Spectral Analysis of the Left and Right Hand Radial Artery Doppler Signals using the Welch Method to Diagnose Rheumatoid Arthritis Disease

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***Abstract*— In this study, 40 healthy control group and 40 patients with rheumatoid arthritis (RA) and Doppler signal from radial artery of the left and right hand were recorded. This non-parametric Welch Periodogram method to signal attributes of the signs were removed and the artificial neural network (ANN) classification method was utilized in order to recognize diseased and healthy control group individuals. Then, multilayer feed forward ANN trained with a Levenberg - Marquardt (LM) back propagation algorithm was applied to lineament extracted from left and right hand Radial artery Doppler signals for classifying RA disease. The combination of Welch Periodogram method with ANN achieved the classification accuracies of 91.25 % left hand and 90 % right hand Radial artery Doppler signals in the diagnosis of RA disease. Radial artery left hand and right hand for the ROC curves and AUC values were calculated. DAS 28 for RA showing the extent of disease, classification of result values was correlated with each other. The suggested approach in this study is of potential to help with the early diagnosis of RA disease for the specialists who dealing with this subject.**

Keywords—* *Rheumatoid Arthritis, Radial Artery, Welch Periodogram Method, Artificial Neural Networks, Back Propagation Algorithm of LM

I. INTRODUCTION

Rheumatoid arthritis (RA) is defined as an autoimmune disease of unknown etiology which firstly targets the synovial tissue, bone and cartilage [1]. It is a form of inflammatory arthritis with a prevalence of between 0.3 % and 1 % in most industrialized countries [2]. Although RA disease affects people of any age, the peak incidence has been observed for the mid-age range of the working population. Epidemiological studies have shown that RA can shorten life expectancy by around 6 -10 years [3]. Whilst the clinical course of RA is extremely variable, its symptom involved pain, stiffness in the joints and tiredness, particularly in the morning or after inactive periods. It affects the synovial joints, producing pain and eventual deformity and disability. The disease can progress very rapidly, causing swelling and damaging cartilage and bone around the joints. The bones those are mostly affected by RA present in the hand, feet and wrists. RA can also affect the heart, eyes, lungs, blood and skin [3]. The ratio of 2.5:1 indicates that the occurrence frequency of RA in woman is higher than that of RA in men [4].

The Radial artery appears, from its direction, to be the continuation of the brachial, but it is smaller in caliber than the ulnar artery. It starts at the bifurcation of the brachial, just below the bend of the elbow, and passes along the radial side of the forearm to the wrist. Thus, the radial artery is of three portions, first in the forearm, second at the back of the wrist, and third in the hand [5].

The diagnosis of RA disease is still achieved clinically. The clinical diagnostic criteria were established by the American Rheumatism Association in 1987 criteria, and it was revised in 1994 and, they are still applied [6]. Correlations with RA disease severity are of two basic laboratory tests, which are erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) level [7].

The Doppler Effect is utilized in ultrasonic Doppler instruments for the measurement and imaging of blood flow transcutaneous. In these instruments, ultrasonic waves are launched into a blood vessel by an ultrasonic transducer and the scattered radiation from the moving red cells is detected by either the same or a separate transducer. Suitable instrumentation is combined in order to extract the Doppler frequency, which is proportional to the red cell velocity [8]. The rebounded echoes are Doppler shifted. The Doppler shift is related to the flow velocity by.

$$f_{Doppler} = f_t - f_r = \frac{2\upsilon Cos\theta}{c} f_t \quad (1)$$

Where $f_{Doppler}$ is the mean frequency of the Doppler spectrum, f_r is the frequency of the returned echo, f_t is the frequency emitted by the transducer, υ is the flow velocity, θ is the Doppler angle and c is the velocity of sound in blood. For an ultrasound transmitting at frequencies between 1&15 MHz [8], blood flow velocities in the human body constitute Doppler-shifted echo frequencies in the audio range.

