

# **Skin Characterization with High-Frequency Ultrasound**

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# Skin Characterization with High-Frequency Ultrasound

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## **Abstract:**

Recent development of high-frequency ultrasound transducers has led to a vast range of applications in dermatology, such as the evaluation of tumors, burn injuries, skin aging, etc. The question examined in this research is "Can tissue structure changes be quantified with 15 MHz ultrasound?" Ultrasound data are collected in the pulse-echo mode from *in vivo* studies in normal volunteers from the mid-anterior and posterior forearm. The data are displayed as B mode intensity images. To help differentiate between different states of tissue the rf data are converted into the frequency domain and the Integrated Backscatter, a spectral feature based on the power spectrum, is analyzed.

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## Table of Symbols and Abbreviations

<b>Abbreviation</b>	<b>Definition</b>
A-line	Ultrasound echo reflected by the scatterers within the resolution cell volume presented as a voltage versus time plot
B-scan	Two-dimensional brightness image
GUI	Graphical User Interface
IDL	Interactive Data Language
RF	Radio frequency

# 1. Introduction

The objective of this research is to design a rigorous method to characterize skin using an ultrasound imaging system. The goal for this research is to provide an alternative to biopsy routinely used in dermatology. Biopsy is an invasive method which leaves scarring on the patient's body. This kind of method may leave emotional scars as well. A patient will not have to undergo a biopsy check for cancerous tissue if more research is done in this area. Ultrasound is a non-invasive method with no side effects. Ultrasound may also be used to determine how much of the skin the surgeon has to remove for malignant skin cancer. Ultrasound may be useful in achieving the goal for the surgeon which is to improve the assessment of the volume needed for removal.

This research is a stepping stone in accomplishing the large aim of providing an alternative to biopsy. Ultrasound B-scan images are first be created and inspected visually in order to get a qualitative estimate of tissue structures within the volume under interrogation. A global integrated backscatter method is applied to the data and differences, if any, are estimated using a t-test. The hypothesis of this research is, "Are there significant differences between the anterior and posterior mid-forearm regions of tissue structure imaged with a 15 MHz transducer?" Imaging at 15 MHz provides enough resolution and penetration so that these changes will manifest themselves as a change in the backscattered signal and may be evident in a B-mode image. The method is tested on normal volunteers.

Ultrasound technology is evolving rapidly and high-frequency transducers are readily available. This gives physician easier access to high-frequency transducers. Non-invasive objective assessment of skin condition is possible. Ultrasound penetrates through the skin surface thus giving the user a chance to see beyond into the underlying structure. With this technology, identification of skin layers is feasible thus giving the user more information.

Tissue characterization is a difficult problem because little is known on tissue scattering properties. An ultrasound B-mode image is not enough to understand tissue function and pathology. It is necessary to extract information from the radio frequency data. Tissue characterization techniques include spectral methods, signal processing, statistical characterization.

This work is divided in several sections. Ultrasound background and theory are presented in Section 2. Section 3 addresses the experimental methods used in the analysis of data. Section 4 describes the experimental protocol while Section 5 presents the analysis. Finally, conclusions and future work are discussed in Sections 6 and 7.

## 2. Background and Theory

Ultrasound is used in medical imaging for the detection and measurement of tissue motion and blood flow (Kremkau 2002). Ultrasound is a safer medical tool than X-rays due to its properties of being a non-invasive and non-ionizing technology. Ultrasound equipment is cheaper to manufacture as well compared to other imaging technologies. At frequencies above 10 MHz, researchers have shown that the technology provides enough resolution to characterize microstructures (Cammarota 1998 & Lebertre 2002).

Recent development of high-frequency ultrasound transducers has led to a vast range of applications in dermatology, such as the evaluation of tumors (Raju 2001 & 2003), burn injuries (Thiboutot 1999), skin aging, water content (Eisenbeiss 2001), etc.

In dermatology, most of diagnoses are done by visual inspection and palpation of the skin. High-frequency ultrasound can give a measurement of volume so that if malignant tissue needs to be removed the surgeon knows exactly how much tissue needs to be removed.

