AM-FM Texture Image Analysis of the Intima and Media Layers of the Carotid Artery

Christos P. Loizou*, Victor Murray, Marios S. Pattichis, Christodoulos S. Christodoulou, Marios Pantziaris, Andrew Nicolaides, and Constantinos S. Pattichis

Department of Computer Science, School of Sciences, Intercollege, P.O. Box 51604, CY-3507 Limassol-Cyprus
loizou.c@lim.intercollege.ac.cy, vmurray@ieee.org, pattichis@ece.unm.edu, cschr2@ucy.ac.cy, pantzari@cing.ac.cy, andisnicolai@gmail.com, pattichi@ucy.ac.cy

Abstract. The purpose of this paper is to propose the use of amplitude modulation-frequency modulation (AM-FM) features for describing atherosclerotic plaque features that are associated with clinical factors such as intima media thickness and a patient's age. AM-FM analysis reveals the instantaneous amplitude (IA) of the media layer decreases with age. This decrease in IA maybe attributed to the reduction in calcified, stable plaque components and an increase in stroke risk with age. On the other hand, an increase in the median instantaneous frequency (IF) of the media layer suggests the fragmentation of solid, large plaque components, which also lead to an increase in the risk of stroke. The findings suggest that AM-FM features can be used to assess the risk of stroke over a wide range of patient populations. Future work will incorporate a new texture image retrieval system that uses AM-FM features to retrieve intima and intima media layer images that could be associated with the same level of the risk of stroke.

1 Introduction

Atherosclerosis causes enlargement of the arteries and thickening of the artery walls. Thus clinically the intima-media thickness (IMT) is used as a validated measure for the assessment of atherosclerosis [1,2] (see Fig. 1). It was proposed but not thoroughly investigated [3], that not only the IMT but rather the media-layer (ML), its thickness [4,5] its textural characteristics [3], and amplitude modulation-frequency modulation (AM-FM) [6] characteristics may be used for evaluating the risk of a patient to develop a stroke and account in general the risk of the cardiovascular disease (CVD) by differentiating between patients at high and low risk for stroke. The objective of this study is to investigate the application of amplitude-modulation frequency-modulation (AM-FM) analysis of intima media complex (IMC), media layer (ML), and intima layer (IL) of the common carotid artery

* Corresponding author.

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(CCA). Only one study [7] investigated AM-FM representations of the atherosclerotic carotid plague of the CCA but not for the IMC, IL, and ML.

As shown in Fig. 1, the IL is a thin layer, the thickness of which increases with age, from a single cell layer at birth to $250\mu m$ at the age of 40 for non-diseased individuals [8]. In ultrasound images the media layer (ML) is characterized by an echolucent region, predominantly composed of smooth muscle cells, enclosed by the intima and adventitia layers (see Fig. 1, band Z6) [2,9]. Earlier research [10], showed that the media layer thickness (MLT) does not change significantly with age ($125\mu m <$ MLT $< 350\mu m$). In recent studies by our group the median (IQR) of IMT, MLT and intima layer thickness (ILT), were computed from 100 ultrasound images from 42 female and 58 male asymptomatic subjects aged between 26 and 95 years old, with a mean age of 54 years to be as follows $0.66mm$ (0.18), $0.23mm$ (0.18), $0.43mm$ (0.12) respectively [3,4,5].

In [11] a method has been presented for quantifying the reflectivity of the ML of the distal CCA. It was shown that the GSM of the intima media layer is the earliest change representing atherosclerotic disease in the arterial wall that can currently be imaged in vivo. This may be the first marker of atherosclerosis and may precede the development of a significant increase in IMT. This would enable earlier identification of high-risk individuals based on the analysis of the CCA artery wall textural and AM-FM characteristics. In [12] the authors reported on the properties of the GSM of the IMC from a random sample of 1016 subjects aged exactly 70. They found that the GSM of the IMC of the CCA is closely related to the echogenecity in overt carotid plaques.

There are several studies reported earlier suggesting that the instability of the carotid atheromatous plaque can be characterized from B-mode ultrasound images [9,13]. In [9,13] the echogenecity in atherosclerotic carotid plaques was evaluated through the GSM, where as in [3] the IMC the ML, and IL were characterized based on texture feature analysis. It is evident from the visual inspections of the IMC in the CCA that a great variation in echogenecity does exist. However, the usefulness of this information has not yet been studied.

