (hypertrophy) of *media*, while arteriosclerosis causes hypertrophy of *intima*. For differential diagnosis therefore is very important clear distinction of two layers as well as accurate measurement of absolute thickness.

Structure of carotid artery and acoustical model

Prior to ultrasonic investigation of structure of AC walls anatomical structure should be related to the acoustical model. Ultrasonic echoscopy is based on reflection and scattering of incident ultrasonic pulses by changes of acoustical impedance of the object under investigation. Relation between anatomic and acoustic layers (changes in acoustic impedance) was established in [10, 11] and potential possibility to measure thickness was proven.

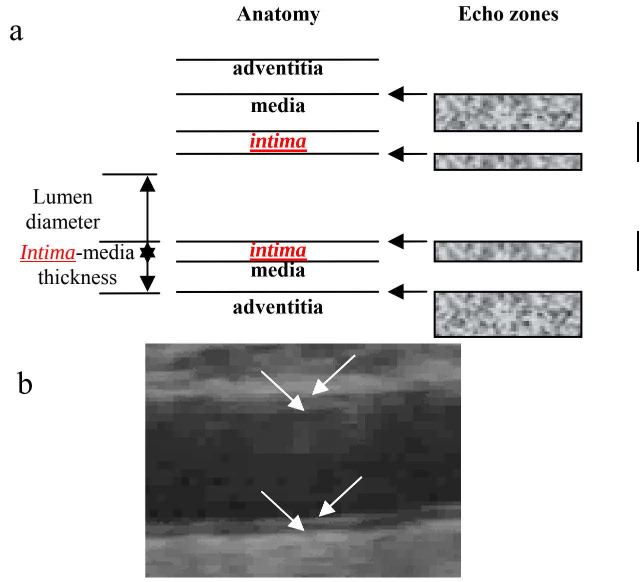

Fig. 1. **Correspondence of anatomical structure of AC to the zones of acoustic reflections: a - scheme of AC anatomy and ultrasound image echo zones; b - typical B-scan image of AC. White arrows corresponds to the black ones on a**

Since an ultrasonic transducer beam hits the artery from one side (supposedly from the top of Fig.1), zones of *andventitia*, *media*, *intima* consequently causes reflections. More convenient for thickness measurements are the AC wall on the far side from the transducer. In this case reflections from the boundaries blood-*intima* and *media*-*adventitia* (elastic outer layer of the artery) are taken into consideration (see Fig.1.). Of course, both walls can be measured simultaneously, or with the use of the high frequency transducer can be effectively used near wall of artery. The far wall has better reflections due to the interface blood–*intima*-*media*-*adventitia* acoustics impedance sequence, what is seen in Fig. 1.

Common AC (before it's bifurcation on it's upper end) is accessible within about 10 cm along the artery. Therefore longitudinal variances of *intima-media* thickness can be measured or (with some assumptions) longitudinal information can be used for averaging of measurement results. Anyway repeatable measurements give the possibility to raise the accuracy [12]. The general purpose echoscopy systems are usually used for the arteria carotis examinations. It is because transducers of these systems are suitable for such investigations. The 7-8 MHz linear scanning transducers are usually used for carotid artery examinations. Both A and B scanning methods can be used for ultrasonic investigations. B scan is used more frequently, since it gives overall view of the artery and general picture can be obtained for a quite long segment of the vessel.

Median population values of *intima-media* thickness range between 0.4 – 1.0 mm [10]. IMT is thickening with age with 0.01 to 0.3 mm per year. The theoretical axial resolution of a 7 MHz transducer is about 0.3 mm. If IMT is thinner than 0.3 mm, the two echo interfaces cannot be clearly separated. If IMT is thicker than 0.3mm, thickness can be measured directly. Images acquired with Toshiba PV ultrasound scanner with linear 7.5MHz transducer were used for measurements in our study. One image pixel in the digitised ultrasound image (in our case) has the size 0.1x0.1 mm. Maximal deviation from the true value will be half a pixel, or 0.05mm. But due to the measurements in pixel pairs, maximal deviation from the true distance will therefore be 0.1mm. To increase the precision of measurements, the more than one pair of pixels on the *intima-media* boundaries should be marked. It is common to use the average result of IMT measurement of the 10mm section of the carotid artery. In the case of manual selection of *intima-media* points, 10 pairs of measurements can be performed. By interpolating these points 100 boundary points can be obtained in 10mm artery segment (see Fig.2). Such a measurement theoretically decreases the error by $\sqrt{N}$, where N is a number of independent measurements. The precision increases when more than one image from an arterial segment is recorded and a mean value is calculated (in this way potential measurement error of 0.005 mm could be achieved in ideal conditions [12]).

