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Study of the Effects of Individual Characteristics on the Vessel Wall Changes using Ultrasound RF Time Series

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Abstract

This study investigates the changes caused by aging on the vessel wall vibrations and changes of acoustic and statistical parameters of the wall tissue using ultrasound radio frequency signals on healthy people of different ages. This study aims to find the vessel wall features discriminating the healthy people from the patients. In this method, the RF signal of the carotid vessel of 31 volunteers was first recorded using echocardiography, and then the raw RF signal was processed using matlab software. Phase tracking method was used to extract the radial movement of the vessel wall. The discrete wavelet transform was used to obtain the low amplitude and high-frequency vibrations. The peak-to-peakamplitude and the dominant frequency are obtained from the vibrations signal. Also, to investigate the changes of acoustic and statistical parameters of the carotid vessel wall tissue, the Nakagami distribution parameters of vessel wall are extracted. To analyze the data, the Pearson correlation test is used. Also, the data is applied to the SVM neural network using the Leave one out cross-validation (LOOCV) to be classified into two classes of young (<50 years) and old (>50 years). As age increases, the peak-to-peakamplitude and dominant frequency of the signal and Nakagami parameters are affected (P<0.05). The vibrations amplitude and dominant frequency of the vibrations signal decrease as the age increases. Also, the Nakagami parameters increase as age increases, and the number of scatterers and the back-scattered power increases. The results of the neural network show that the classification accuracy is 93.5%. Our results raise hopes that the proposed approach may be effective in diagnosing atherosclerosis.

Keywords: Ultrasound RF signal, Carotid vessel, fluctuation signal, Nakagami parameter, Scaling parameter

1. Introduction

Today, one of the main death factors in the world is the heart and brain strokes. In these diseases, the arteries obstruct, the progress symptoms are hidden and do not show up. Today, the threats play a vital role in human life, because they can be present in most daily activities of the human. All threats can be minimized through applying proper management levels. An integrated method with a neutrosophic analytical hierarchy process (N-AHP) and neutrosophic technique has been proposed for this purpose [1]. Changes in the carotid vessel wall like an increase in the wall thickness (intima-media) are the main features of atherosclerosis. The plaques' strength can be estimated using a sclerometer to describe the correlation between plaque strength and the carotid ultrasonography before surgery [2]. Larson et al. used the ultrasound speckle tracking method to estimate the carotid vesselstiffness and atherosclerosis [3]. Optical stream methods have also been used to measure plaque movements and the sheer pressure in one heart cycle [4]. A non-invasive method that studies the mechanical characteristics of the soft tissue called acoustic radiation force imaging has been presented as a new method for detecting plaques [5].

Previous studies show that there is a relationship between changes of the carotid vessel wall with coronary vessel diseases based on the radio frequency signal reflected from the wall [6]. Diameter of the arteries in the systolic phase that blood exits the heart, increases, and decreases in the diastolic phase where blood flows towards the bottom of the vessel tree. Therefore, during the heart cycle, changes in blood pressure and stream move the vessel wall in a radial direction. As a natural operation, the arteries move proportional to their elasticity, and as a result, the stress and strain distribution of the walls change. The official mechanical index of the carotid wall, which is used to study the vessel diseases is the radial movement of the wall [7]. The radial movement of the carotid vessel is estimated quantitatively using image-based methods applied to B-mode images' time-sequence. Tracking the vessel walls' position on the time sequence of the B-mode images for studying the obstruction of the arteries in the hole heart cycle of the B-mode sonography images might be time-consuming. Specific solutions have been proposed to track the position of the vessel walls in B-mode sonography images. One of these solutions is to use the block matching method that updates the reference block using the pixel-oriented Kalman filter [8] and computer edge detection [9].