The Doppler signals are the reflection of the amount of red blood cells that pass or move in the image plane and the speed with which they pass [9]. For the last decades, Doppler sonography has been widely used in medical practice because of the fact that it provides a noninvasive, convenient and cheap method for measurements of blood velocity and blood flow volume in vessels [10].

Signals power spectral density is estimated by using the method of spectral analysis. By using the Welch Periodogram method time domain, which is a non-parametric method of spectral analysis, Doppler signal is converted into the frequency domain. In addition, ANN is a commonly used method especially in biomedical signal processing. ANN, which is capable of using parallel computing techniques of artificial neurons connected to each other in establishing a relationship between the inputs and outputs, is a system producing complex and nonlinear models [11].

In the literature, it is seen that healthy and RA diseased people who received Doppler ultrasound and magnetic resonance medical imaging devices [12-14]. Studies about using the Doppler signal in the diagnosis of various diseases are also available [15, 16]. Based on this background, the radial artery Doppler signal processing and the artificial intelligence technique applied to the RA in terms of disease diagnosis in our study is a new approach.

As a result, deformation in joint of RA patients leads to variation in vessel structure. Because of affected blood flow velocity in vessel, Doppler signals alternates and features obtained from Doppler signals (Welch Periodogram method) for RA patients and healthy persons show alteration.

II. MATERIALS AND METHODS

A. *Participants and Study Design*

The Radial arterial Doppler ultrasound signals were obtained from the left and right hand Radial arteries of 40 patients with RA diseases and 40 healthy control group volunteers. The healthy control group volunteers involved in 10 males and 30 females, between 44 and 73 years of age, with a mean age and standard deviation of 57 ± 9.1 years. The patients are included 8 males and 32 females, between 38 and 70 years of age, with a mean age and standard deviation of 51 ± 9.6 years [17].

The study was approved by the local ethical committee. Prior to the study, all subjects gave their written informed consent.

Doppler signal acquisition was performed with a General Electric LOGIQ S6 Power Doppler Ultrasound Unit from the Radiology Department in the Meram Faculty of Medicine of Necmettin Erbakan University. The system hardware was comprised of a Power Doppler Ultrasound unit that can be operated in the pulsed mode, a linear ultrasound probe (12 MHz) and a laptop computer. A computer was needed for storing, displaying and performing spectral analysis of the obtained Doppler data.

Before Doppler data was recorded, a color and pulsed Doppler ultrasound examination of the left and right hand Radial arterial was performed for elimination of presence of a hemodynamically significant stenosis. A linear ultrasound probe of 12 MHz was used to transmit pulsed ultrasound signals into the left and right hand Radial arterial. Signals reflected from the arterial were recorded for extraction of the Doppler shift frequencies. In all examination on the healthy and patients subjects, the insonation angle and the presetting of the ultrasound were kept fixed. Both manually & via electronic steering methods were used for adjustment of insonation angle to a constant value of 60 degrees on a longitudinal view. The sampling volume was placed within the center of the arterial. The amplification gain was carefully set to obtain a clean spectral output with minimized background noise on the spectral display [17-23]. The audio output of the ultrasound units was sampled at 44.1 kHz and then it was sent to a computer.

Fig. 1 depicts the Doppler signals for a healthy control group subject on the left hand Radial artery, while Fig. 2 represents the Doppler signals for a patient group subject on the right hand Radial artery with RA disease. Transforming the Doppler signals from the time domain to the frequency domain using the Welch Periodogram methods, RA disease was successfully diagnosed.