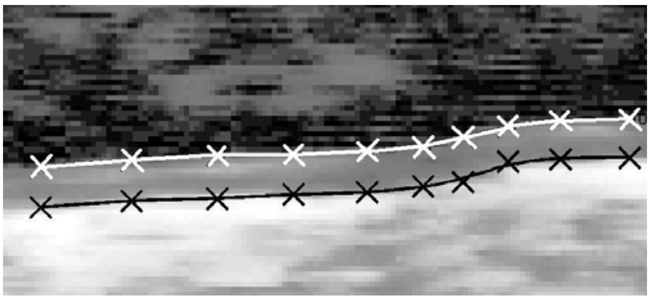

Fig.2. **Interpolation of measurements results**

Overall thickness of *intima* and *media* layers is the most important diagnostic parameter. However thickness of separate layers would be useful for some kinds of pathology differentiation. Since boundary between *media* and *intima* isn't well distinctive in terms of acoustic parameters, in most cases *intima-media* layer thickness is concerned only.

The aim of the present study is to choose and analyse the accurate and reliable method for *intima-media* thickness measurement by use of B-scan images.

Comparative analysis of measurement methods

Measurements can be performed by the physician “by hand”, using conventional means of scales. Most of scanners also have possibility to fix “by hand” special markers and to measure distance between markers.

The most advanced is the method of automated measurements, possibly with some elements of interactivity with physician. Therefore special graphical user interface (GUI) is needed. IMT measurement is performed automatically tracing *intima-media* boundaries and then subtracting *y* coordinates of curves, corresponding to the boundaries.

Four main algorithms could be distinguished from several automatic methods used for the carotid artery *intima-media* thickness measurements [13]:

- Dynamic programming;
- Maximum gradient;
- Model based;
- Matched filter.

The dynamic programming algorithm is an optimization of the cost function by finding optimal polyline, corresponding to artery boundary. The cost function is a weighted sum of echo intensity, intensity gradient and boundary continuity cost terms at each image pixel.

The maximum gradient algorithm searches intensity image along a path perpendicular to the boundary and picks up the point of maximum gradient for measurement.

The model based algorithm fits a parameterized model to the image intensity profile in a direction perpendicular to the approximate boundary.

The matched filter algorithm cross-correlates a reference profile, or template, with the intensity profile in the direction perpendicular to the boundary.

In Table 1 the features of the algorithms are presented for comparison. Here you can find some parameters, subjectively ranked in sequence order. The parameters are:

- Accuracy, defined as the correlation between manually obtained reference values and automated IMT measurements;
- Variability between manual and automated IMT measurements;
- Computational complexity;
- Amount of training required to perform the measurement.

Table 1. **Comparison of the IMT measurement algorithms features (according to [13]):**

	Dynamic programming	Maximum gradient	Model-Based	Matched Filter
Correlation	Highest	High	Lowest	Moderate
Inter Method Variability	Smallest	Low	Highest	High
Computation Complexity	Moderate	Moderate	High	Low
Amount of training	Moderate	None	Moderate	Moderate

The best results have been shown by the dynamic programming algorithm. This algorithm has highest correlation to the manual measurements and smallest inter method variability. The second best method could be evaluated to be the maximum gradient method. It requires no training and computation complexity is lower than for dynamic programming.

The comparison of algorithms impose that combination of best features of most advanced algorithms is most reasonable way for further development.

Development of measurement algorithm

Three algorithms for the far wall *intima-media* boundaries detection were composed, implemented and evaluated. Two algorithms are semi-automatic. They require user interaction specifying the region for the artery analysis and to set up the reference points on the *intima-media* interface. Methods are based on the variations of dynamic programming and maximum gradient algorithms. The third implemented algorithm was with the use of manual boundaries selection. The manual measurements were performed for comparison with automated ones. One reference image was used for evaluation of all algorithms on the 10 mm length carotid artery wall.

