DETECTION OF VENOUS GAS BUBBLES WITH COMPUTERIZED DOPPLER ULTRASOUND

by

Kadir Tufan

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APPROVED BY:

Assoc.Prof. Ahmet Ademoğlu ....
(Thesis Supervisor)

Assist. Prof. S. Murat Egi ....
(Thesis Co-supervisor)

Assoc. Prof. Hale Saybaşılı ....

Assist. Prof. Ata Akın ....

Assist. Prof. Nurullah Arslan ....

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ABSTRACT

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Venous Gas Embolism (VGE) may occur during the brain and neck surgery where the operative site is higher than the heart. Medium where the pressure changes significantly like diving, aviation and space missions also promote VGE. For this reason, early detection of VGE is very crucial. The Doppler Ultrasound Audio (DUA) signals recorded from two divers are analyzed to detect the embolic waveforms. The optimal pass band characteristics of the embolic events are determined by an extensive band pass filtering analysis and the optimum band is determined as 4.5-8 KHz. A nonlinear Teager operator and and adaptive thresholding is also applied to the filtered DUA for automatic detection of the embolic events. As a last step, a software that can perform all the operations from digitizing the DUA recordings to detecting the embolic events is developed for off-line processing.

Keywords: Doppler Ultrasound Audio, gas bubble, Teager energy operator, venous gas embolism, frequency band analysis

ÖZET

TOPLARDAMAR GAZ KABARCIKLARININ BİLGİSAYARLI İŞİTSEL DOPPLER SESÖTESİ İLE YAKALANMASI

Toplardamar gaz embolisi (TGE) ameliyat bölgesinin kalpten yukarıda olduğu beyin ve boyun ameliyatlarında oluşabilir. Dalma, havacılık ve uzay çalısmaları gibi basıncın belirgin ölçüde değiştiği durumlar da TGE'ye yol açabilir. Bu nedenle TGE'nin erken farkedilmesi çok önemlidir. İki dalgıçtan işitsel Doppler sesötesi (İDS) sinyalleri kaydedilerek embolik dalgaların sezimi için incelendi. Kapsamlı bir bant geçirgen süzgeçleme incelemesiyle embolik olaylara özgü en iyi bant geçirgen özellikler belirlenerek en iyi bant olarak 4.5 - 8 KHz saptandı. Embolik olayların otomatik sezimi için süzgeçlenmiş İDS sinyallerine doğrusal dışı bir Teager işleci ve ayarlı bir eşikleme de uygulandı. Son aşama olarak kayıt sonrası işleme için İDS kayıtlarını sayısallaştırmaktan embolik olayları sezimlemeye kadar tüm işlemleri yapabilen bir yazılım gerçekleştirildi.

Anahtar Sözcükler: İşitsel Doppler sesötesi, hava kabarcığı, teager enerji operatörü, toplardamar gaz embolisi, sıklık band analizi

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LIST OF ABBREVIATIONS

CWDU	Continuous Wave Doppler Ultrasound
DCS	Decompression Sickness
DUA	Doppler Ultrasound Audio
FES	Fat Embolism Syndrome
FFT	Fast Fourier Transform
FIR	Finite Inpulse Response
GUI	Graphical User Interface
İDS	İşitsel Doppler Sestesi
PDU	Pulsed Doppler Ultrasound
RBC	Red Blood Cell
SD	Standard Deviation
TBR	Transient-to-Background Ratio
TEO	Teager Energy Operator
VGE	Venous Gas Embolism
WDS	Wave Decoding System
WT	Wavelet Transform

1. INTRODUCTION

1.1 Motivation and Objectives

VGE may occur during the brain and neck surgery where the operative site is higher than the heart. Medium where the pressure changes significantly like diving, space missions also promote VGE. If not done properly, removing or inserting central venous catheter can cause VGE. VGE is a serious event which can cause serious injury or death. For this reason, early detection of VGE is very crucial. There are several detecting methods like capnography, 2D echocardiogram but utilizing the DUA is accepted as a great promising technique due to its practical and noninvasive nature.

Listening to the DUA by experts is a practical way to detect embolic signals. But there are some drawbacks of this method. Firstly, it needs continuous listening which decreases attention to other monitors in operating room. Adaptive nature of ear is another problem. Additionally, subjectivity of this method is obvious because it relies on the subjective judgement of listeners.

There have been several attempts to detect VGE by computerized processing of DUA [1], [2], [3]. In vivo studies are carried out with human and animal data [1],[3], [4]. Since VGE has severe risks, studies performed on the human subjects are scarce. Human data is generally obtained from divers.

The aim of this study is to analyze the embolic DUA signals to count the occurence of embolic events. The digital Finite Impulse Response (FIR) filter is used as preprocessing technique and the filtered signals are transformed through a nonlinear Teager Energy Operator (TEO) for emphasizing the embolic event while suppressing the background activity. The optimum bandpass filter characteristics are determined by studying the DUA data from several subjects using different bandpass filters. Once the filter characteristics are determined, a software program with a Graphics User

Interface is developed for routine analysis of embolic DUA data.

With this study, the frequency characteristics of embolic signals for human subjects are investigated. After determining the frequency characteristics, the TEO is applied to increase the Transient-to-Background Ratio (TBR). As a result, number of missed embolic signals and false alarms are decreased.

1.2 Outline of The Study

The outline of the thesis is as follows; In Chapter 2, the mechanism of embolism and its various types, its detection methods are discussed.

Chapter 3 explains the materials and methods used in this study for digitizing, filtering, transforming and detecting the embolic DUA signals.

Chapter 4 includes the results obtained from the application of the technique to the DUA signals. In Chapter 5, the conclusions and the further recommendations for future studies are presented.

2. THE EMBOLUS AND ITS FORMATION

2.1 Embolism

An abnormal clot that develops in a blood vessel is called a thrombus. Once a clot has developed, continued flow of blood past the clot is likely to break it away from its attachment, and such freely flowing clots are knows as emboli[5]

2.1.1 Gas Embolism

An insoluble gas bubble travelling in the vessel can stop the blood passage and gas embolism occurs. Also, the changes in the hemodynamic and medium parameters can cause gas bubbles to form in blood vessels from the gas molecules in blood.

During the coronary angiography or coronary angioplasty, gas embolism can occur [6],[7]. During these operations; incomplete aspiration of catheters, raptures occuring in balloon, insinuation of gas during balloon catheter placement and/or withdrawal, structural failures of operational equipments and gas entrance from outside can lead to gas embolism [8].

Gas embolism is also a potential complication in central venous access [9]. Gas embolism can occur spontaneously when there is an open venous structure 5 cm or more above the heart or if the gas is delivered under pressure into the venous system, such as during a laparoscopy or mishaps with infusion bags. Likewise, initial placement of catheter, disconnection or breakage on catheter can cause to gas embolism [10].

Gas embolism can also be seen in media where the environment pressure changes significantly. SCUBA diving, caisson working, aviation and space mission are common places where the gas embolism can occur.

Gas embolism can also occur if a hysteroscope is connected incorrectly [11]. This is a minimum risk diagnostic operation but it must be managed carefully. Gas can be pumped into the uterus rather than fluid, which results in the gas to be introduced into the patient coronary arteries and causing a gas embolism. When the gas embolism occurs, it becomes a life-threatening phenomenon.

Haemodialysis procedures require an extracorporeal blood circulation using haemodialysis machine. This can lead to a gas embolism. In vivo studies showed that gas embolism is formed by the blood pump of the haemodialysis machine [12].

2.1.2 Fat Embolism

Fat embolism mainly occurs in traumatic injuries [13]. Fat Embolism Syndrome (FES), however, is estimated to occur in a low percentage in all long bone fractures. Despite the fact that FES is known and discussed in traumatic and surgical literatures for more than 100 years, the exact nature of it is unknown.

2.1.3 Cholesterol Embolism

Cholesterol embolism is generally a complication of vascular surgery, thrombolysis, arteriography, and anticoagulation in elderly patients [14], [15], [16]. More generally, cholesterol embolism can result from medical interventions that disrupt the surface of an atherosclerotic plaque. Aortic surgeries, aortography, left heart catheterization, and angioplasty are other processes where one can find cholesterol embolism. Moreover, cholesterol embolism should be considered after the surgical kidney operations of elderly patients. It can be seen in patients with arteriosclerosis.

2.1.4 Thrombus Embolism

Blood clots (fibrin clots) are the clumps that result from coagulation of the blood. A blood clot that forms in a vessel or within the heart and remains there is called a thrombus. A thrombus that travels from the vessel or heart chamber where it formed to another location in the body is called an embolus and the disorder, an embolism [17].

2.1.5 Amniotic Fluid Embolism

Amniotic fluid embolism occurs when amniotic fluid enters to a woman's bloodstream [18]. If any means, the amniotic fluid which is normally isolated from maternal intravascular compartment, enters to the maternal intravascular compartment, it starts to affect lung, heart, and brain.

2.2 VGE

VGE is a severe event especially in clinically ill patients. Clinical presentations of VGE are non-specific and a wide variety of signs and symptoms can occur [19]. The only specific sign is the "mill wheel" murmur, which is not detected frequently.

If VGE occurs, gas bubbles start to navigate within the blood circulation system. First, they are collected in the right atrium of the heart. Then they pass to the right ventricle where the blood is pumped to the lungs to oxygenate. There is a chance of these emboli to be filtered out in the lungs. But, if the filtering capacity of lungs is exceeded, these bubbles return to the left atrium of the heart. Also, if there is a passage between the left and right side of the heart, bubbles can pass through this shunt to the left side of the heart. Existence of patent foramen ovale is a common sickness which allows this passage. If gas bubbles reach to the left side of the heart, it becomes a serious phenomenon because from the left ventricle, the blood is pumped to all parts of the body.