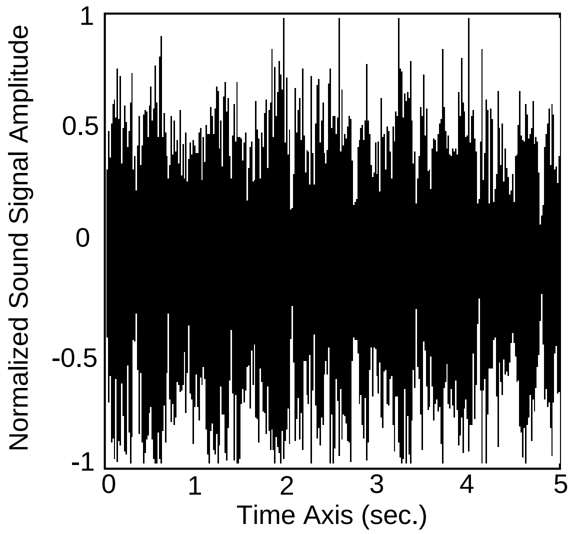

Fig. 1. Doppler signals for a subject (no:32) with a healthy left hand Radial artery

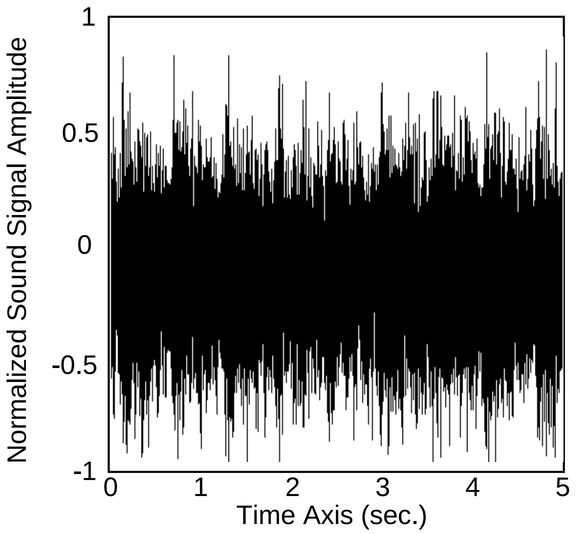

Fig. 2. Doppler signals for a patient (no:10) having RA disease on the right hand Radial artery.

B. Disease Activity Score-28 (DAS-28)

Based on the American College of Rheumatology (ACR) criteria, 40 patients diagnosed with RA were evaluated. In order to minimize the human factor, clinical evaluation was carried out by the same rheumatologist throughout the study. The DAS-28 was estimated by considering the number of swollen and tender joints using 28 joint counts (28 swollen and 28 tender). The measurement of Erythrocyte Sedimentation Rate (ESR) was performed millimeters per hour. In addition, based on the physician evaluation, the general health of 40 RA patients was measured on a visual analogue scale (VAS) of 0 mm to 100 mm. For each patient joint swelling and tenderness were scored as “present” or “absent” [24,25]. RA disease also affects mainly synovial joints. The human body possesses 28 synovial joints, with 24 in our hand (12 in each hand).

The DAS-28 was determined according to the following equation:

$$\text{DAS-28} = 0.56 \times \sqrt{\text{TEN-28}} + 0.28 \times \sqrt{\text{SW-28}} + 0.7 \times \ln(\text{ESR}) + 0.014 \times (\text{VAS}) \quad (2)$$

where, TEN-28 is the tender joint number, SW-28 is the swollen joint number, ESR is the erythrocyte sedimentation rate (in mm after one hour) and VAS is the visual analogue score in mm. Statistics values (mean, standard deviation, minimum and maximum) DAS-28, VAS, TEN-28, SW-28, ESR and CRP belonging to the 40 RA patients are shown in Table 1.

A DAS-28 score under 2.6 correspond to remission (2 patients), while a score between 2.6 and 3.2 indicates low disease activity (one patient), between 3.2 and 5.1 means moderate disease activity (21 patients), and above 5.1 indicates high disease activity (16 patients).

TABLE I. STATISTICAL VALUES OF DAS-28, VAS, TEN-28, SW-28, ESR AND CRP BELONGING TO THE 40 RA PATIENTS.