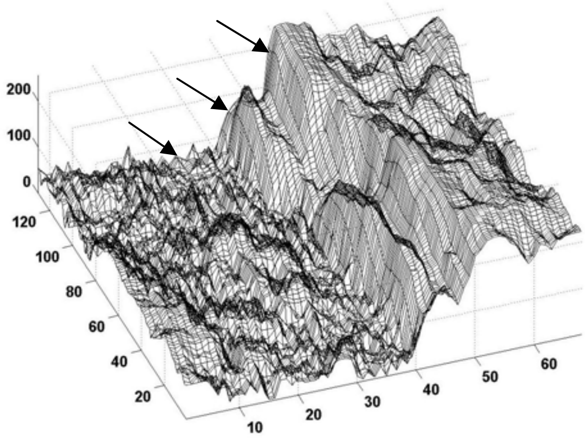

Fig. 3. **Ultrasound image 3D view of the carotid artery far wall**

As seen in the ultrasound B images (Fig.1), the *intima-media* is recognized as middle step of intensity from three intensity steps in the image (Fig.3). These steps are indicated by the derivative of image amplitude (see Fig.4, a, - derivative (or gradient) in y direction is presented here). Generally we'll use image gradient properties for IMT measurements too. The image gradient amplitude is defined as:

$$|\nabla f(x,y)| = \sqrt{(\partial_x f(x,y))^2 + (\partial_y f(x,y))^2}\ , \qquad (1)$$

where $\partial_x f(x,y)$ and $\partial_y f(x,y)$ are image gradients (derivatives) in x and y directions.

The first algorithm, what we call "live-wire" [14] algorithm, is based on finding a local minimum of the cost function for the each pixel of propagating "wire" from one reference point to another. So, the first step is to place reference points on the image (see Fig.5,- white and black crosses). Reference points are placed by hand and they are snapped to the local (size of 5x5 image pixels) image gradient maximum. Then the boundaries outlining begins. The search of the boundaries begins automatically from the

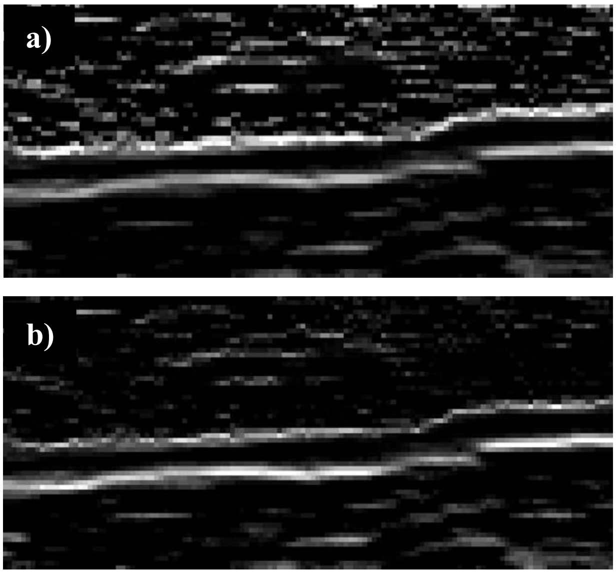

Fig. 4. **Gradient image of the carotid artery far wall: a gradient of image in vertical direction; b image in a, multiplied by intensity image**

first reference point, calculating local image pixels costs the from current point p to all directions (i.e. to points q) and choosing one point with the smallest cost value (see Fig.6). By this algorithm is consequently tracking of the chosen boundary performed. The local cost function consists from the following feature costs: image gradient amplitude value, gradient direction and distance from the point p to the next reference point:

$$l(p,q) = k_G \cdot f_G(q) + k_D \cdot f_D(p,q) + k_{DIS} \cdot f_{DIS}(p,q)\ . \qquad (2)$$

Here each k is the weight of the corresponding feature of the cost function. Values of these coefficients can be determined empirically (as we have done) or can be the object of optimisation. Using multiple images recorded for AC we have chosen k_G=0.6, k_D=0.1 and k_{DIS}=2.5.

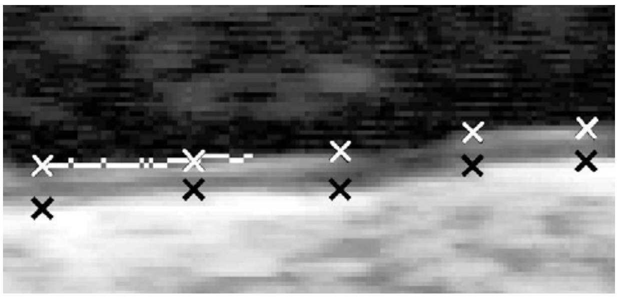

Fig. 5. **Reference points and the propagating "live-wire" on the carotid artery wall image**

The gradient magnitude feature, f_G is scaled and inverted using an inverse linear ramp function:

$$f_G = 1 - \frac{|\nabla f(x,y)|}{\max(|\nabla f(x,y)|)}\ . \qquad (3)$$

The gradient direction f_D feature cost associate a high cost for sharp changes in the boundary direction [14].