2.2.1 Surgical Operations

VGE may occur in some surgical operations where the operative site is higher then the heart [2]. If the incision of vessel is 5 cm or higher than the heart [3] the pressure of the vein which is cut becomes less than the atmospheric pressure. Due to this pressure gradient, gas can be sucked into the blood circulatory system as bolus. In brain and neck surgery, patients are held in sitting position. So, the incision sites become higher than the heart level. Therefore, VGE may occur in these types of operations.

2.2.2 Hyperbaric Environments

Hyperbaric environments are also very suitable places where VGE can be seen [20], [21], [22], [23], [24]. If a diver has been beneath the sea long enough so that large amounts of nitrogen have been dissolved in his body and then he suddenly comes back to the surface of the sea, significant quantities of bubbles can develop in his body fluids either intracellularly or extracellularly, and these can cause minor and serious damage in almost any area of the body, depending on the amount of bubbles formed; this is the decompression sickness (DCS) [5]. In hyperbaric environments, DCS can be seen after the mission. For that reason, there is a chance for treatment.

2.2.3 Hypobaric Environments

Altitude DCS describes a condition characterized by a variety of symptoms resulting from exposure to low barometric pressures that cause inert gases (mainly nitrogen), normally dissolved in body fluids and tissues, to come out of physical solution and form bubbles. Altitude DCS can be seen at high-altitude balloon and aircraft flights and space missions [25]. Unlike hyperbaric environments, DCS is seen during the mission. Therefore, detection is more important.

2.2.4 Catheterization

Removing or inserting a central venous catheter can cause a fatal VGE if these processes are not managed properly. If a break occurs in the intra venous (IV) system above the level of the heart and a patient takes in gas by coughing, sneezing or taking a deep breath, the change in intrathoracic pressure can draw up to 10 to 15 cc of gas into the venous system as a bolus [26].

VGE can occur at the placement, removal or at any time during the catheterization. If it occurs in hospitals, preventive precautions can be taken immediately to protect the patient from unwanted results. However, if it occurs at home, for example; during home infusion therapy, results may be much dangerous.

2.3 Current Detection Methods

Since the consequences of the VGE could be extremely dangerous, early and reliable detection is very important. There are several methods to detect the VGE. Two dimensional echocardiography is accepted as gold standard. It can be applied transthoracic or transoesophageal. Gas bubbles can be observed visually with this method. Since it offers a visual inspection, it is accepted as a highly reliable technique. But, it is not suitable to use in critical situations because it is not practical.

There are some other methods to detect gas bubbles in veins. For example, a sudden increase in the central venous pressure can be a sign of VGE. Also, an acute right heart strain detected by echocardioagram is a suspect of gas bubbles. These two methods are less definitive in detection of the VGE.

One easy and reliable means to detect emboli is to use DUA. It is a very sensitive and non-invasive technique. Also, it can be applied quickly and easily in critical situations. It can be used and is accessible at bed site of the patient. These features make the DUA a very popular means of detecting gas emboli circulating in vessels.

2.4 VGE Detection by Using DUA

Bodies may be detected by sound when they have acoustic characteristics that differ from those of the surrounding medium so they scatter sound, absorb it, or change its speed of propagation [27]. There is a considerable acoustic impedance mismatch between the gas bubble circulating the blood vessel and its surrounding fluid, namely the blood [2]. When a blood vessel is ensonified, scattering and reflection of a wave (sound) will have different intensities for the gas bubble and for the blood [28]. DUA can be utilized to detect the suspected gas emboli in several ways. The simplest one is that the DUA is listened to by an expert. Since the expert is good at differentiating the embolic sounds from the remaining part of DUA, gas emboli are detected by ear.

2.4.1 Aural Counting

The Doppler audio contains both amplitude and frequency information and can be used to detect gas bubbles without quantitative calibrating [4]. If there is no embolus circulating in the blood vessel, the DUA is almost smooth. If the Doppler audio contains an embolic signal, a transient, aurally distinguishable sound is heard. This embolic sound is described as a "chirp", a "squeak", or a "click" [4]. An experienced person can easily identify and count gas bubbles by listening to the DUA signal.

Detecting VGE aurally is an easy method but it has some drawbacks. Firstly, the method is subjective which means that one can accept a signal as embolic while another can accept as non-embolic. Moreover, ear is an adaptive organ. Therefore, the sensitivity of it will decrease with time. During a surgical operation, the DUA must be listened to for hours, so as the time elapses, the sensitivity of listener will decrease. This will negatively affect the detection of VGE. Limitation of it is another problem. If there are several emboli in one heart cycle, discriminating and counting each individual embolus become impossible. Anesthesiologist must concentrate on the DUA in order to catch gas emboli in vessel. This will diminish the attention to other monitors. This is a very important problem in critical surgical operations. In the operating room, it is the primary purpose to detect whether there is any embolus in veins. In DCS, however, the number and the frequency of the embolic signals are the values interested in.

The acoustic signals returned by the Doppler instrument are complex and must be interpreted by trained Doppler raters [29]. There are two codes, Kisman-Masurel [30] and Spencer [31] codes, to score the DUA and assign its grade. These two codes are useful to provide an estimation of the number and relative size of bubbles, but they are significantly subjective [29].

Due to all significant disadvantages described above, DUA must be processed and more improved emboli detection systems must be designed.

2.4.2 Spectral Analysis of DUA

DUA carries both amplitude and frequency information. Superior to the aural counting method, spectral characteristics of DUA can be used to enhance the performance of the emboli detection system. A DUA signal is composed of a transient, nonstationary random process called embolic waveform, and a complex background signal affected by several factors. The background is mainly due to the scattering from Red Blood Cells (RBC) flowing through the vessel of interest, from the movement of the vessel walls and from the moving of extracellular tissues [4]. Sounds from the heart muscle and heart valves can also be found in the background. One important point is that the DUA characteristics can change from one person to another. Likewise, orientation of the Doppler ultrasound transducers is very effective on the recorded Doppler audio characteristics.

In order to detect embolic signals from DUA, spectral analysis should be used. By applying a spectral analysis, amplitude, frequency and duration information about the embolic waveform can be obtained.

In the literature, although there are some information about the frequency characteristics of embolic signals for animals, such an information is lacking for human subjects [1].

Kisman used the transient spectral analysis technique to detect gas bubbles in DUA taken from the posterior vena cava and pulmonary arteries of decompressed animals. DUA is recorded before the dive and soon after the dive. Since the physiology of animals are different from that of human, transient spectral analysis of DUA also yielded different results. But, he recognized that after the dive, certain high frequency components which are due to gas bubbles were detected as seen in Figure 2.1 [4]. Here, we can say that the gas bubbles are the cause of the higher frequency components in the DUA.

There are some *in vivo* studies for both human and animal data. Human studies mainly based on DUA recorded from scuba divers taken after the diving process. Animal studies, however, are based on different techniques including direct injection of known volume of gas [3] and gas bubbles formed after the decompression at a diving process [2]. There are some constraints in human studies, mainly due to ethical considerations.

From the studies on spectral analysis of DUA, we know that gas emboli empower the higher frequency components. But, the frequency band where the embolic signal can be separated from the background signal is not declared. Brent *et. al.* [2] performed

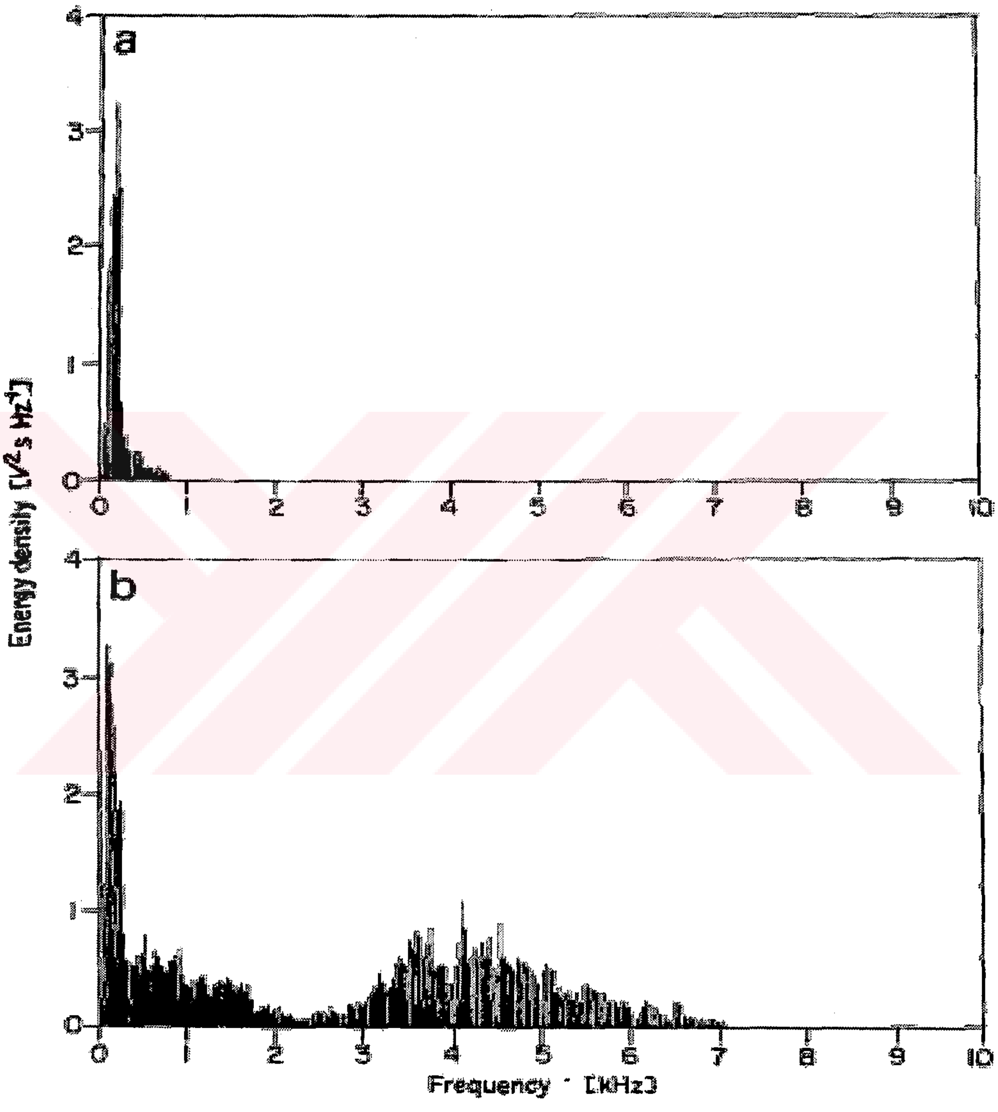

Figure 2.1 DUA Spectrum of a decompressed rabbit a)Predive b)after dive [4]

a good research on the anesthetized dogs to determine the spectral characteristics of gas emboli. They found that while the normal heart sound was below the 400 Hz, embolic components were at 400 Hz-1.2 KHz. They injected known amount of gas bubbles to dogs and analyzed the DUA. They preferred dogs to perform this study, they assumed dogs and human beings showed quite similar physiological properties.