Value	Mean	Standard Deviation	Max. Value	Min. Value
DAS-28	4.804	1.373	7.49	2.16
VAS (mm)	51.5	19.81	80	10
TEN-28	10	9.526	28	1
SW-28	1.3	1.689	7	0
ESR (mm/h)	33.2	18.34	75	3
CRP (mg/L)	20.53	21.16	78.5	3

In the presented study, a system involved three stages is proposed. First, the left and right hand Radial arterial Doppler signals are acquired; second, feature extraction is accomplished using the Welch Periodogram method; and third, an ANN is used to classify RA diseases based on left and right hand Radial artery Doppler signals. Fig. 4 indicates the flowchart of the classification system. The suggested method will be explained in more detail according to the following sub-sections.

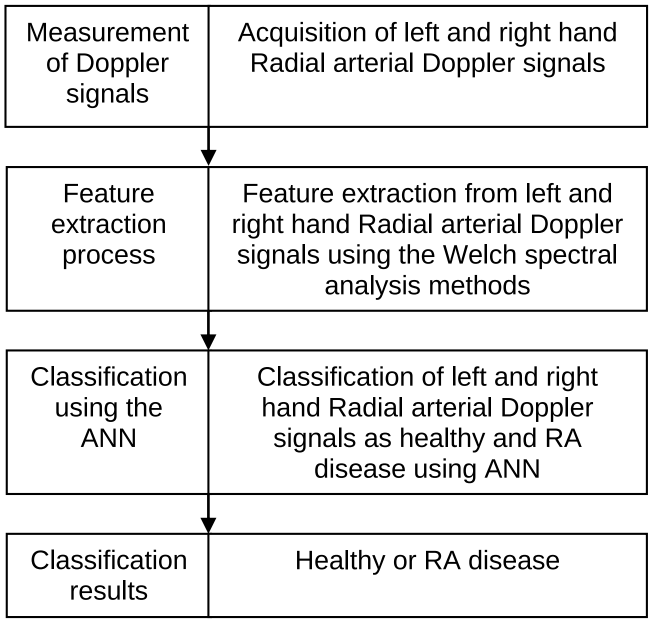

Fig. 3. The flowchart of the classification systems.

C. Process of Feature Extraction with the Method of Welch Spectral Analyze

Periodogram method, Fourier transform-based method, is known as classical spectral estimation methods. Periodogram improved method proposed by Welch and these methods may overlap on top of the signal time series into sections based on the principle of separation. Periodogram each overlapping portion of the data received was developed and then it is obtained by taking the average Periodogram. Periodogram mean all data developed by single Periodogram estimation variance decreases [26]. Even if overlap between sections leads to unnecessary data, this influence decreases overlapping with the use of non-rectangular window the weight of the samples in the final section.

Welch method of power spectral density is estimated by taking the average periodogram improved [27,28] m’st improved periodogram,

$$P^{m}{}_{XX}(f) = \frac{1}{MU}\left|\sum_{n=0}^{M-1} x_m(n).w(n).e^{(-j2\pi fn)}\right|^2 \quad (3)$$

Here $f = f_S$ is the normalized frequency variable. M is the normalizing constant, $w(n)$ is the windowing function and U is total average of [27,28].

$$U = \frac{1}{M}\sum_{n=0}^{M-1} w(n)^2 \quad (4)$$

As a result, the power spectral density is determined as

$$P^{Welch}{}_{XX}(f) = \frac{1}{L}\sum_{i=0}^{L-1} P^{i}{}_{XX}(f) \quad (5)$$

D. Normalization and Classification of the Left and Right Hand Radial Artery Doppler Signals Using an ANN

Normalization of data is of importance in order to improve the performance of ANN. Normalization is a data pre-processing technique. The purpose of normalization is to scale the data in to predefined range. Normalization methods which are used for application in engineering are z-score normalization, min–max normalization and decimal scaling normalization methods and so on. All data were converted in the range of (0-1) by application of min-max normalization to Doppler data in this study [29,30].