We propose to study changes in AM-FM characteristics that can be associated with disease progression for different age groups and different gender. Here, we note that for fully developed plaques in the CCA, texture features derived from statistical, model based, and Fourier based methods, have been used to characterize and classify carotid atheromatous plaques from B-mode ultrasound images [13].

To the best of our knowledge no other study carried out ML and IL ultrasound AM-FM measurements for investigating their relationship with the increase of age and gender, and the risk of stroke based on their AM-FM characteristics. We do note that the best known (related) results were presented in [14,15] where it was shown that IMT increases linearly with age.

The objective of our study is to investigate whether AM-FM characteristics extracted from the IMC, the ML, and the IL of the CCA, segmented manually by an expert and automatically by a snakes segmentation system [5,16] can be associated with the increase of IMT, MLT or ILT and how these are affected by

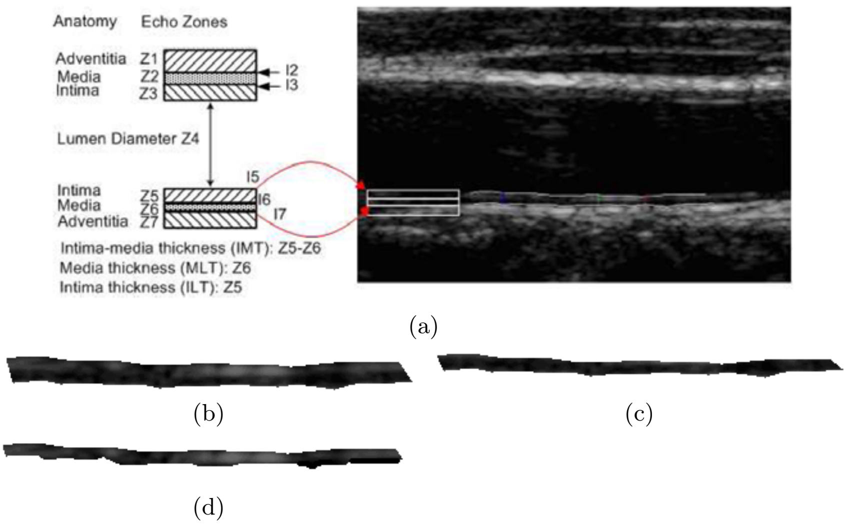

Fig. 1. (a) Illustration of the intima-media-complex (IMC) of the far wall of the (b) common carotid artery and the automatic IMC segmentation [4,16]. The media layer (ML) is defined as the layer (band) between the intima-media and the media-adventitia interface (band Z6), (c) extracted automated IMC, (d) extracted automated media layer (ML) and e) extracted automated intima layer (IL).

age and gender. Ultimately, AM-FM characteristics that vary with age, gender, or IMT, MLT or ILT might be used to assess the risk of stroke.

The paper is organized as follows. In Section 2, we provide materials and methods for the current study. Results are given in Section 3. We provide discussion in Section 4, and give concluding remarks in Section 5.

2 Materials and Methods

2.1 Recording of Ultrasound Images

A total of 100 B-mode longitudinal ultrasound images of the CCA were recorded using the ATL HDI-3000 ultrasound scanner (Advanced Technology Laboratories, Seattle, USA). For the recordings, a linear probe (L74) at a recording frequency of 7 MHz was used. Assuming a sound velocity 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 $0.11 mm$ [16]. 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 $0.06 mm$). Furthermore, the images were normalized as described in [17]. The grayscale-normalized image was obtained through algebraic (linear) scaling of the image 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. The images were partitioned into three different age groups. In the first group, we included 27 images from patients who were younger than 50 years old. In the second group, we had 36 patients who were 50 to 60 years old. In the third group, we included 37 patients who were older than 60 years old.

2.2 Manual Measurements

A neurovascular expert manually segmented (using the mouse) the IMC [16] the ML, and IL [4,5] on each image after image normalization by selecting 20-40 consecutive points for the adventitia, media and intima at the far wall. The measurements were performed between $1-2cm$ proximal to the bifurcation of the CCA, on the far wall [2], over a distance of $1.5cm$. The bifurcation of the CCA was used as a guide and all measurements were made with reference to that region.