2.5 Doppler Ultrasound

In this section, the principles of ultrasonic Doppler sensors used in this study are explained.

The Doppler Principle is a wave theory that describes the relationship between the velocity of a moving object and transmitted or received wave frequency [32]. An Austrian Physicist, Christian Doppler at Royal Bohemian Society of Science in Prague, first described this theory in 1842. Later, this theory is applied to measure the speed of moving objects in almost every field, from medical applications to detect speeding vehicles in high ways.

In medicine, Doppler methods are employed to collect information related to the function of an organ rather than its morphology [33]. Moreover, their noninvasive nature promises to apply in critical medical situations.

There are two kinds of Doppler ultrasound transducers used, the Pulsed Doppler Ultrasound (PDU) and the Continuous Wave Doppler Ultrasound (CWDU) to detect the VGE.

2.5.1 Doppler Effect

The Doppler effect is the change observed in the wavelength / frequency of sound waves due to relative motion between a wave source and a wave receiver [33]. When a wave is reflected from a moving object, the frequency of the observed wave is different than the source wave. This frequency difference is called as the "Doppler Shift". The Doppler Shift depends on:

1. Speed of motion
2. Frequency of source wave
3. The angle between the sound wave direction and the moving object direction.

This is illustrated in Figure 2.2 [34] and formulated as

$$f_d = 2 f_e \frac{v}{c} \cos\theta \tag{2.1}$$

Where

c: Speed of sound in medium

v: Speed of moving object

f_e: Emitted wave frequency

f_d: Doppler shift frequency

θ : Angle between sound beam and the direction of moving object

Doppler shift frequency is detected by Doppler instruments. But, one is interested in the speed of the motion or the blood flow speed. So Doppler equation can be rearranged as follows:

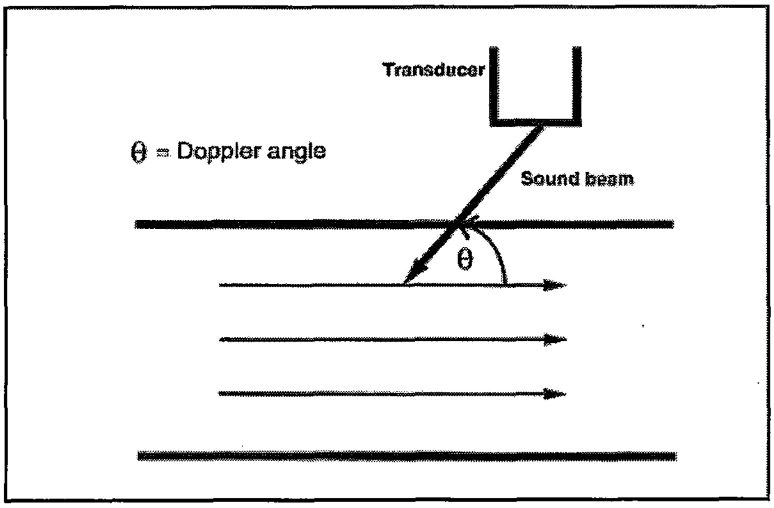

Figure 2.2 A classic implementation of a Doppler instrument[34]

$$v = 77(\frac{f_d}{f_e \cos\theta}) \tag{2.2}$$

Where

f_d : Doppler shift frequency (KHz)

f_e : Emitted wave frequency (MHz)

v : Speed of moving object (cm.s^{-1})

To make this simplification, take the speed of the sound in blood as approximately 1540 m/s [35]. As seen in Eq. 2.1 and 2.2, Doppler shift is proportional to the operating frequency of the instrument, i.e, at higher frequencies higher Doppler shift is obtained. However, attenuation of the ultrasound in tissue increases with frequency, which means when frequency increases, the penetration capacity decreases. A suitable solution to optimize the Doppler shift is to choose the frequency by considering the application type. In medical applications, 2-10 MHz operating frequency can be used.

Doppler shift also depends on the Doppler angle, the angle between sound beam and the direction of moving object. This is in the form of cosine, i.e, if the Doppler angle is parallel to the direction of moving object, positive maximum (when both in the same direction) or negative maximum (when they are opposite direction) is obtained. At large angles, error in estimation of Doppler angle is more critical than it is at small angles. Additionally, Doppler shift becomes very small at large angles, which reduces the system sensitivity. As a result, Doppler angles more than 60^o to 70^o are not used.

2.5.2 Doppler Ultrasound in Medicine

Doppler ultrasound has been used in medicine for many years [36]. In general, it is used to detect the flow deficit. At the beginning, it is used to measure the flow in the carotid artery. Later, it started to be employed in other fields thanks to the development in ultrasound technology. Nowadays, it is used in almost every branch of medicine, including cardiology, surgery, pediatrics, obstetrics and radiology.

2.5.3 Continuous Wave Doppler Ultrasound

Both source and receiver are stationary in CWDU. Additionally, transmitter and receiver transducers are not in line, there must be an angle between them , as seen in Figure 2.3 [32].

CWDU gives little information about the flow of blood in vessels [37]. It is very accurate in high speed flows, but it is unable to provide range resolution [38],[39].

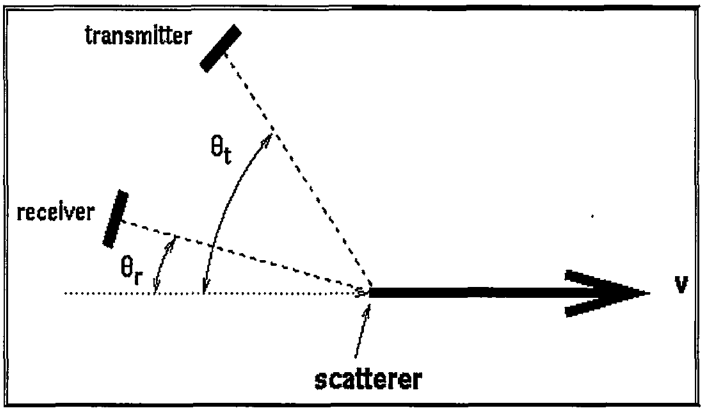

Figure 2.3 Continuous Wave Doppler Ultrasound [32]

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2.5.4 Pulsed Doppler Ultrasound

In PDU, the transmitting and the receiving transducers are the same. After a burst is sent to the tissue, the received reflection is collected after a certain time and the collection is stopped. By changing the time of reception of returning signal, depth of measured flow can be adjusted. The region where the flow velocity is measured is called as "Sample Volume" [39].

By changing the time of reception of returning signals (reflections), depth flow can be changed. In other words, we can measure velocities at a specific location, which is called range resolution [38],[39]. Here the velocity of flow as well as the direction of flow are measured. This is another advantage of Doppler ultrasound. PDU has a limitation of speed, i.e, if the velocity of flow exceeds certain values, then the measurement involves errors in accuracy. The highest velocity which can be measured accurately is called the Nyquist Limit.

3. MATERIALS AND METHODS

3.1 Data

3.1.1 Obtaining Data

Doppler recordings were obtained from divers during the high altitude diving expedition performed in 1994. Divers were monitored with a continuous Doppler ultrasound device (2-3.5-5 MHz Mini Dopplex, Huntleigh Healthcare Ltd, UK) after surfacing from test dives to develop new dive tables for diving at high altitude[40],[41].

3.1.2 Digitizing Data

DUA stored on magnetic tapes were digitized in order to be processed by the computer. To accomplish this, a computer (Quasar Pentium PIV 800) having a sound card (Creative Sound Blaster PCI, Creative Technology Ltd, Singapore), a magnetic cassette player (Aiwa TX456, Sony Marketing Inc.) were used. The data on the magnetic tapes was transferred to the computer through the microphone input of the sound card. For recording the sound, the software provided with the sound card was used.

DUA was digitized with the specifications given in Table 3.1.

The sampling frequency was chosen such that the Nyquist frequency (half of the sampling frequency) of DUA was around 20 KHz, which is the upper bound of audible sound. This was because the embolic signals are in audible range. Data format was chosen as 16 bit. File format was the default format of the sound recorder program.

Table 3.1
DUA recording specifications

	Setting
Sampling Frequency	44.1 KHz
Channel Mode	Mono
Data Format	16 Bit
File Format	Windows PCM Wave (*.wav)

3.1.3 Marking Embolic Places

Embolic signals within DUA should be marked by an expert. With a sound player program (Cool Edit 2000, Syntrillium Software Corporation, Phoenix, AZ), DUA waveforms were displayed. The hard copies of each segment were printed out.

As an expert in identifying embolic waveforms in DUA signals, S. Murat Egi, Ph.D., examined the DUA both visually and auditory and marked the embolic events.