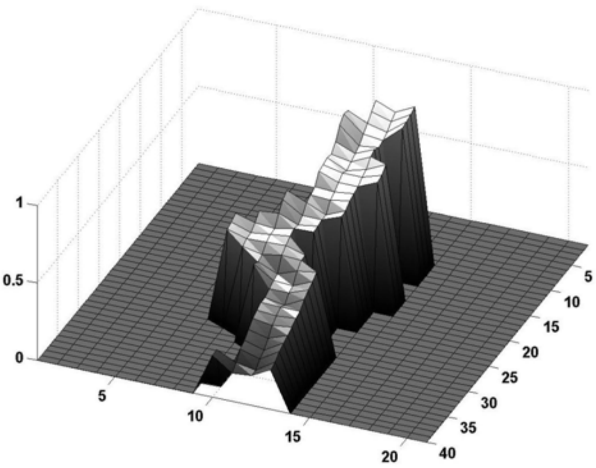

Fig. 6. **“Live-wire” goes down from “local costs hill”**

The feature of the distance from current point to next reference point f_{DIS} is the distance $d(x,y)$, normalized to the distance between reference points L:

$$f_{DIS} = \frac{d(x,y)}{L}. \qquad (4)$$

Second algorithm is based on the maximal gradient findings. The reference points are placed in the middle of the *intima-media* layer (see Fig.7 black crosses). Then the points are connected by lines and the scanning of the image line by line in horizontal direction is performed. The gradient of the each vertical line is calculated. For reducing speckle-like noise in the image of gradient in y direction we multiply it by the original intensity image (see Fig.4, a, b). *Intima-media* layer boundaries are searched for local maximums of image line’s gradient to the left and to the right from the predefined middle line (Fig.8). The boundaries are located as local maximums of image profile gradient curve to the left and to the right from the reference line (central vertical line on the Fig.8).

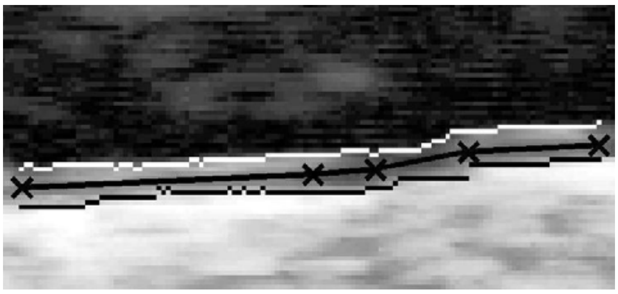

Fig. 7. **Reference “middle” line for neighbouring maximal gradient search and findings of the algorithm**

Manual IMT measurements with the use of **third algorithm** were performed labelling by hand 10 pairs of points (top and bottom of the *intima-media* layer) and then interpolating between them (see Fig.2). Then labelling points, first the upper boundary is selected and then the algorithm places the marker exactly at the same horizontal position for each point. Here the user should mark *media-adventitia* boundary of the wall in a vertical direction with no care to the horizontal marker placement.

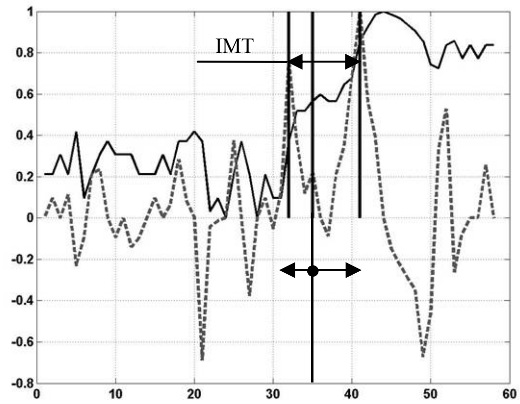

Fig. 8. **Finding boundaries of the *intima-media* layer in the profile of the image. Solid curve - image profile; dotted curve - image profile gradient multiplied by profile; central vertical line - reference line. Arrows shows boundaries search directions**

Implementation and measurement results

The graphical user interface for measurements was designed in Matlab programming environment (Fig.9). The interface enables easy management of images under investigation, pointing markers, choosing the processing algorithm, setting appropriate parameters and running measurements algorithms. The design of the interface is intended to meet the needs of a clinical physician and also can be used for adjusting of measurement algorithms. It is good to have it for algorithms evaluations purposes and going forward real program design. It could be modified quite simply in Matlab environment and there is no need to transfer Matlab algorithms to other programming languages.