The phase tracking method was first presented to evaluate the elasticity of one area of the vessel wall [10]. In this method, a small change in the vessel wall can be detected based on its speed estimation accuracy. The vessel movement speed in the radial direction is estimated based on the echos phase-shift, which is related to the change in the bidirectional delay of ultrasound beams between the ultrasound probe and the vessel wall. Eliminating the large movement of the carotid vessel caused by the bloodstream is necessary for extracting the vibrations of low amplitude. In the study conducted by Salehi et al., this parameter is calculated through calculating the time delay generating the maximum mutual correlation between the wavelet transform of the RF signals of two subsequent frames [11]. Wavelet transform is performed using the transferred pulse as the mother wavelet. In this method, after compensating the time delay, the small vibrations can be obtained using the average phase change of the Hilbert transform of the windowed signals of each layer of the vessel wall along the depth of the vessel wall. Yosefi Rizi et al. have presented a novel method based on phase tracking on the continuous wavelet transform of the RF echos to extract the radial movement of the carotid vessel wall. To extract the vessel wall vibrations, which are riding the radial movement, the experimental mode decomposition (EMD) algorithm has been used. Accordingly, the features of the radial movement and the wall vibrations can be used to diagnose the carotid vessel wall stiffness and advanced atherosclerosis, even before the appearance of symptoms and increased thickness of intima-media [12]. Also, in another study, the chaotic characteristics of the vibrations by age are studied. The results indicate that by increase in age and wall stiffness, the vibrations signal becomes irregular and complicated [13].

Some of the proposed methods employ the peak amplitude of the autocorrelation between echos or the phase of the complex autocorrelation function to estimate the wall movement and measure the tissue strain. In the modified phase tracking method presented by Hasegawa et al. in 2006, the vessel wall's instantaneous position is tracked through estimating the wall movement speed [14]. In the prediction method proposed by this group [15], the wall movement speed is estimated based on the phase shift of the echos based on the time delay of the bidirectional ultrasound propagation between the ultrasound probe and the vessel wall. The estimated speeds are integrated to calculate the displacement of the moving vessel wall. The existing phase tracking methods are used to measure the partial changes in the wall thickness and estimate the wall elasticity [16-17].

Most of the methods used to diagnose vessel wall sclerosis are based on B-mode sonography images obtained by demodulating the RF echo signals to calculate the envelope of the RF signal. Therefore, multiple processing steps, including time compensation of the gain, filtering, rectification, and logarithmic compression, should be applied to the RF signals to generate the corresponding B-mode images. Since these steps are performed differently in each sonography device, the images recorded by different devices are not comparable. These processing steps might result in loss of information of the RF signal, which might prevent using the received signal completely for automatic diagnosis. The assumption based on which, we are looking to study the wall is that if the carotid vessel wall becomes stiffness, the wall vibrations change. The above characteristic can be used to diagnose wall stiffness before the intima-media thickness is increased or the elasticity changed. Age increase and the presence of factors that increase the probability of atherosclerosis and other coronary diseases like obesity and high blood pressure increase the risk of vessel wall stiffness that changes the wall vibration speed.

Thus, to achieve a more precise view of the previous studies in the context of RF signals [18-20], we present a novel method based on time-discrete wavelet transform to extract low amplitude, high-frequency vibrations. Also, we study features like peak-to-peakamplitude and dominant frequency of the vibrations, and the Nakagami distribution parameters on the carotid wall vessel to study the changes in acoustic and statistical parameters of the carotid vessel wall tissue.

2. Materials and Methods

2-1. Experimental data

The basis of this study is to use the RF signals, which are raw signals containing all information about the propagation of the acoustic waves in the tissues and the mutual effects of the tissue and the acoustic waves. Before carotid vessel sonography, the individuals are asked to rest for at least ten minutes so that their heart rate and blood pressure become stable. The arrangement of the individuals and the probe should be such that it is ensured that the wall movement is only the result of the bloodstream. While recording, the individuals should sleep on the back with their head at a maximum height of 45^0 and 30^0 towards left (to record data of the right carotid vessel). In each recording, the best image of the movement blood-intima boundaries in M-mode data is tracked for several heart cycles in six seconds. Our effort is to minimize the patient's movements, and the individual is asked to keep his breath and avoid ingestion. In the current study, MyLab™60 (ESAOTE, Italy) equipped with the linear array probe (3-13 MHz) is used where its frame rate is 60 frames per second, and it is connected to a computer for probable processing and recording data. Each data record includes 355 frames, including 6-8 heart cycles, considering the heart rate of the individual. Thus, the right carotid vessel is scanned longitudinally, and the resulting RF signals are converted into matrix data using MATLAB. The matrices are 2526×129×355. The number of sample points in depth is 2526, the number of RF echo lines is 129, and 355 frames are recorded in six seconds for each individual. The RF data of the right carotid vessel of 31 healthy volunteers (19 men and 12 women in the age range of 37.54±14.89) without any coronary diseases, blood pressure, and diabetes is recorded. The characteristics of the subjects are given in Table 1.