3.1.4 Converting the Data to Matlab Format

In order to process the DUA in the computer, a file conversion operation has been carried out. A conversion software (AwaveAudio v7.2, FMJ-Software, Hagersten, Sweden) was utilized for this purpose. It could convert Windows PCM Wave (*.wav) format to Matlab (Matlab 5.3, The MathWorks Inc, Natick, MA) format (*.mat). Also, the sampling frequency can be changed. This was suitable for downsampling the original data. Moreover, sampling frequency could be set to any value, rather than choosing a value from a limited list.

3.2 Signal Processing

To develop a bubble detection system, the frequency characteristics of embolic signals must be determined first. As stated before, there is a limited number of studies which propose a frequency range for the DUA in the literature. This study started with trying the frequency bands stated in earlier studies[1].

3.2.1 Bandpass Filter Design

Filtering of the DUA to determine the optimal filter pass band characteristics were performed by Fourier transforming, rectangular windowing in frequency domain and then inverse Fourier transforming. A Matlab routine that performs the bandpass filtering for a given frequency band was designed. It requires four parameters from the user; the signal array, the lower cutoff frequency value, the upper cutoff frequency value and the sampling frequency of the signal to be analyzed.

3.2.2 Selecting Appropriate Frequency Band

DUA in Matlab array was filtered by using the bandpass filter explained above. Then, it was thresholded with appropriate multiples of the standard deviation (SD) of filtered DUA signal. SD is calculated from the first 0.5 second of processed signal. This region was called as the "test region". Then, this value was thresholded. For the remaining part of detection process, it was assumed as constant. From the end of the test region to the end of processed signal, a proper number of samples is taken into an array and its SD was calculated. The number of sample in this array was called as "trial length". Trial length is 100 samples in this study. Those parts of the signal exceeding the threshold value were counted as embolic signals. When the threshold value was exceeded, a flag that that marks the beginning of an embolic signal is set. If the SD of consequent trial length was also higher than the threshold value, it was accepted as the continuation of the embolic signal, rather than an individual bubble. An embolic signal ended when the SD a trial length falls below the threshold value. In other words, not only the embolic places are going to be found, but also an information about the length of these signals were aimed to be established. If an embolic signal was missed, it was called as "(M)", if a non-embolic signal was detected as embolic, it was called as "False Alarm (FA)".

Choosing the appropriate frequency range where the signal to background ratio was maximum was the crucial phase of this study. The frequency range found in the literature was tested first. It was observed that it eliminated the low frequency components but it was not satisfactory to differentiate embolic signals properly as seen in Figure 3.1. The power spectrum of the DUA showed that there was not a significant signal power over 11 KHz (Figure 3.2). Therefore, it was decided to study the frequency band from 0 Hz to 11 KHz.

A systematic comparison of the filtered signals from 1 KHz to 11 KHz with a 1 KHz bandwidth were tried. Then, the same test was repeated with a 2 KHz bandwidth. Then, the bandwidth was increased to 4 KHz which yielded the highest number of embolic waveforms among all frequency band tried. To fine tune the bandwidth, the value was decreased to 3.5 KHz and 1-4.5 KHz and 4.5-8 KHz band were tested. This yielded the the optimal bandwidth. All the embolic waveforms marked by the expert were detected in the 4.5-8 KHz band.

3.2.3 Using a Nonlinear Operator

Transients, by nature, have short durations with respect to the observation interval. They are often weak signals, i.e, their TBR is quite low. Their influence on the total spectrum is limited due to their small energy content and short time duration. A non-linear operator can be used jointly with time-frequency method to increase the TBR. A normal blood flow having embolies and breathing sounds having respiratory crackles are examples of these kinds of physiological events. [42].

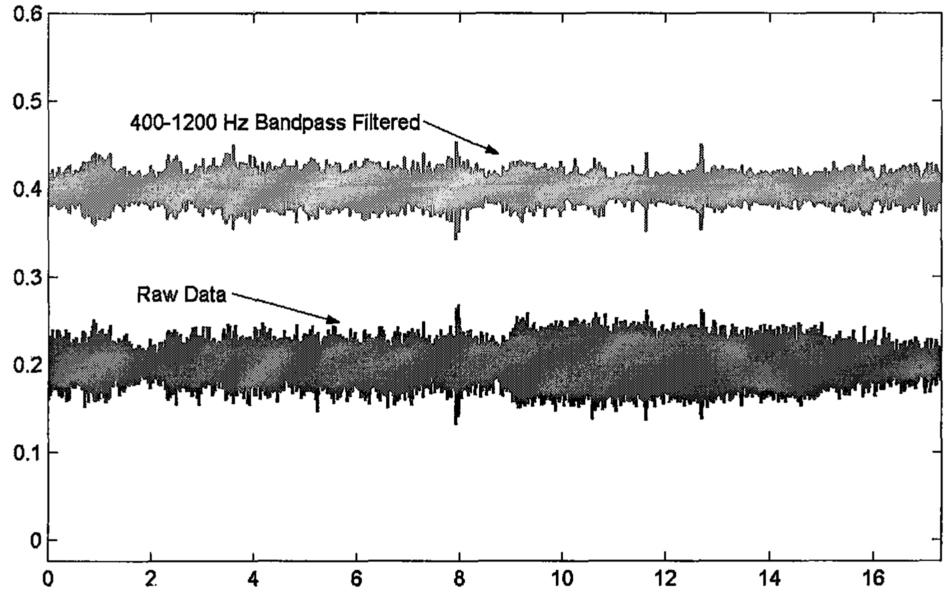

Figure 3.1 Raw data and 400 Hz-1.2 KHz Bandpass filtered data

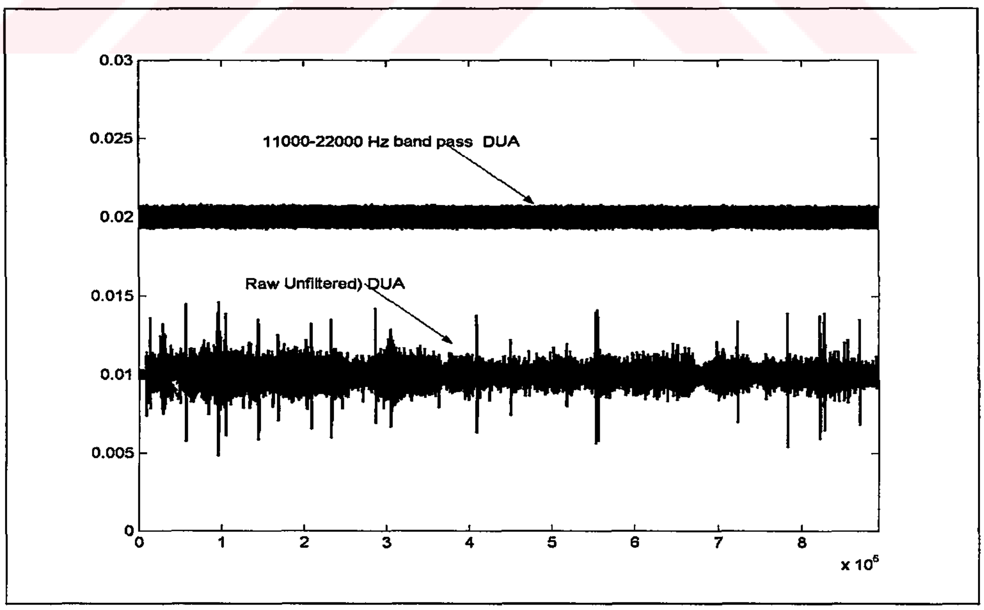

Figure 3.2 Raw DUA and 11-22 KHz filtered DUA.

The determined frequency band did not miss any embolic signal but there are some false alarms. To eliminate this drawback, a nonlinear operator, the TEO was applied to the bandpass filtered signal in order to increase the TBR.

Teager [43], [44] did extensive research on nonlinear speech modelling and pioneered the importance of analyzing speech signals from an energy point of view [45]. He devised a simple nonlinear,energy tracking operator, for a continuous time signal x(t) as follows:

$$\Psi_c[x(t)] = [x^{'}(t)]^2 - x(t)x^{''}(t) \tag{3.1}$$

For the discrete-time signal x(n) TEO can be formulated as:

$$\Psi[x(n)] = x^2(n) - x(n-1)x(n+1) \tag{3.2}$$

These operators were first introduced systematically by Kaiser [46], [47]. TEO can be used to enhance the burst type of signals over noisy signals.

3.3 Designing Graphical User Interface (GUI)

During the testing and optimization process, different steps were accomplished using different tools. The DUA was recorded by using a tape recorder. The recorded data was digitized in Windows PCM Wave format by using the sound card. The sounds were converted to Matlab specific file format by using the AwaveAudio program. All signal processing was performed by using the Matlab program. The whole process from recording the DUA to analyzing and displaying the detected embolic signals must be performed in the same software for a routine analysis. Designing a compact, user-friendly GUI was one of the most important steps of this study.

A functional and easy to use GUI was designed by using the Microsoft Visual Basic 6.0 (Visual Studio 6.0 SP5,Microsoft Inc, Seatle WA) programming language. The source code of the program was provided in the Appendix B.

3.3.1 Saving Microsoft Wave Format

The output of the Doppler ultrasound sensor was used as the microphone input of the sound card of computer. Recorded data was saved as Windows PCM Wave format. For recording and saving sound data, "Microsoft Multimedia Control (MM-Control.OCX)" ActiveX Control was used. The sampling frequency, channel mode, data format and file format could be set. The same control could also be used to playback the recorded sounds.

3.3.2 Extracting Sound Data

Microsoft PCM Wave format sound data should be processed in order to extract the sound data into an array form. This was crucial because this format includes some nonsound information about recording mode, total length of the sound data, recording frequency, data encoding, etc.