Ultrasound penetrates through the skin; therefore assessments of appearance are possible as well as observation of the skin layers below the surface. The challenge is to characterize the different skin conditions such as skin lesion, mole, and normal skin. In the ultrasound tissue characterization field it has been an ongoing question to identify the main scatterers at a given frequency. It is impossible to truly identify the structure due to the complexity of the scattering properties, furthermore as ultrasound frequency is increased these properties may change and some of the underlying assumptions may not hold. Thus statistical methods have been developed to address this question. The purpose of this paper is to design a robust method to differentiate between normal skin, moles, and skin lesions with the acquired high-frequency ultrasound data. The experiment was performed with a high frequency piston focused transducer on human skin in vivo described in detail in the next sections.

Tissue characterization has been an ongoing research in the Ultrasound Imaging Lab. Studies have been conducted in breast tissue, both normal and abnormal, liver, and skeletal muscle. Statistical methods, such as the second normalized intensity moment have been used to differentiate between normal and diseased breast tissue and obtain the effective number of scatterers within the resolution cell volume. Micro-structure characterization has also been investigated by performing frequency sweeps and quantifying the inter-scatterer distance.

Spectral methods, such as the integrated backscatter have been successfully applied to the study of skeletal muscle and differentiation between normal volunteers and patients suffering from Duchenne's muscular dystrophy. This study was performed while having volunteers exercising their biceps. Results are shown in Figures 1 and 2 (Helguera, 1990).

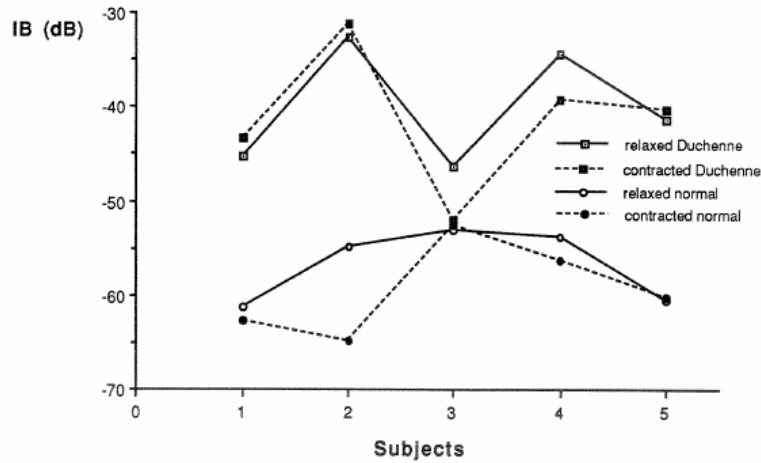


Figure 1. Changes in integrated backscatter (IB) with exercise in normal volunteers and patients with Duchenne’s muscular dystrophy.

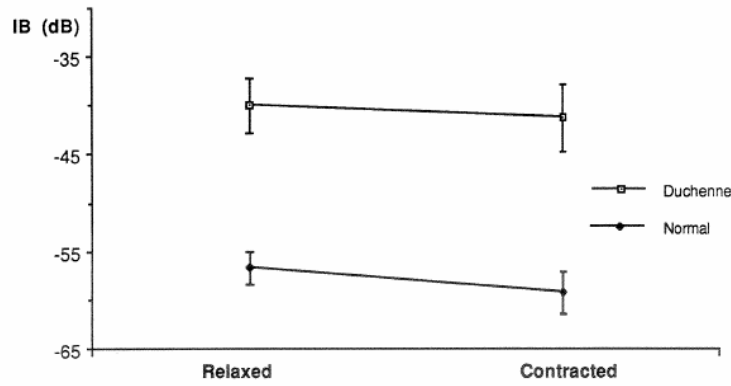


Figure 2. Integrated backscatter (IB) from afflicted patients is consistently higher than that of normal volunteers.

This spectral method has also been use by other research groups in the ultrasonic study of skin at 20 MHz (Fournier, 2000).

The present work investigates skin at 15 MHz. It is important to theoretically characterize the transducer’s lateral and axial resolutions to provide us with a framework.