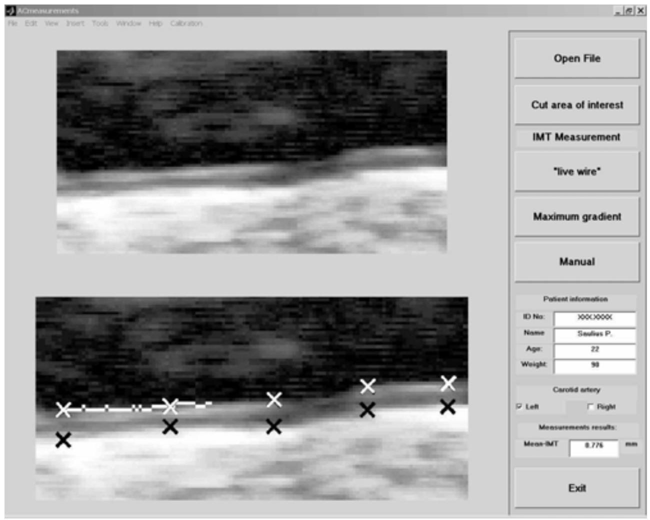

Fig. 9. **Graphical user interface for carotid artery far wall *intima-media* thickness measurements (implemented in Matlab)**

The measurement results for all three developed algorithms are presented in Table 2 for comparison. The mean IMT value and standard deviation along 10 mm artery wall from 22 measurements were calculated. Means of the standard deviations of each measurement were calculated also.

Table 2. **Comparison of the implemented algorithms for repeatable measurements of the same image (n=22)**

Method	Mean±standard deviation, mm	Mean standard deviation of measurements, mm
Manual	0.774±0.022	0.052
“Live-wire”	0.728±0.007	0.082
Maximal gradient	0.753±0.003	0.086

To increase accuracy and repeatability of measurements the artery wall orientation should be taken into a count and corrections of IMT must be done. For such a correction the orientation of the *media-adventitia* boundary to the horizontal direction should be used. This boundary is taken to be reference boundary, because it is closer to the outer of the artery wall and is more stable then the blood-*intima* boundary, where *intima* is thickening to the blood side. The correction is done in this way:

$$IMT_{Corrected} = IMT \cdot \cos(\arctan(\partial_y B_{m-a})), \qquad (5)$$

where B_{m-a} is the media-*adventitia-boundary* curve. It was not used in our calculations because it does not have influence to the results in the case of one image measurements comparison.

Discussions

As we see in Table 2, the measurement results obtained by three methods differ a little. As was supposed, manual tracing of the *intima-media* layer boundaries gives higher deviation of results or is less repeatable. The most repeatable is the maximal gradient method. It seems, that manual tracing gives a more stable thickness result (as shows mean standard deviation of measurements). It could be explained as a subjective factor of a measuring person to select the comparable thickness. Our “live-wire” method gives less reproducibility compared with the maximal gradient. It seems that implemented method is more sensitive to the image noise and to the reference points position. Depending on a ultrasonic image quality, automated methods IMT tracing results can require manual corrections.

It could be concluded that automated algorithm for IMT measurements is preferable for monitoring patient’s carotid artery state. It gives better reproducibility of results and is less time-consuming. Different *intima-media* boundary finding algorithms can give different results of IMT and for large volume monitoring the same measuring methods should be used or comparative studies should be done. We prefer to use maximal gradient algorithm for IMT measurements.

Acknowledgement

We are thankful to MD J. Marcinkevičienė from Kaunas Medical University Clinics Cardiology Department for ultrasonic images of artery carotis.

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D. Jegelevičius, A. Lukoševičius

Ultragarsiniai žmogaus miego arterijos sienelės *intima*-media sluoksnio matavimai

Reziumė

Straipsnyje aprašytos žmogaus miego arterijos sienelės *intima-media* storio (IMS) matavimo ypatybės. IMS matavimams naudojami ultragarsiniai arterijos carotis B vaizdai. Apžvelgti monitoringo matavimams paspartinti bei tikslumui padidinti naudojami automatizuoti matavimo metodai. Realizuoti ir palyginti trys matavimo algoritmai. Matavimams Matlab aplinkoje atlikti pasiūlyta naudoti IMS nustatymo maksimalaus gradiento metodą bei vartotojo interfeisą.

Pateikta spaudai 2002 06 17

DOI: 10.5755/j01.u.43.2.8123