The file format of Microsoft PCM Wave was investigated [48] and a "Wave Decoding System (WDS)" was developed. The WDS was tested using another tool called Hexedit, a freeware software that displays a file in hexadecimal format. In Figure 3.4, a Windows PCM Wave file opened in Hexedit program is seen. In the left pane, you see the hexadecimal values and in the right pane, you see the value of the hexadecimal data.

The format of Windows PCM Wave file is tabulated in Table 3.2. It will explained in the following paragraphs [49].

Table 3.2
400 Hz-1.2 KHz Bandpass filter results

File Offset(Bytes)	Field Name	Field Size (Bytes)
0	ChunkID	4
4	ChunkSize	4
8	Format	4
12	SubChunk1ID	4
16	SubChunk1Size	4
20	AudioFormat	4
22	NumChannels	4
24	SampleRate	4
28	ByteRate	4
32	BlockAlign	4
34	BirPerSample	4
36	SubChunk2ID	4
40	SubChunk2Size	4
44	Data	4

This format can be divided into 3 main groups. The first group is the general description of file format and size and the other two groups are the sub-chunks of it. The first subchunk is the "fmt" chunk for file format description and the second chunk is the "data" chunk for exact sound data storage.

The first group has 3 fields, ChunkID, ChunkSize and Format fields. The ChunkID contains the letters "RIFF" in ASCII form. Since each character occupies 1 byte, this filed has total 4 bytes of storage. The ChunkSize field contains the size of the entire file in bytes minus 8 bytes for the two fields not included in this count; ChunkID and ChunkSize. The format contains the letters "WAVE".

The second group, the fmt chunk describes the format of the sound information in the data sub-chunk. Subchunk1ID contains the letters "fmt ". Subchunk1Size is the size of the rest of the Subchunk which follows this number. For Windows PCM Wave the value is 16. AudioFormat is 1 for PCM. If this value is different than 1, it indicates a form of compression. the NumChannels field is 1 for mono,2 for stereo , etc. the SampleRate field contains the sampling frequency of data like 8000, 44100, etc. The ByteRate equals to SampleRate * NumChannels * BitsPerSample/8. The BlockAlign equals to NumChannels * BitsPerSample/8 which is the number of bytes for one sample including all channels. The BitsPerSample field the encoding information. For 8 bits encoding its value is 8, for 16 bits encoding its value is 16, etc.

The third group is the data chunk which indicates the size of the sound information and contains raw sound data. The Subchunk2ID field contains the letters "data". The Subchunk2Size is the number of bytes in the data. It can be formulated as Subchunk2Size = NumSamples * NumChannels * BitsPerSample/8. The data files is the actual sound data.

As an example, here are the opening 72 bytes of a wave file and its graphical interpretation is shown Figure 3.3. It is a 16 bits per sample, 2 channels, 22.05 KHz sampling frequency (sampling rate) PCM Wave file.

After decoding the Windows PCM Wave file format, it was possible to get out raw sound data and store it into an array. The result in array can also be written into a text file.

3.3.3 Signal Processing

Since the optimum filter pass band characteristics were determined, a FIR band-pass filter was designed for permanent use in the software. The advantage of FIR based filtering over the Fourier transform based one is its computational efficiency and its convenience for real time processing. **FIR1** function of the Matlab signal processing

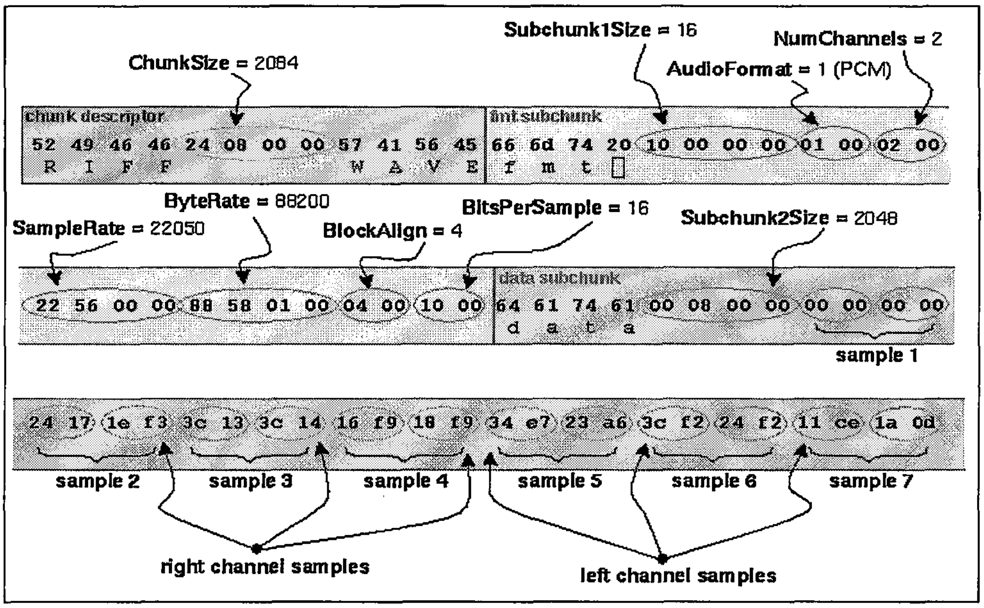

Figure 3.3 A graphical interpretation of a 72 bytes of wave file [49].

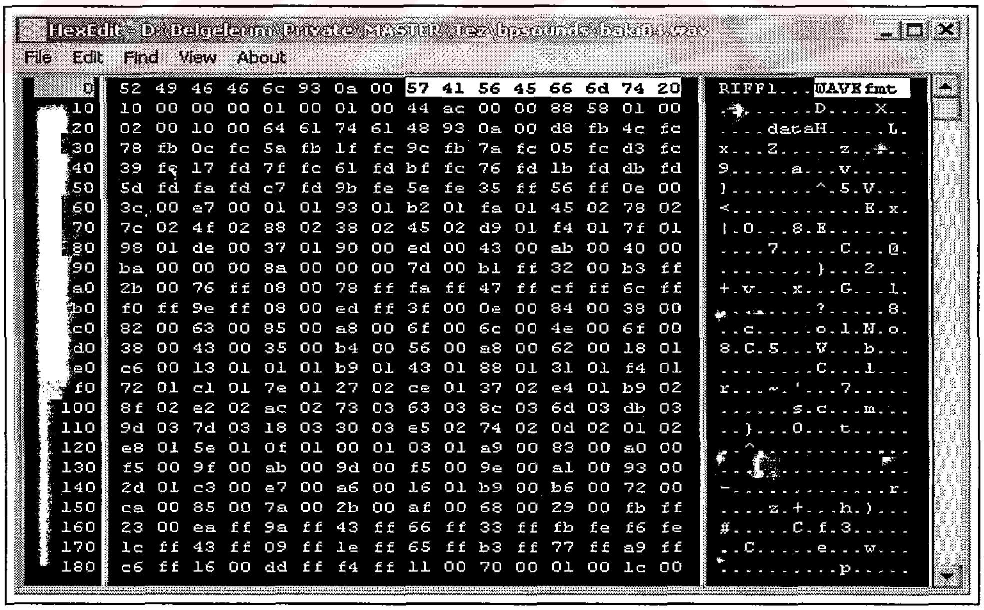

Figure 3.4 A Windows PCM Wave file opened with Hexedit Program

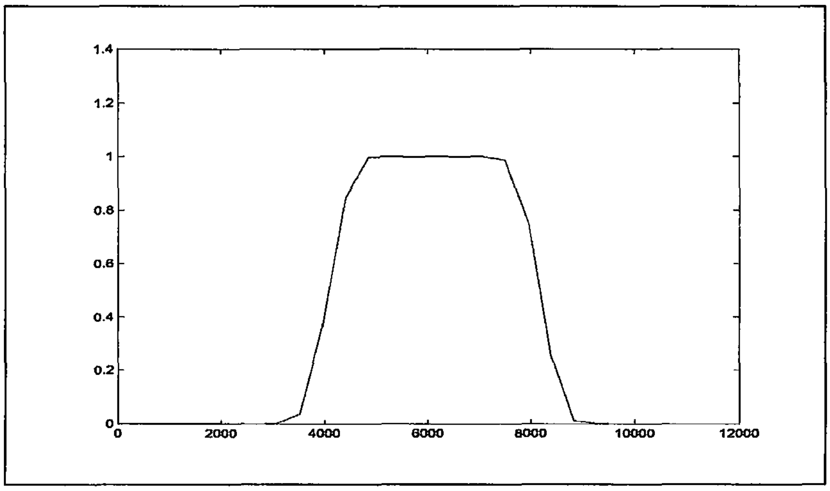

Figure 3.5 Bandpass filter designed with FFT.

software was used. FIR1 is a tool to design finite impulse response (FIR) filter using the window method. Upper and lower cut-off frequencies and the order of filter is set as input. The upper cut-off frequency value can be 1 as maximum and it must be the half of the sampling frequency. The coefficients of this filter are given in Appendix A. The frequency response of this filter is shown in Figure 3.5.

3.3.4 Finishing and Documentation

As the last step, the GUI was redesigned in order to perform all the functions necessary to detect the embolic signals in a user-friendly manner.

Both raw data and embolic signals is displayed at the same screen so that the user can check the results graphically. A scroll bar moving with time is put underneath the graphics so that one can see which part of the file is being played at the time.

After examination, the embolic signals are marked with a line in the figure, graphically. At the same time, embolic portions are displayed in a list form. In the list, the number of embolic signals detected, the length of each embolic signal and its location are stated. The user can save the list for clinical purposes.