2-2. Extracting vibrations of carotid vessel wall

In the proposed method, first, the area of the carotid vessel wall is detected based on two subsequent peaks in the RF echo, indicating the inner and outer sections of the wall. The ROI of the inner or the outer wall is determined depending on whether the inner or the outer wall movement should be estimated. Then, the phase demodulation is carried out using the Hilbert transform. To this end, the signals are substituted in Eq. (1) after applying the Hilbert transform.

Table 1: Characteristics of the human subject population.

Number	31
Age(years)	37.54±14.89
Male (%)	61.3
BMI(kg/m^2)	23.16±2.13
Systolic Blood Pressure(mmHg)	132.45±9.72
Diastolic Blood Pressure(mmHg)	83.90±14.54
Heart Rate(bpm)	77.31±13.91

Data are presented as means±S.D.

$$CC = Max(\sum_{-\frac{k}{2}}^{\frac{k}{2}} |Z_{HIL}(n; x_1(n) + k.\Delta x)|.|Z_{HIL}(n+1; x_1(n) + k.\Delta x)|) \qquad (1)$$

In this study, the phase tracking method based on RF signals is used, which operates based on the phase change of the Hilbert transform of the RF echos received from the two corresponding layers in subsequent frames. In this method, it is assumed that the result of the integral in Eq. (1) is maximum when the correlation of the

Hilbert transform of the two signals is maximum. Therefore, the time delay of the two signals, δ, is calculated using the correlation integral. In this interval, the small phase difference between the two signals is calculated using the phase difference of the Hilbert transform of the two input signals.

$$\Delta\theta_1(n) = \frac{\sum_{-K/2}^{K/2}(\theta_{HIL}(n+1)-\theta_{HIL}(n))}{K} \quad (2)$$

Where $\theta_{HIL}(n)$and$\theta_{HIL}(n+1)$ are the Hilbert transform phase of the two corresponding layers in two subsequent frames, which are convolved to reduce the large difference resulting from phase bounce from π to – π.

The average velocity is described as follows:

$$\hat{v}\left(x,t+\frac{\Delta T}{2}\right) = c_0.\frac{\Delta\theta_1(n)}{2\omega_0\Delta T} \quad (3)$$

By multiplying the obtained velocity by ΔT, the next position of the object, $\hat{x}(t)$, is estimated as follows:

$$\hat{x}(t) = \hat{x}(t-\Delta T) + \hat{v}\left(x,t+\frac{\Delta T}{2}\right).\Delta T \quad (4)$$

Using the next position of the object, $\hat{x}(t)$, and the velocity, $\hat{v}\left(x,t+\frac{\Delta T}{2}\right)$, the position of the object and the vibrations' velocity in a movement with a large amplitude is determined simultaneously.

2-3. The Nakagami Parameter

Among all possible probabilities, the statistical Nakagami distribution has recently attracted attention, because the corresponding Nakagami parameters estimated from the backscattered echos, can be used to detect the returned distributions in ultrasound medical images, and provide the possibility of detecting biological tissues. Since the Nakagami parameters only depend of the statistical distribution structure of the backscattered signal (raw data), this image is less affected by the changes in device operator, and system factors (gain and dynamic range), when only one device is used [21, 22].

The probability distribution function (pdf) of the backscattered ultrasound signals' envelope (R) from Nakagami statistical model, follow the following relationship [21, 23, 24]:

$$f(r) = \frac{2m^m r^{2m-1}}{\Gamma(m)\omega^m}\exp\left(-\frac{m}{\omega}r^2\right)U(r) \quad (5)$$

In which, Γ and U are the Gamma and the unit step functions. r is the possible values for the random variable R about the backscattered envelopes. If E is considered the statistical mean, then the scaling parameter ω and m (Nakagami parameter) are obtained as follows [21,23,24]:

$$\omega = E(R^2)$$

$$m = \frac{[E(R^2)]^2}{E[R^2-E(R^2)]^2} \quad (6)$$

The Nakagami parameter is a function of the concentration of the scatterers, and the scaling parameter describes the mean energy in the backscattered echo, which is calculated by the back scattered signals [21,23,24].

2-4. LOOCV

Since the number of data is low, Leave one out cross-validation method is used to validate data. In the LOOCV method, similar to the Jack Knife sampling method, one observation is extracted from the set of training data, and the parameters are estimated based on other observations. Then, the model error for the extracted observation is calculated. In this method, only one observation is extracted at each step, the times that the process is repeated is the same as the number of the training data. Thus, the time required to calculate the model error is short and can be implemented easily.