The axial resolution of a transducer can be approximated by using the following equation:

$$z = \frac{2c}{f_c} \approx 2\lambda = 0.2mm \tag{1}$$

Where  $z$  is the axial resolution,  $c$  is the speed of sound in the tissue (1500 m/s),  $f_c$  is the center frequency of the transducer (15 MHz),  $\lambda$  is the wavelength.

The lateral spatial resolution in millimeters is calculated from:

$$\lambda = \frac{2c}{f_c} \approx 0.2\text{mm} \quad (2)$$

The lateral resolution is best at the focal length of the transducer, and it gets wider away from this distance into the far field of the transducer due to diffraction.

Skin may be divided into three structures: epidermis, dermis and subcutaneous fat (Thiboutot, 1999). The epidermis about 50 – 100 μm in depth, the dermis is between 1 200 and 1 800 μm in depth. Terminal hair follicles are 1 500 to 4 000 μm. A 15 MHz ultrasound pulse is expected to penetrate about 1.5 cm into the skin. Figure 3 shows a pictorial representation of a volume section.

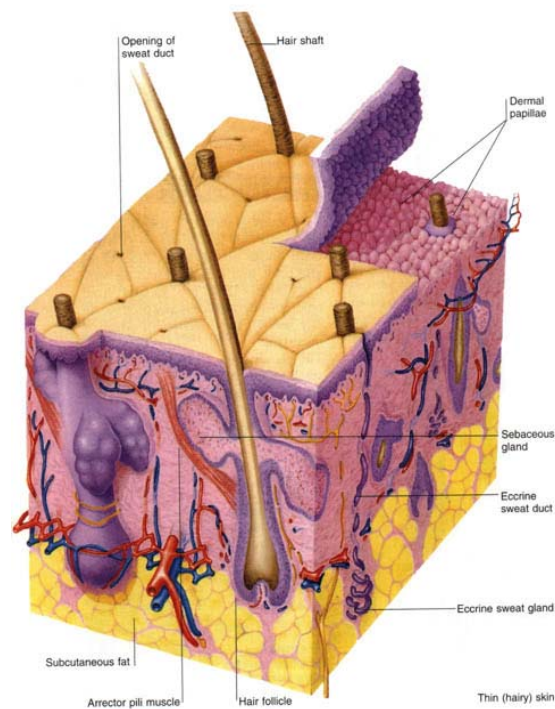


Figure 3. An illustration of skin volume section (Gawkrödger, 1997).

### 3. Experimental Methods

The experimental setup used for this study consists of a single element 15 MHz focused transducer. In order to form an image using the pulse-echo technique, the transducer needs to be scanned perpendicular to the surface to be imaged.

A line of data is collected at each position in the scan. These data contain information of the backscattered signal as a function of depth. 50 to 100 such lines are collected and stacked side by side to form an image of a cross section of the structure under investigation. This process is schematically shown in Figure 4 and an actual A-line is shown in Figure 5. In order to simulate a brightness image, better known as a B-scan, the Hilbert transform is applied to the real data to obtain an imaginary part. From here, the envelope (amplitude) can be calculated as the magnitude of the complex signal

$$E(f(n)) = \sqrt{\Re(f(n))^2 + \Im(f(n))^2} \quad (3)$$

Intensity is the square of the amplitude, therefore the brightness image is created from

$$I(f(n)) = E(f(n))^2 \quad (4)$$

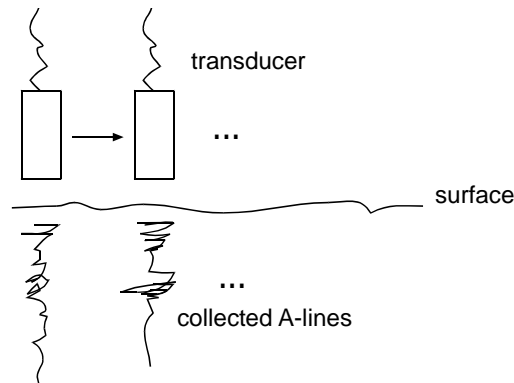


Figure 4. Illustration of data collection.