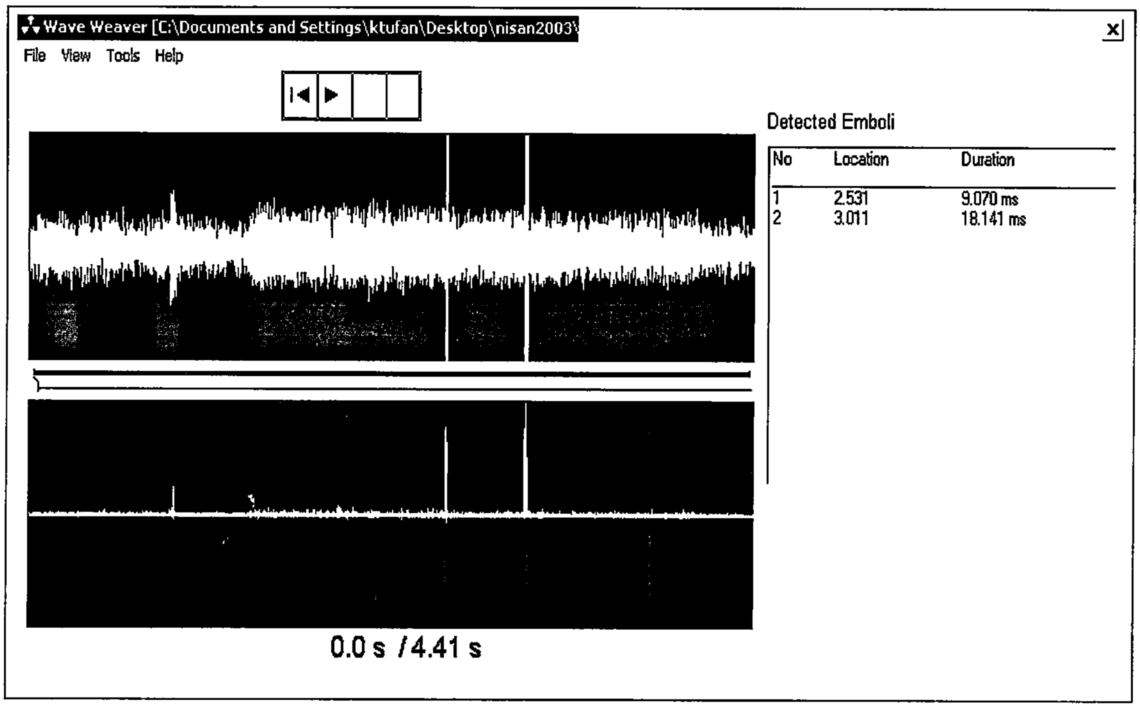

Figure 3.6 A sample view of graphical User Interface

With this software, one can analyze DUA recorded by other ways. To do so, DUA must be digitized in Windows PCM Wave format, 16 bit, mono and 22.05 KHz.

This GUI was prepared with a setup package. With this package, the software can be installed on a computer easily.

A sample view of the GUI is seen in Figure 3.6.

4. RESULTS AND DISCUSSIONS

In this study, DUA waveforms taken from SCUBA divers were investigated. The frequency characteristics of embolic signals were determined. By using the non-linear TEO, emboli detection performance was improved. Then a functional GUI was designed to integrate different phases of emboli detection system, starting from the recording of DUA to analyzing and displaying results.

DUA waveforms used were taken from two subjects each having 8 and 6 embolic signals, respectively. These waveforms were recorded on magnetic tapes. They were listened to by an expert and embolic signals within these signals were marked. Then, they were digitized in Windows PCM Wave file format. Digitized waveforms were converted into Matlab specific format for analyzing. By doing so, sound data within the Windows PCM Wave files were extracted into arrays. A bandpass filter subroutine was designed for simplifying the filtering process. Data in the array was bandpass filtered. It was then thresholded with appropriate multiples of the SD of filtered DUA signal. Places where the threshold value was exceeded were accepted as detected embolic signals.

In the literature, the frequency band of interest for embolic signals was stated as 400 Hz-1.2 KHz. Firstly, this band was used for the bandpass filter. Embolic signals in the DUA waveforms for two subjects were tried to be detected by changing the threshold value. A threshold value that gives minimum number of misses and false alarms for which both subjects was tried to be achieved. As you can see in Table 4.1 at high threshold value, subject1 emboli were detected but none of the embolic signals of subject2 could be detected. In order to detect the embolic signals of subject2, the threshold value should be set to lower values. As seen from the same table, the threshold value was decreased to 2.3 times the SD, where 3 of 6 embolic signals were detected with additional 9 false alarm. While decreasing the threshold value, the number of false alarm for subject1 increased significantly. As a result, filtering and thresholding did not give satisfactory results.

Table 4.1
400 Hz-1.2 KHz Bandpass filter results

SD coefficient for threshold	Subject 1		subject2		Total	
	M	FA	M	FA	M	FA
6	3	-	6	-	9	-
5.5	1	4	6	-	7	4
5	-	5	6	-	6	5
4.5	-	5	6	-	6	5
4	-	7	6	-	6	7
3.5	-	11	6	-	6	11
3	-	11	6	-	6	11
2.5	-	18	5	-	5	18
2.3	-	40	3	9	3	49

Since the detection results of 400 Hz-1.2 KHz band were not satisfactory, a non-linear TEO operator was applied to the filtered signal to improve the TBR. Embolic signals of subject1 was detected at high threshold values with a small number of false alarms. But, none of the embolic signals of subject2 could be detected at high threshold setting. At low threshold values, however, some embolic signals of subject2 were detected but with a significant number of false alarms of both subjects. Further decreasing the threshold value increased the number of false alarm drastically. Therefore, teagering the signal filtered by using a 400 Hz-1.2 KHz bandpass filter did not give satisfactory result, as seen in Table 4.2.

Both unteagered and teagered 400 Hz-1.2 KHz bandpass filtering methods did not yield satisfactory emboli detection result. Therefore, it can be concluded that the frequency characteristics stated for the animals in the literature do not conform with those of the humans. For this reason, the embolic signals were studied extensively for determining the most appropriate filter frequency characteristics by using different bandpass filters.

First, the frequency lower than 400 Hz was tested. As you can see in Table 4.3,

Table 4.2
400 Hz-1.2 KHz Teagered Bandpass filter results

SD coefficient for threshold	Subject 1		subject2		Total	
	M	FA	M	FA	M	FA
7.5	1	1	6	-	7	1
7	-	1	6	-	6	1
6.5	-	2	6	-	6	2
6	-	3	6	-	6	3
5.5		4	6	-	6	4
5	-	4	6	-	6	4
4.5	-	6	6	-	6	6
4	-	7	6	-	6	7
3.5	-	7	6	-	6	7
3	-	7	6	-	6	7
2.5	-	7	3	8	3	11
2.3	-	7	3	21	3	28

50-200 Hz and 100-400 Hz frequency bands were tested. The former band missed twelve of total fourteen embolic signals where it yielded total five false alarms. The later band yielded eleven missed embolic signals and four false alarms. It means that the embolic signals cannot have frequency characteristics below 400 Hz. Therefore, it was decided to search for frequency characteristics of embolic signals at higher frequencies.

Table 4.3
Frequencies lower than 400 Hz

	subject1		subject2		Total		Result
	M	FA	M	FA	M	FA	
100 Hz - 400 Hz	5	4	6	-	11	4	Rejected
50 Hz - 200 Hz	6	5	6	-	12	5	Rejected

The range from 1 KHz to 11 KHz was spanned with a 1 KHz of bandwidth filter. The upper limit was chosen as 11 KHz because after 10 KHz, the filtered signals is almost noise (Figure 4.1). The same process was repeated with 2 KHz and 4 KHz bandwidths. It was seen that 5-9 KHz was the region where the number of misses and false alarms are minimum for both subjects. It was decided to fine tune around

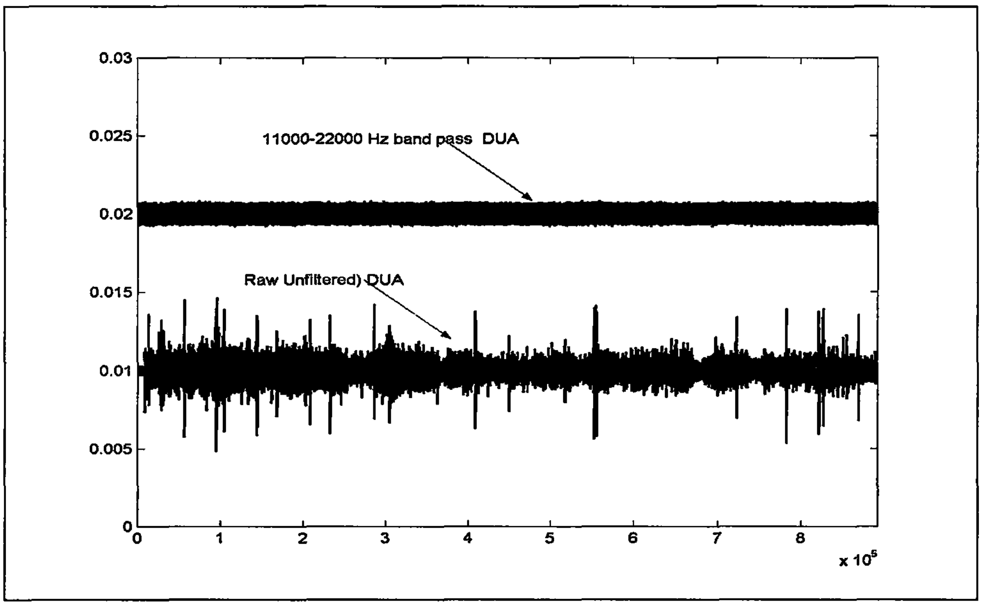

Figure 4.1 Raw DUA and 11-22 KHz filtered DUA.

this value to fix the embolic signal frequency band. To do so, the bandwidth was set decreased to 3.5 KHz. So, 1-4.5 KHz and 4.5-8 KHz bands were tested. At 4.5-8 KHz band, it was observed that, first subject yielded full detection of embolic signals with no false alarm. The second subject also detected all embolic signals while giving only one false alarm. Different bandpass filters and number of missed embolus and false alarms can be seen in Table 4.4

Filtered signal by using 4.5-8 KHz bandpass filter was further processed to increase the detection performance. This was accomplished by applying the TEO to the filtered signal. This application positively affected the emboli detection, because the false alarm of the second subject was eliminated with the application of the TEO, as seen in Table 4.5

With this study, the frequency characteristics of embolic signals for human subjects were investigated. After determining the frequency characteristics, the TEO was applied to increase the TBR. As a result, number of missed embolic signals and false alarms were decreased.