2.3 IMC, ML and IL Snake Segmentations

All images were automatically segmented to identify the IMC, ML, and IL regions. Automatic segmentation was carried out after image normalization using the snakes segmentation system proposed and evaluated on ultrasound images of the CCA in [4,5,16]. The segmentation system is based on the Williams & Shah method [18]. Using the definitions given in Fig. 1, we first segment the IMC [16] by extracting the I5 (lumen-intima interface) and I7 boundaries (media-adventitia interface). The upper side of the ML (see Fig. 1, Z6) was then estimated by deforming the lumen-intima interface (boundary I5) by $0.36mm$ (6 pixels) downwards and then deformed by the snakes segmentation algorithm proposed in [16] in order to fit to the media boundary.

2.4 Amplitude-Modulation Frequency-Modulation (AM-FM) Methods

Two AM-FM estimates were computed from the automated IMC, ML, and the IL segmented regions of interest as follows: a) the instantaneous amplitude (IA) and b) the instantaneous frequency (IF).

The IA models average intensity variations and the IF provide us with information at a pixel level related with orientation variations, or structures in an image region. We use the IF in terms of both its amplitude and its angle. Thus, for each input image we estimate the information about: (i) the IA, (ii) the IF, and (iii) the instantaneous frequency angle. Then, for each of the three AM-FM parameters, we compute the histograms over the IMC, ML, and IL segmented regions.

We consider a multi-scale AM-FM representation of digital non-stationary images given by [19,20]:

$$I\left(k_1,k_2\right) \approx \sum_{n=1}^{M} a_n\left(k_1,k_2\right)\cos\varphi_n\left(k_1,k_2\right), \tag{1}$$

where $n=1,2,\ldots,M$ denote different scales, $a_n\left(k_1,k_2\right)$ denotes slowly-varying instantaneous amplitude (IA) function and $\varphi_n\left(k_1,k_2\right)$ denoted the instantaneous phase (IP). The basic idea is to let the frequency-modulated components

$\cos\varphi_n(k_1,k_2)$ capture fast-changing spatial variability in the image intensity. The IF $\nabla\varphi_n(k_1,k_2)$ is defined in terms of the gradient of the IP: $\nabla\varphi_n(k_1,k_2) = (\partial\varphi_n/\partial k_1(k_1,k_2), \partial\varphi_n/\partial k_2(k_1,k_2))$.

For a single-scale AM-FM representation ($M = 1$ in (1)), the IA and the IP are estimated using [21]:

$$\hat{a}(k_1,k_2) = |\hat{I}_{AS}(k_1,k_2)| \text{ and} \tag{2}$$

$$\hat{\varphi}(k_1,k_2) = \arctan\left(\frac{\text{imag}(\hat{I}_{AS}(k_1,k_2))}{\text{real}(\hat{I}_{AS}(k_1,k_2))}\right), \tag{3}$$

respectively, where $\hat{I}_{AS}(k_1,k_2)$ is an extended version of the one-dimensional analytic signal computed with $\hat{I}_{AS}(k_1,k_2) = I(k_1,k_2) + j\mathcal{H}_{2d}[I(k_1,k_2)]$, where $\mathcal{H}_{2d}$ denotes a two-dimensional extension of the one-dimensional Hilbert transform operator.

The IF is computed using a variable spacing, local quadratic phase (VS-LQP) method as described in [19,20]:

$$\frac{\partial\varphi(k_1,k_2)}{\partial k_1} \cong \frac{1}{n_1}\arccos\left(\frac{\bar{I}_{AS}(k_1+n_1,k_2)+\bar{I}_{AS}(k_1-n_1,k_2)}{2\bar{I}_{AS}(k_1,k_2)}\right), \tag{4}$$

and similarly for $\frac{\partial\varphi(k_1,k_2)}{\partial k_2}$. In (4) $\bar{I}_{AS}(k_1,k_2) = \hat{I}_{AS}(k_1,k_2)/|\hat{I}_{AS}(k_1,k_2)|$, and n_1 is a variable displacement from 1 to 4.

We generate a 96-bin feature vector using the histograms of each of the three AM-FM estimates described (IA, IF magnitude (|IF|), and IF angle, 32-bin each) on the ROI of IMC, ML, and IL segmentations. Additionally, the normal histogram of the ROI of the IMC, ML, and IL segmented regions, was computed for 32 equals width bins used and was used as another feature set for comparison purposes.