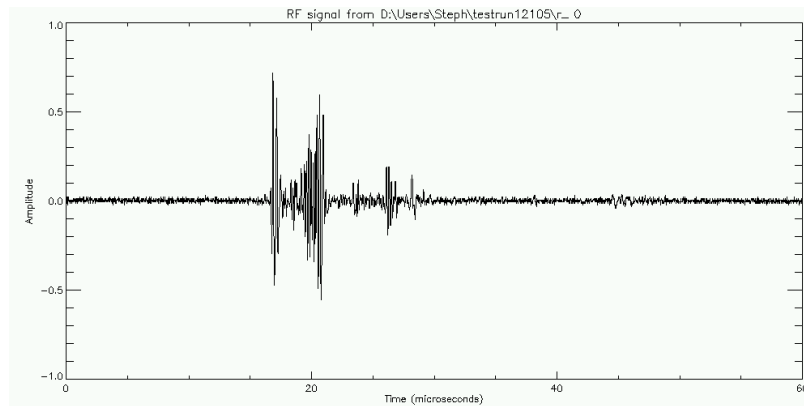


Figure 5. Experimental A-line. First large signal amplitude on the left is produced by the skin surface. Signal to the right comes from dermis and epidermis.

Structural information is inferred from the A-line since depth is encoded in the horizontal axis via

$$c = \frac{2d}{t} \quad (5)$$

Where  $c$  is the speed of sound in tissue, in average 1500 m/s,  $d$  is distance and  $t$  is time. The factor 2 is necessary to take into account the round trip.

Echoes return to the transducer wherever an impedance mismatch occurs. Impedance is defined as

$$z = \rho c \quad (6)$$

Where  $\rho$  is the density of the tissue and  $c$  is the speed of sound. Impedance is measured in Rayls.

The B-mode image thus produced is shown in Figure 6.

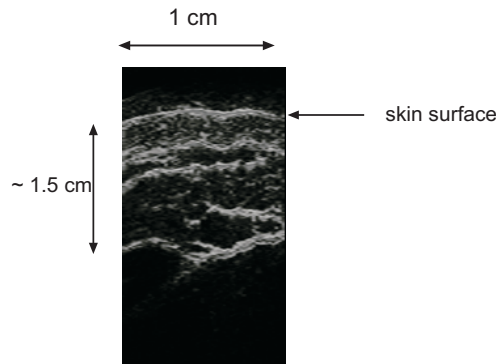


Figure 6. B-scan image of skin in the anterior mid-forearm. Visible structures show epidermis at the top of the image, dermis scattering underneath.

A major factor in determining the resolution of an ultrasound image is attenuation, which limits penetration. Attenuation increases with higher center frequencies and thus penetration decreases. Put it in other words, the farther the sound travels the greater the attenuation. Fine resolution is difficult to achieve at deeper depths.

Attenuation includes absorption (conversion to heat), and reflection and scattering of the sound as it encounters tissue interfaces. Absorption is the main factor that contributes to attenuation.

Attenuation can be described by an exponential law with distance:

$$A(z, t) = A_0 e^{i(\omega t - kz)} e^{-\alpha z} \quad (7)$$

Equation (7) represents a plane wave affected by a multiplicative amplitude loss term due to attenuation.  $\omega = 2\pi f$  is the frequency of the transducer,  $k$  is the wave number,  $z$  is depth and  $\alpha$  is the attenuation coefficient.

Echoes from reflection and scattering are essential to create an image but contribute little to attenuation.

Attenuation can also be quantified in decibels (dB) via the following equation:

$$A(\text{dB}) = 1/2 \times f \times z \quad (8)$$

Where  $f$  is the center frequency of the transducer in MHz and  $z$  is the path length in cm.

In spite of these limitations, an ultrasound image is very detailed and “geometrically” correct. The image represents a map of the mechanical properties of the structure under evaluation which depend on density and stiffness or elasticity.