From recording of DUA on magnetic tapes to analyzing it and reporting embolic

Table 4.4
Different Frequency band results between 1-11 KHz.

Frequency Band	subject1		subject2		Total		Result
	M	FA	M	FA	M	FA	
1 KHz - 2 KHz	-	6	6	-	6	6	Rejected
2 KHz - 3 KHz	-	7	-	31	-	38	Rejected
3 KHz - 4 KHz	-	6	-	1	-	7	Rejected
4 KHz - 5 KHz	-	4	-	-	-	4	Rejected
5 KHz - 6 KHz	-	2	2	-	2	2	Rejected
6 KHz - 7 KHz	-	-	2	-	-	2	Rejected
7 KHz - 8 KHz	3	-	2	-	5	-	Rejected
8 KHz - 9 KHz	7	1	6	-	12	5	Rejected
9 KHz - 10 KHz	8	-	6	-	14	-	Rejected
10 KHz - 11 KHz	8	-	6	-	14	-	Rejected
1 KHz - 3 KHz	-	5	5	-	5	5	Rejected
3 KHz - 5 KHz	-	4	-	14	-	18	Rejected
5 KHz - 7 KHz	1	-	2	-	3	-	Rejected
7 KHz - 9 KHz	4	-	6	-	10	-	Rejected
9 KHz - 11 KHz	8	-	6	-	14	-	Rejected
1 KHz - 5 KHz	-	4	5	-	5	4	Rejected
5 KHz - 9 KHz	-	-	1	1	1	1	Rejected
1 KHz - 4.5 KHz	-	4	5	-	5	4	Rejected
4.5 KHz - 8 KHz	-	-	-	1	-	1	OK
8 KHz - 11 KHz	5	-	6	-	11	-	Rejected

signals, there are some steps accomplished by using different tools. A functional GUI was prepared to integrate all the steps into one window.

There are four titles of menu in this software. The first menu is the File menu which includes New, Open, Save As and Exit tools. With New tool, one can record a DUA input from the microphone input of the sound card. Open tool is used to open a sound file recorded earlier. File to be opened must be mono channel, 16 bits, 22050 Hz sampling frequency Windows PCM Wave format. Save As tool is used to save recorded sound. Exit menu item is used to quit the program (Figure 4.2).

Table 4.5
Teagered and unteagered results of 4.5-8 KHz band

	subject1		subject2		Total		Result
	M	FA	M	FA	M	FA	
Teagered	-	-	-	-	-	-	OK
Unteagered	-	-	-	1	-	1	OK

The second menu is the View menu including Show Info, Show Wave and Show Filtered tools. Show Info is used to display the characteristics of sound wave file. Show Wave tool is used to show the waveform characteristics of raw DUA digitized as sound wave file. Show Filtered tool is used for displaying processed DUA waveform. Since the processed signal is displayed underneath the raw signal, one can see the difference of raw signal and processed signal (Figure 4.3).

The third menu, Tools menu, holds the tools for signal processing tools. First one is the Apply Filter tool which is used to filter the DUA and teagering this filtered signal. The second tool is the Detect Embolus tool used to compare processed signals with threshold value to detect the embolic signals. Detected embolic signals are listed in a list box. The third tool in this menu is the Write To File tool used to write detected embolic signals into a text file. The last menu item in this menu is the Advance tool. For average users, the threshold value and the trial length are constant. For the researchers, however, an option to change these values is provided. If one click on this menu, he or she can change the coefficient of SD of test region, in other words, the threshold value and the number of samples in trial length. This tool act as a toggle switch between advanced and standard mode. After choosing the advance mode, one can return to the standard mode by clicking again this menu item. Tools menu and its content can be seen in Figure 4.4. The GUI is in the advance mode is seen in Figure 4.5.

The last menu is the Help menu. Help menu opens a help file prepared in html file format. It describes the functions of menu items and other objects of the software (Figure 4.6). A setup tool is prepared for easy installation of the software. With

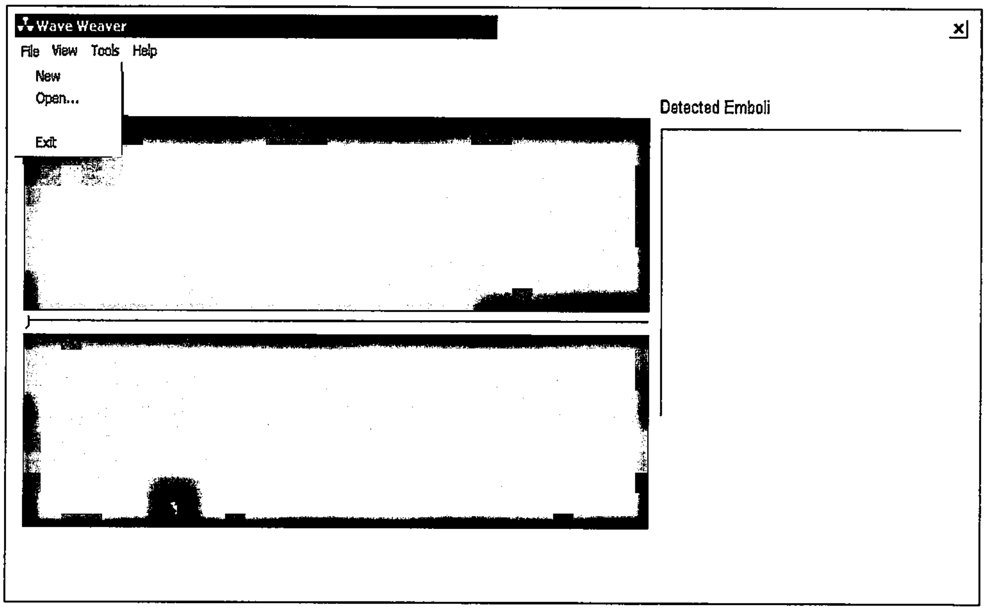

Figure 4.2 File menu content of GUI

this tool, executable of the GUI and necessary components can be set to their correct locations automatically.

A multimedia tool is used in this software. A DUA taken from the microphone input of sound card can be recorded with this tool. After recording phase, a standard window, the "Save As" window is called and the recorded data is provided to be saved permanently. After saving, analysis of the data is triggered automatically. Data in the opened wave file is extracted into an array firstly. Then it is bandpass filtered and TEO is applied. Results are displayed graphically on the form and list of detected emboli is written in the list box. In the raw data plot which is at the top of processed data, embolic places found are marked. It is possible to listen the DUA by pressing the "Play" button of the multimedia tool. A slider control which is sliding towards the right with speed of sound wave. Therefore, visual and aural inspections can be applied simultaneously. For the functions of buttons on the multimedia control, refer to the help of the software.

In this study, we have a limited number of subjects and DUA waveforms. More data from different subjects must be used to improve the reliability of this emboli detection system.