2.5 Statistical Analysis

The Mann-Whitney rank sum test (for independent samples of different sizes) was used in order to identify if there are significant differences (SD) or not (NS) between the extracted AM-FM features. For significant differences, we require $p < 0.05$, and compare between age groups. Similarly, for comparing independent samples from equal populations, we use the Wilcoxon rank sum test. We use the Wilcoxon rank sum test to detect AM-FM feature differences between the IL, ML, and IMC, for the automated segmentations. We use regression analysis to investigate the relationship between the IMT, MLT, and ILT and medium IF (MIF) and medium IA (MIA) and age.

3 Results

Fig. 1 illustrates an original normalized ultrasound image of the CCA with the automated segmentation of the IMC in (b) and the extracted automated IMC, ML and IL in (b), (c) and (d), respectively.

Table 1. Comparison between the High, Medium and Low AM-FM features extracted from the IMC, ML, and IL for the automated segmentation measurements based on the Mann-Whitney rank sum test for the three different age groups, Below 50 (< 50), Between 50 AND 60 (50-60) AND Above 60 (> 60) years old

			Automated segmentation measurements for the IA and IF																	
			Instantaneous Amplitude (IA)									Instantaneous Frequency (IF)								
			IMC			ML			IL			IMC			ML			IL		
			<50	50-60	>60	<50	50-60	>60	<50	50-60	>60	<50	50-60	>60	<50	50-60	>60	<50	50-60	>60
Automated Segmentation measurements	High	<50		NS (0.65)	NS (0.65)		NS (0.56)	NS (0.21)		NS (0.77)	NS (0.82)		NS (0.4)	NS (0.69)		NS (0.4)	NS (0.62)		NS (0.64)	NS (0.67)
		50-60			NS (0.15)			NS (0.56)			NS (0.19)			S **(0.001)**			S **(0.044)**			NS (0.79)
		>60																		
	Medium	<50		NS (0.15)	S **(0.014)**		NS (0.18)	NS (0.8)		NS (0.16)	NS (0.89)		NS (0.19)	NS (0.67)		NS (0.34)	NS (0.32)		NS (0.13)	NS (0.34)
		50-60			NS (0.32)			NS (0.69)			NS (0.11)			NS (0.68)			NS (0.79)			NS (0.65)
		>60																		
	Low	<50		NS (0.07)	NS (0.34)		S **(0.033)**	NS (0.16)		NS (0.08)	NS (0.82)		NS (0.76)	NS (0.59)		NS (0.22)	NS (0.46)		NS (0.75)	NS (0.67)
		50-60			S **(0.03)**			NS (0.31)			S **(0.0264)**			NS (0.97)			NS (0.24)			NS (0.35)
		>60																		

IMC: Intima-media complex, *ML*: Media layer, *IL*: Intima layer. The p value is shown in parentheses (*S*=Significant difference at p<0.05, *NS*=Non significant difference at p>0.05).

The measurements were extracted using the automated IMC/ML/IL segmentations.

Regression was also carried out for the media IA and media IF of the ML in order to investigate their relationship with age. It was found that the IA of the ML linearly decreases with age (IAml=0.825-0.00373*age, $p = 0.005$), while the IF of the ML linearly increases with age (IFml=-0.046+0.00178*age, $p = 0.001$).

Table 1 presents a comparison among the high, medium and low AM-FM features extracted from the IMC, ML, and IL for the automated segmentation measurements based on the Mann-Whitney rank sum test for the three different age groups, namely below 50 (< 50), between 50 and 60 (50-60) and above 60 (> 60) years old. It is shown that it is possible to differentiate between the three different structures (IMC, IM, IL) using AM-FM features. The AM-FM features were computed at different frequency scales, considering only horizontal oriented filters, of the three-scale filter bank used: (i) Low frequencies (11.3 to 32 pixels wavelengths), (ii) Medium frequencies (5.7 to 16 pixels wavelengths) and (iii) High frequencies (2.8 to 8 pixels wavelengths). It is shown from Table 1, that there is no single feature differentiating between ML and IL, and between the age groups.

More specifically the following observations are made using the information from Table 1:

1. It is possible to differentiate IMC:
   (a) For the ages < 50 and > 60 years old using medium IA.
   (b) For the ages 50 to 60 and > 60 years old using low IA or high IF.
2. It is possible to differentiate ML:
   (a) For the ages < 50 and 50 to 60 years old using medium IA.
   (b) 15BFor the ages 50 to 60 and > 60 years old using high IF.
3. It is possible to differentiate IL:
   (a) For the ages < 50 and > 60 years old using medium IA.
   (b) For the ages 50 to 60 and > 60 years old using low IA.
4. There is no single feature differentiating between ML and IL, and between the age groups.