3. Results

In this study, a new wavelet transform method is used to extract the vessel wall vibrations with low amplitude and high frequency. The wavelet transform provides the possibility to decompose a signal to its frequency components and determines the times at which these components have occurred. This transform can be represented as a dot product of the signal$x(t)$, and the wavelet function$\varphi_{a,b}(t)$, as follows:

$$W_{\varphi}X(a,b) = < x(t), \varphi_{a,b}(t) > \qquad (7)$$

The mother wavelet function used in this study is db10. The wall movement signal is decomposed, and the approximation and the partial coefficients are obtained. As the wavelet transform coefficients are obtained, the signal is reconstructed in Vj and Wj subspaces. The reconstructed signal is W5 subspace includes high-frequency components of the wall movement (the wall vibrations shown in Figure (1)).

3-1. Peak-to-Peak Amplitude and the Dominant Frequency of the Vibration Signal

To better illustrate the peak-to-peakamplitude of the changes and the dominant frequency of the wall vibrations signal, the relationship between the values of these parameters and the individuals' characteristics using Pearson correlation is shown in Table 2. As shown in Table 2, the peak-to-peak amplitude, and the dominant frequency of the vibrations signal are correlated with age. But these parameters are not correlated with the systolic and diastolic blood pressure and sex.

Also, the linear regression analysis is performed using the age parameter related to the peak-to-peak amplitude and the dominant frequency of the vibration signal. The age parameter is obtained as an independent parameter affecting the peak-to-peak amplitude and the dominant frequency of the vibrations signal.

Since one of the main assumptions in this study is that the dominant frequency and amplitude of the carotid vessel wall vibration decreases as age increases due to wall stiffness, it is studied in two age groups of young and old. The peak-to-peakamplitude is correlated with the age ($p<0.001$), and this value is smaller is elderlies older than 50 years, as shown in Figure (2).

Also, the dominant frequency is correlated with age ($p<0.001$), and it is smaller in elderlies older than 50 years, as shown in Figure (3).

3-2. Nakagami Distribution Parameters

In this section, it is assumed that the number of scatterers and the power scattered back is different in young and old groups, and the effect of the number of scatterers and the power

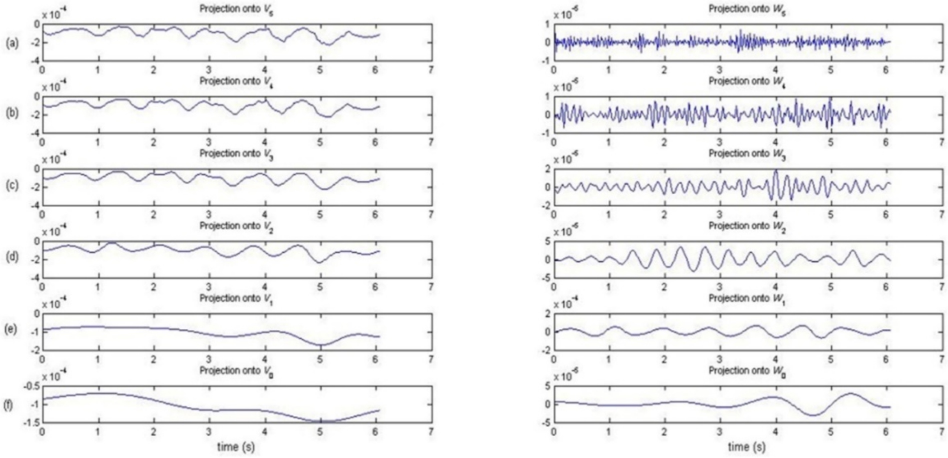

Fig.1. The reconstructed signals in partial subspace *Wj*

Table 2:Relationship of the peak-to-peak amplitude, and the dominant frequency of the vibrations signal with people characteristics.

	Peak-to-Peak amplitude		**Dominant frequency**	
Variables	*r* –value	*p* -Value	*r* value	*p* -Value
Age	-0.475	$6.432\times10^{-6*}$	-0.693	$3.315\times10^{-6*}$
Systolic blood pressure	-0.184	0.432	0.240	0.212
Diastolic blood pressure	0.025	0.327	0.027	0.687
Sex	0.062	0.631	-0.038	0.514