## 4. Experimental Protocol

The experiment is performed by holding the high-frequency transducer perpendicular to the skin with the focal zone at the surface of the skin as shown in Figure 7:

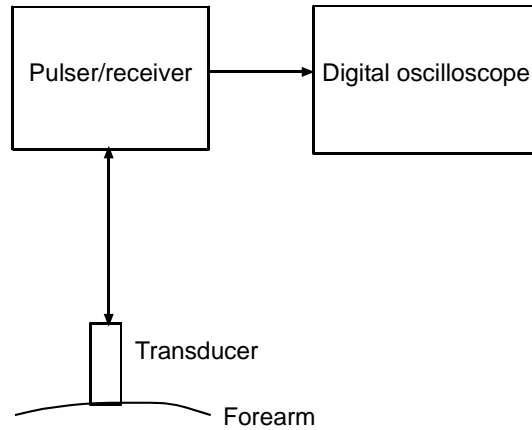


Figure 7. General experimental setup.

Experiments are conducted on normal, healthy volunteers. Volunteers are seated with their arm resting on a table shown in Figure 8.

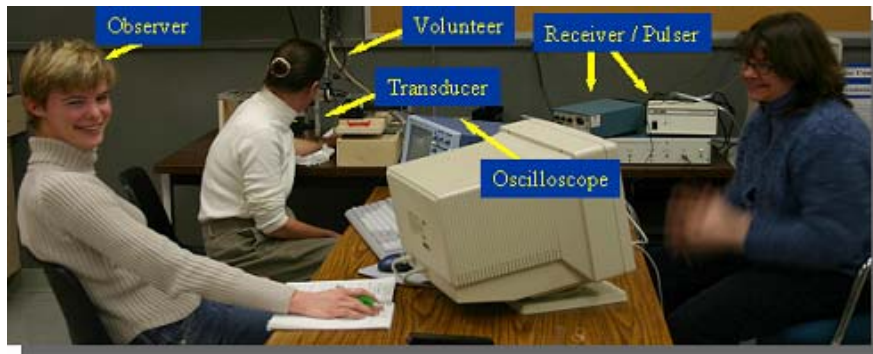


Figure 8. Experimental setup with a volunteer.

The 15 MHz focused transducer with a water-filled standoff is placed on the skin of the forearm. Initially, a line of 10-20 mm on the surface of the skin is imaged by collecting A-lines on a line scan mode of at least 50 to 100 sites. Coupling gel is added between skin surface and standoff to improve transmission. The actual setup is shown in Figure 9.

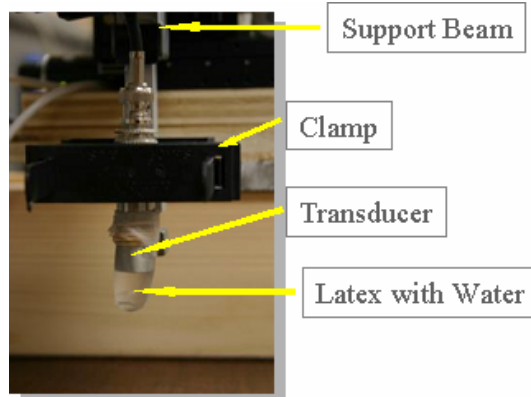


Figure 9. Experimental setup for transducer standoff.

The water-filled standoff is implemented with a finger section of a common latex rubber glove used in laboratory work, attached to the transducer with a rubber band. Care is taken to eliminate air bubbles. The flexibility of the standoff provides control over the focal length for various depths within the skin. The transducer is controlled by a programmable x-y stepper motor system.

The digital oscilloscope samples the data at a sampling frequency of 500 MHz. The digitized data are then transferred to the computer for further analysis. An example of A-line is shown with the water standoff and skin signals in Figure 10.