4 Discussion

In this study AM-FM of the IMC, ML, and IL of 100 longitudinal ultrasound images of the CCA of asymptomatic subjects were investigated. AM-FM analysis reveals the IA of the ML decreases with age. This decrease in IA maybe attributed to the reduction in calcified, stable plaque components and an increase in stroke risk with age. On the other hand, an increase in the median IF of the ML suggests the fragmentation of solid, large plaque components, which also lead to an increase in the risk of stroke. Our study also showed that the IA high, medium, and low components for the IMC, ML, and IL show an increasing trend from high to low, while the IF high, medium, and low components for the IMC, ML, and IL show a decreasing trend from high to low. The findings suggest that AM-FM features can be used to assess the risk of stroke over a wide range of patient populations.

Our study also showed that the IA high, medium, and low components, for the IMC, ML, and IL show a decreasing trend from high to low, while the IF high, medium, and low components, for the IMC, ML, and IL show a decreasing trend from high to low. It was also shown that the AM-FM features performed slightly better than the traditional texture features and gave better results than simple histogram. It is also shown that almost all AM-FM (expect for the ML) features increase with increasing age.

Texture features analysis was also carried out on the same dataset in another study [3]. It is very important to note that texture features provided complementary information in the discrimination between age groups when compared to the AM-FM features extracted in this study. More specifically, for the ML when comparing the age groups < 50 and 50-60, there is significant difference for the AM-FM IA low component (see Table 1), whereas for the texture features GSM and SS-texture energy laws are significantly different [3]. Also, when comparing the age groups < 50 and > 60 only texture features (GSM, contrast, complexity, coarseness) are significantly different.

It has also been observed that there is an increase in the granularity in association with atherosclerotic disease [22]. A granular IMC indicates more advanced atherosclerosis, which may precede the development of significant IMT thickening. In [11] a method has been presented for quantifying the reflectivity of the IM layer of the distal CCA. It was shown that the GSM of the IM layer is the earliest change representing atherosclerotic disease in the arterial wall that can currently be imaged in vivo. This may be the first marker of atherosclerosis and may precede the development of significant increase in IMT. This would enable earlier identification of high-risk individuals based on the analysis of the CCA artery wall textural characteristics.

In [7] the use of AM-FM representations for the characterization of carotid plaques ultrasound images for the identification of individuals with asymptomatic carotid stenosis at risk of stroke was investigated. To characterize the plaques using AM-FM features, the authors computed (i) the instantaneous amplitude, (ii) the instantaneous frequency magnitude and (iii) the instantaneous frequency angle in order to capture directional information. For each AM-FM feature, they compute the histograms over the plaque regions. The study showed that the AM-FM features performed slightly better than the traditional texture features and gave better results than simple histogram. In previous work [13] on the same problem a large number of features were extracted for the classification of carotid plaques including the traditional texture features, statistical features, and shape.

5 Concluding Remarks

The AM-FM analysis presented in this study was performed on the IMC, ML, and IL, on 100 ultrasound images of the CCA of asymptomatic subjects. It was shown that the (IA) of the media layer decreases with age and that the median instantaneous frequency (IF) of the media layer increases with age. AM-FM analysis reveals the instantaneous amplitude (IA) of the media layer decreases with age. This decrease in IA maybe attributed to the reduction in calcified, stable plaque components and an increase in stroke risk with age. On the other hand, an increase in the median instantaneous frequency (IF) of the media layer suggests the fragmentation of solid, large plaque components, which also lead to an increase in the risk of stroke. The findings suggest that AM-FM features can be used to assess the risk of stroke over a wide range of patient populations. It may also be possible to identify and differentiate those individuals into high and low risk groups according to their cardiovascular risk before the development of plaques. The proposed methodology may also be applied to a group of people, which already developed plaques in order to study the contribution of the ML texture features to cardiovascular risk. Both groups of patients may be benefited by prognosing and managing future cardiovascular events. The use of AM-FM representations will also be utilised in order to provide new feature sets, which can be used successfully for the classification of the IMC, ML and IL structures in normal and abnormal. Future work will incorporate a new texture image retrieval system that uses AM-FM features to retrieve intima and intima media layer images that could be associated with the same level of the risk of stroke.

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