***** $p < 0.00001$

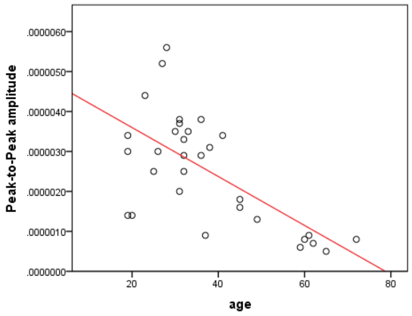

Fig.2. Correlation diagram of the values of peak-to-peak amplitude

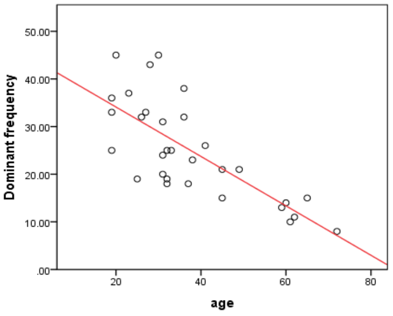

Fig.3. Correlation diagram of the values of dominant frequency

scattered back on the parameters ω and m, is studied. To estimate these two parameters, first, the Hilbert transform on the signals in each line of the obtained frame is calculated and then windows of the same length are used to segment the signal such that an ROI region including the carotid vessel wall is selected and the parameters ω and m are estimated in the region of interest using Eq. (6) and Eq. (7).

The relationship between the parameters ω and m and the individuals' characteristics are evaluated using the Pearson correlation, and the results shown in Table 3 indicate that these parameters are correlated with age. But they are not correlated with systolic and diastolic blood pressure and age.

The values of ω and m are correlated with age ($p<0.001$), and the values are larger in elderlies older than 50 years, as shown in Figure (4).

3-3. Classification

The SVM neural network is used to classify the data into young (<50 years) and old (>50 years). In the LOOCV method, first, one data is used as test, and the rest of the 30 data is used as training data; the process is repeated 31 times. Such that all data is used both as test data and training data, and then their average is calculated. To study the results of the neural network, four parameters of Accuracy (ACC), Specificity (Sp), Sensitivity (Se), and Positive Predictive Value (VPP) are calculated as given in the following:

$$Accuracy(\%) = \frac{TP+TN}{TP+TN+FP+FN} \times 100$$

$$Specificity(\%) = \frac{TN}{FP+TN} \times 100$$

$$Sensitivity(\%) = \frac{TP}{TP+FN} \times 100$$

$$PositiveP\ redictiveV\ alue(\%) = \frac{TP}{TP+FP} \times 100$$

- True Positive (TP) : Correctly detected as elderly (> 50 years) subjects
- True Negative (TN) : Correctly detected as young (< 50 years) subjects

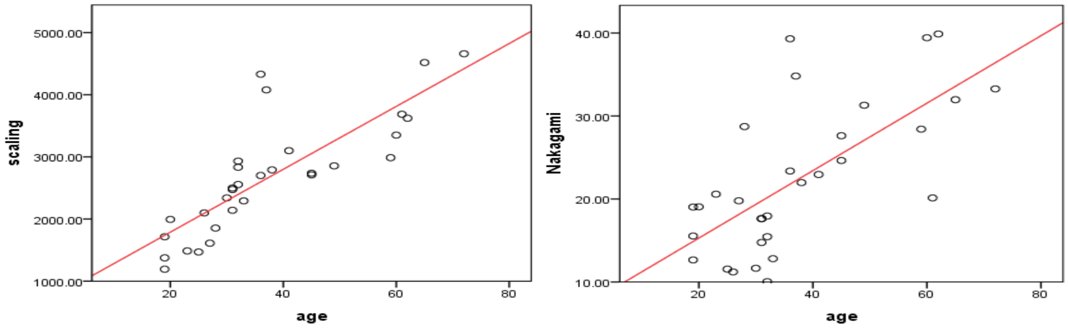

Fig.4. Correlation diagram of the values of scaling and Nakagami parameters

Table 3: Relationship of the Peak-to-Peak amplitude, and the dominant frequency of the vibrations' signals with people characteristics.

	ω		***m***	
Variables	r –value	p -Value	r value	p -Value
Age	0.813	$2.659\times10^{-8*}$	0.678	$2.8\times10^{-5*}$
Systolic blood pressure	0.171	0.321	0.230	0.431
Diastolic blood pressure	0.024	0.567	0.245	0.649
Sex	-0.047	0.615	-0.026	0.731

* $p < 0.0001$

- False Positive (FP) : Incorrectly detected as elderly (> 50 years) subjects
- False Negative (FN) : Incorrectly detected as young (< 50 years) subjects

The results of Acc, Sp, Se, and PPV are given in Table 4.