The basic definition of ANN is a process information algorithm, using parallel computing technique. ANNs provide accurate results and convergence speed is of importance in terms of training algorithms. Back propagation algorithm is one of the most widely employed algorithms for biomedical signal processing [11] Back propagation algorithm involves three layers; the input, hidden and output layers. Because of the output of the error in the calculation, the output layer to the hidden layer and then spread back to the input layer, this algorithm is called as back propagation algorithm [11]. In recent years, one of the most commonly used Back propagation algorithm is the Levenberg - Marquardt (LM) algorithm. In this study the reasons for the use of LM algorithm are because it learns quickly, and the maximum fine could converge on the idea that an established neighborhood features, i. e., the method of calculation.

As seen in Fig. 4, in this study, LM algorithm trained neural network structure includes three layers, input layer 129 features (neurons), hidden layer 10 neurons and output layer of two neurons (healthy control group or RA patients).

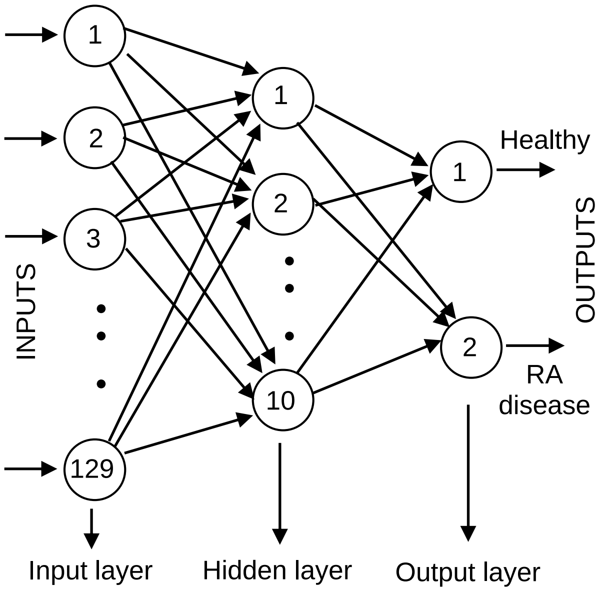

Fig. 4. Structure of ANN trained with LM algorithm.

E. Performance Criteria`s

The classifiers and data pre-processing methods have been used for both classification of medical data sets and determination of the performance of some statistical measurements as well. In this study, the performance compared to 10-fold cross-validation data sets, sorting, classification accuracy, sensitivity and specificity, and receiver operating characteristic (ROC) and ROC curve area under value (AUC) were used. Classification accuracy, sensitivity and specificity of the formula can be given by following equations.

$$Classification\ Accuracy\ (CA) = \%\ \frac{TP+TN}{TP+FP+TN+FN} x100 \quad (6)$$

$$Sensitivity\ (SEN) = \%\ \frac{TP}{TP+FN} x100 \quad (7)$$

$$Specificity\ (SPE) = \%\ \frac{TN}{FP+TN} x100 \quad (8)$$

where TP, FP, TN, respectively FN and true positive, false positive, true negative and false negative.

TP: a subject with RA disease is detected as a patient diagnosed with RA disease.

FP: a healthy control group subject is detected as a patient diagnosed with RA disease.

TN: a healthy control group subject is detected as normal.

FN: a subject with RA disease is detected as normal.

In this study, 10-fold cross-validation and separation of the data sets were used. At the beginning our data set (40 healthy control group and 40 RA patients) was divided into 10 equal parts, nine parts were used for training data set, one part for the testing data set. Then the test set became the last second part and the remaining part was selected as the training data set. This process continued, respectively until the last part of the test data set. Therefore the data set of training data each time for 90 % of the remaining 10 % was allocated for the test data. Used data sets of 40 RA patients and 40 healthy people Doppler signals (a total of 80 data sets), the ANN is to train and to test data, 10-fold cross-validation process % in 90/10 (72-8), respectively, to train / test process has been subjected Therefore training input data set of 36 healthy and 36 RA patients (72 × 129 samples), whereas the test data set of four healthy and four RA patients (8 × 129 samples) are available. MATLAB software program was used for all evaluation in this study.