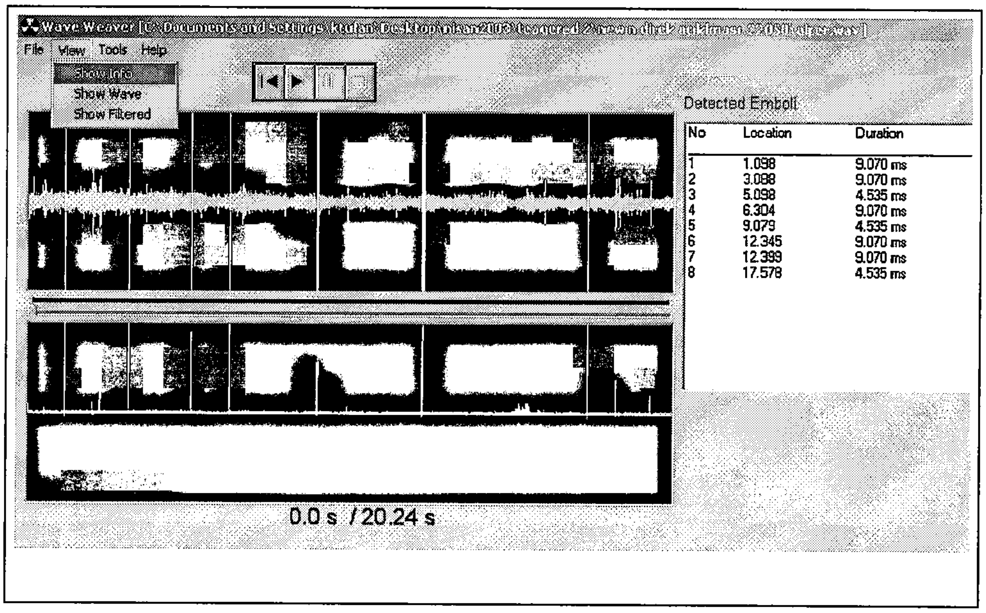

Figure 4.3 View menu content of GUI

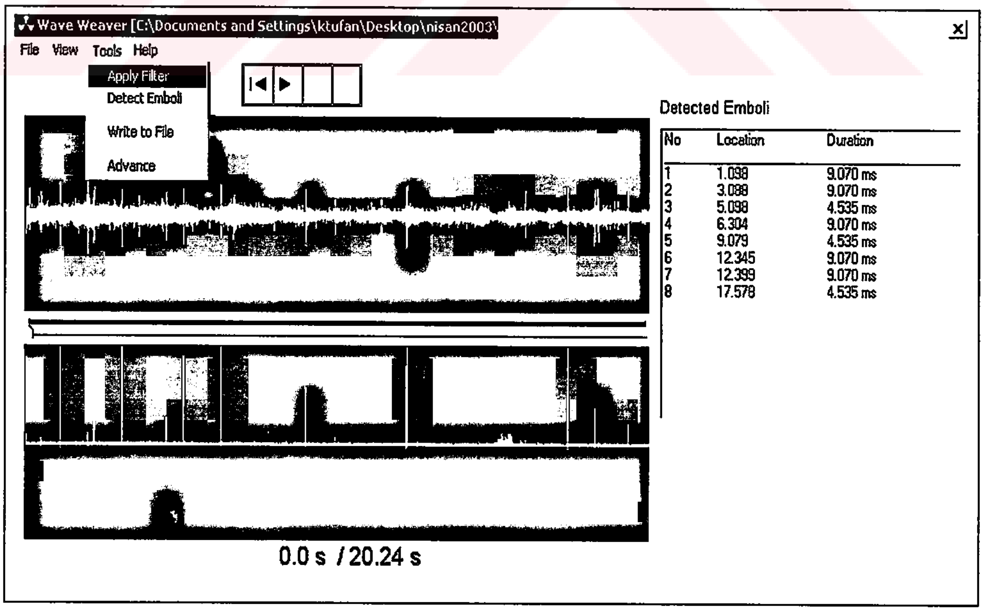

Figure 4.4 Tools menu content of GUI

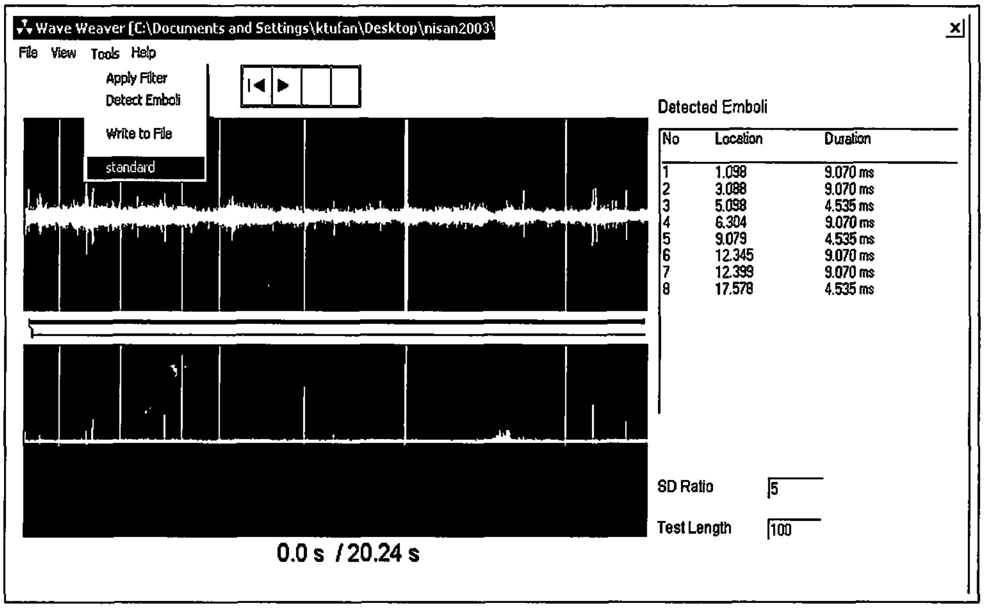

Figure 4.5 Emboli detection system is in advance form.

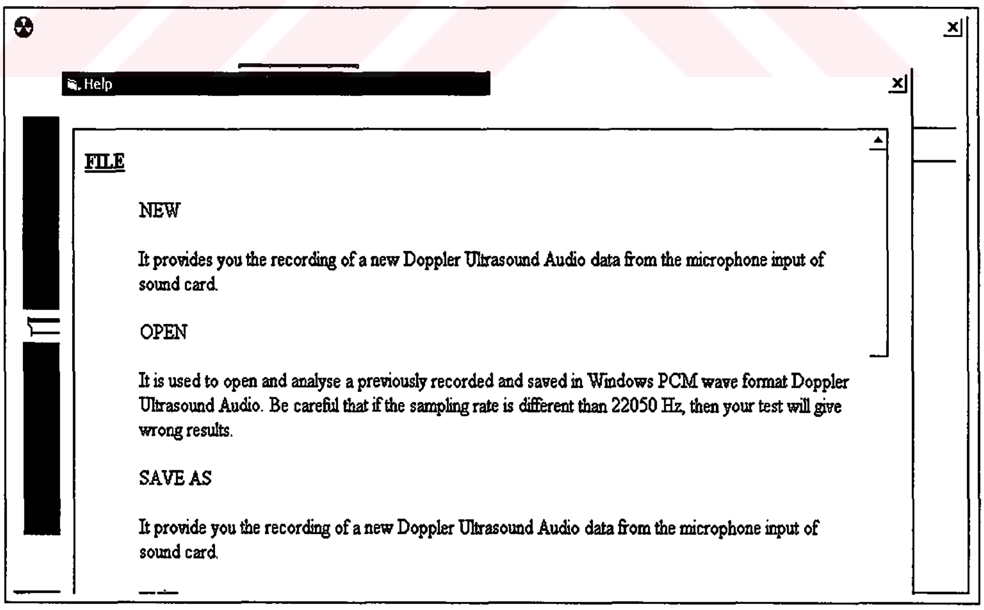

Figure 4.6 Help menu of GUI

5. CONCLUSIONS

The aim of this study was to understand the characteristics of embolic signals in DUA and develop an reliable and easy method to detect gas bubbles circulating in veins.

The proposed method is based on band pass filtering and nonlinear thresholding and is tested by using DUA recorded from two subjects each having eight and six embolic signal waveforms, respectively.

The frequency characteristics of embolic signals are examined. It is found that the 4.5-8 KHz frequency band is the desired band for subclavian DUA. After setting the frequency band, the TEO is used for amplifying the TBR and enhancing the the reliability of the system. No missed signal and no false alarm is achieved. A functional and easy to use GUI is designed. All the modules from recording the DUA to finding embolic signals are integrated into a software.

In this work, there is limited number of subjects and embolic signals. The DUA is taken from two subjects and there are total fourteen embolic signals. The number of subjects and the number of embolic signals must be increased. Also, there is only one expert to mark the embolic signals (Mr. S. Murat Egi). In future studies, more experts should listen to the DUA samples and mark embolic signals.

This GUI tools designed to detect embolic signals is for offline DUA analysis. In future, it must be modified for online (real-time) DUA processing. This way, the system can be used clinically, as well.

Therefore, a future work should address the objectives of testing the system with more DUA samples taken from different subjects, having more experts for marking the embolic signals and modifying the software for real-time operation.

6. APPENDIX A

The band pass filter used in the GUI software is designed by using the FIR1 function of Matlab software. In this appendix, the coefficients of this filter is tabulated.

Table 6.1
Band pass filter coefficients of 4.5-8 KHz.

No	Value	No	Value	No	Value	No	Value
1	-0.0002	2	-0.0004	3	0.0023	4	-0.0003
5	-0.0034	6	0.0014	7	0.0003	8	0.0030
9	0.0037	10	-0.0133	11	-0.0002	12	0.0130
13	-0.0020	14	0.0073	15	-0.0192	16	-0.0212
17	0.0483	18	0.0052	19	-0.0259	20	-0.0042
21	-0.0610	22	0.0915	23	0.1210	24	-0.2412
25	-0.0634	26	0.3182	27	-0.0634	28	-0.2412
29	0.1210	30	0.0915	31	-0.0610	32	-0.0042
33	-0.0259	34	0.0052	35	0.0483	36	-0.0212
37	-0.0192	38	0.0073	39	-0.0020	40	0.0130
41	-0.0002	42	-0.0133	43	0.0037	44	0.0030
45	0.0003	46	0.0014	47	-0.0034	48	-0.0003
49	0.0023	50	-0.0004	51	-0.0002	52	-

7. APPENDIX B

GUI software codes are included with the attached CD. In the CD, an installation package is also included to the source codes in order to install the executables on any computer.

There are two folders in the CD, the Source Code and the Package folders. The file lists of them are tabulated below.

Table 7.1
Files in the Source Code Folder

File Name	Explanation
prjEmboliDetect.vbp	Visual Basic Project file
frmtest.frm	Visual Basic form
Help.frm	Visual Basic form for help file monitoring
Bubble.htm	HTML help file
MSSCCPRJ.scc	Source safe status file
prjEmboliDetect.PDM	PDM file
frmTest.frx	Visual Basic form binary file
prjEmboliDetect.vbw	Visual Basic workspaces

Table 7.2
Files in the Package Folder

File Name	Explanation
Setup.exe	Setup file
Setup.lst	List file
WW.cab	Zipped cabinet file
setup.exe	Setup Bootstrap for Visual Basic Setup Toolkit
Setup1.exe	Visual Basic 6.0 Setup Toolkit
Setup.lst	List file
WW.exe	Application file
WW.bat	MS-DOS Batch File
MCI32.OCX	ActiveX Control
MSCOMCTL.OCX	ActiveX Control
COMDLG32.OCX	ActiveX Control
ASYCFILT.DLL	DLL file
COMCAT.DLL	DLL file
OLEAUT32.DLL	DLL file
OLEPRO32.DLL	DLL file
VB6STKIT.DLL	DLL file
msvbvm60.dll	DLL file
Project1.DDF	DDF file
ST6UNST.exe	uninstall application
Bubble.htm	HTML help file
Alper.wav	Windows PCM Wave file
Baki.wav	Windows PCM Wave file

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