Table 4:Summarized evaluation results

Method	Acc%	Sp%	Se%	PPV%
LOOCV	93.5	96	83.3	83.3

Besides, the classification results can be seen in the Confusion matrix represented in Table 5. The results show that the accuracy of the neural network in classifying the data into young and old groups based on peak-to-peak amplitude, the dominant frequency of the vibrations, and the parameters ω and m is 93.5%.

Table 5:Confusion matrix

Predicted	**Old (> 50 years)**	**Young (< 50 years)**
Old (> 50 years)	5	1
Young (< 50 years)	1	24

4. Discussion

In the previous studies, age, body mass index (BMI), systolic blood pressure, and lipemia were used as essential parameters which are independently related to elasticity of the carotid vessel elasticity [25-27]. However, the statistics show that half of the people that experience brain stroke and coronary diseases have a normal cholesterol level.

Various studies have been done on the internal wall of the carotid vessel using methods like determining the thickness of the internal carotid wall, determining the vesselstiffness index, elastography of the areas suspicious of stiffness, and wall movement in longitudinal and latitudinal directions to diagnose atherosclerosis and the start of plaque formation in the carotid vessel wall. Previous studies in the context of non-invasive measurement of mechanical characteristics, like elasticity of the vessel walls, are used to diagnose atherosclerosis and vesselstiffness. Because there is a significant difference between the elastic module of the normal vessel wall and a wall affected by atherosclerosis. The purpose of the current study is to extract and evaluate the radial movement and the vibrations of the carotid vessel wall while blood flows, and evaluate the individuals' characteristics on wall movements and vibrations so that they can be used for early diagnosis of carotid atherosclerosis. Since the B-mode sonography images are obtained after multiple processing steps of the RF signal, they contain less information. Thus, in this study, the carotid wall sclerosis is studied regarding the RF echo signals, which contain more information. Although, the large radial movements of the carotid vessel wall present useful information about the vessel health, the carotid vessel wall has vibrations with higher frequency and lower amplitude compared to the radial movements. Since these vibrations are inherently small signal, the changes in characteristics of the vibrations caused by pathogen conditions is superior over larger radial movements of the vessel; this issue has been less investigated in the previous studies. One of the main objectives of this study is to find indicators of changes in the wall vibration signal characteristics instead of changes in the radial movement.

In the following, the factors affecting the carotid vessel wall stiffness, which are usually involved in the brain stroke, age, sex (atherosclerosis mainly occurs in men), systolic and diastolic blood pressure, and heart rate are studied. In this study, the effect of each factor on vibrations of the carotid vessel wall of the volunteers was studied, and the results after studying the time and frequency characteristics of the vibrations indicate that the dominant frequency of the vibrations decrease as age increases. Also, the strength of wall movements at higher frequencies is mainly seen in elderlies, indicating that the wall vibrations of the young people have more components.

Since the corresponding Nakagami parameters are estimated from the backscattered echos, they can be used to detect the backscattered distribution in ultrasound medical images and provide the possibility to detect biologic tissues. To this end, the effect of the number of scatterers and the backscattered power on the scaling and Nakagami parameters in people of different ages is studied. One of the assumptions of this study is that the number of scatterers and the backscattered power is different. The results show that the value of these parameters increases as age, number of scatterers, and the backscattered power increases, and the vessel wall becomes more obvious. Considering the presented results, it can be concluded that the scaling and Nakagami parameters in the Nakagami distribution can be effectively used for diagnosing the wall vesselstiffness.

There were some constraints in extracting the wall vibrations, including the limited frame rate of the ultrasound device. The output recording parameters of this device could not be changed. Some heart cycles were eliminated from the data of each volunteer because of not repeating the heart cycle pattern, which might be due to breathing, swallowing, small movements, or contracting the neck muscles.

5. Conclusion

The purpose of this study is to present a non-invasive method for extracting new features from the carotid vessel wall that might be useful in evaluating the elasticity of the vessel wall and diagnosing atherosclerosis compared to the existing methods. In this study, the potential of RF signals in evaluating the carotid vessel wall changes is represented. To this end, the effect of age on wall characteristics is used. For this purpose, the effect of individuals' age on the peak-to-peak amplitude and the dominant frequency of the vibrations signal and Nakagami parameters of the RF ultrasound echos are used, and it is concluded that these features are correlated with age; as age increases, these parameters also change. Finally, the proposed method might be useful and effective in evaluating the carotid vessel wall in early diagnosis of atherosclerosis.

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