The ROC curves are employed as measures for the accuracy of diagnostic tests in medicine and other fields. The ROC curve is one of the best methods in order to assess the performance of a test and defining appropriate decision threshold. The ROC curves shows the relationship between true positive rate (sensitivity = y-axis) and the rate of false positives (1-specificity = x-axis) as shown in the two-dimensional graphics are drawn [31]. According to the results of the ANN test ROC curves in this study, Radial artery Doppler signals of left and right hand are plotted in Fig. 5.

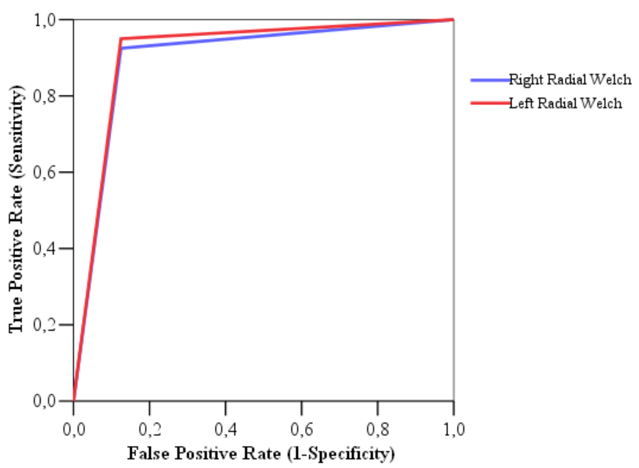

Fig. 5. According the results of the ANN test ROC curves are plotted Radial artery Doppler signals of left and right hand.

III. Results and Discussion

In this study, the Welch method has been used to extract the significant features from the left and right hand Radial artery Doppler signals for diagnosing the RA disease. RA disease has been diagnosed using an ANN classifier. TABLE II shows, 10-fold cross-validation ANN classifier with test results obtained.

TABLE II. 10-FOLD CROSS-VALIDATION TEST RESULTS OBTAINED BY ANN CLASSIFIER.

	TP	FP	TN	FN	CA (%)	SEN (%)	SPE (%)
Right Radial Arterial	37	3	35	5	90	88.1	92.1
Left Radial Arterial	38	2	35	5	91.3	88.4	94.6

In this study, we developed an expert diagnostic system for the interpretation of the left and right hand Radial artery Doppler signals using signal processing and ANN methods.

It can be seen in TABLE III that the combination of Welch Periodogram method and ANN achieved the classification accuracies of 90 % right hand and 91.25 % left hand Radial artery Doppler signals in the diagnosis of RA disease.

Comparing DAS-28 values belonging to 40 patients and classification accuracy results obtained with the ANN, a compatible correlation between the compliant was determined. The results shows that classification accuracy has not overlapped with DAS-28 values for only five of right-hand radial artery patients and only four of left hand radial artery patients. The consistent results have yielded with all the classification accuracy of the results concerning patients' DAS-28 values (Table 3).

TABLE III. CORRELATION OF DAS 28 VALUES WITH RESULTS OBTAINED BY ANN CLASSIFIER.

	Number of Disease	Number of True Correlation	Number of False Correlation	CA (%)
Right Radial Arterial	40	35	5	87.5
Left Radial Arterial	40	36	4	90

It can be seen in TABLE II and III that the right hand Radial artery for ANN and classification accuracy of 90 % while the DAS-28 values correlated with 87.5 %, the left hand Radial artery for the ANN with a classification accuracy of 91.3 %, while DAS-28 values with the correlation of 90 % were observed. As a result, a method used in the diagnosis of RA disease and compatible with the DAS-28 values was developed.

The proposed method in this paper is a novel study about diagnosis of RA disease using right and left hand

Radial artery Doppler signals belonging to healthy subjects and patients. This system can help physicians make final decisions for the early diagnosis of RA disease without hesitation.

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