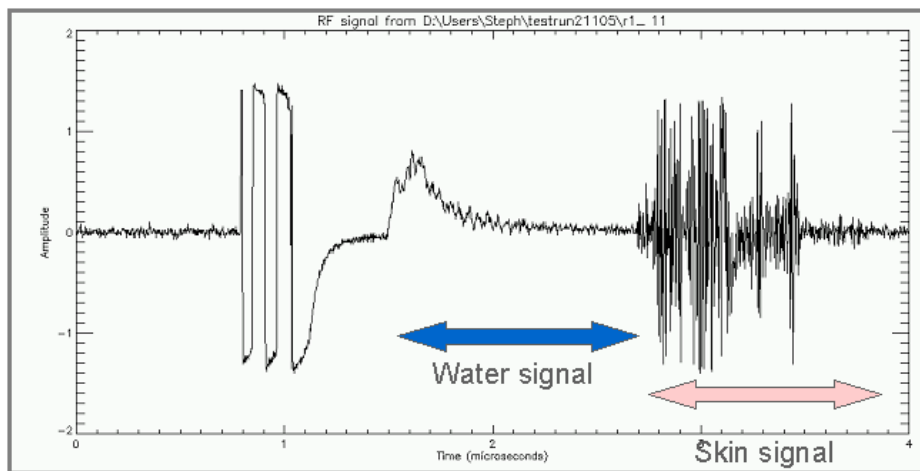


Figure 10. A plot of radio frequency for a single A-line.

## 5. Analysis of Experimental Results

IDL© programs were used in this analysis. A-lines are displayed using the IDL© graphical user interface shown in Figure 11.

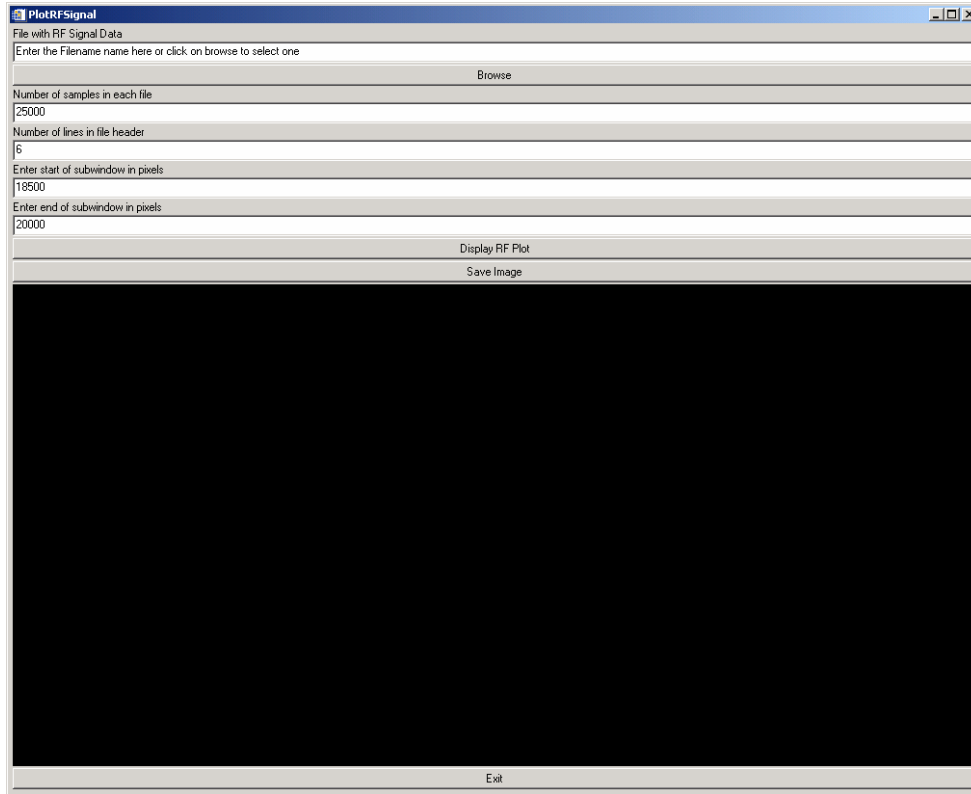


Figure 11. GUI to display RF data.

The A-line GUI displays the RF data one line at a time allowing inspection of different regions by selecting the length of the zoom window. This way scattering from epidermis and dermis can be separated for further studies.

Once the A-lines are collected a B-scan image is created by calculating the envelope of each line. This process is implemented with the user interface developed in IDL©, shown in Figure 12.

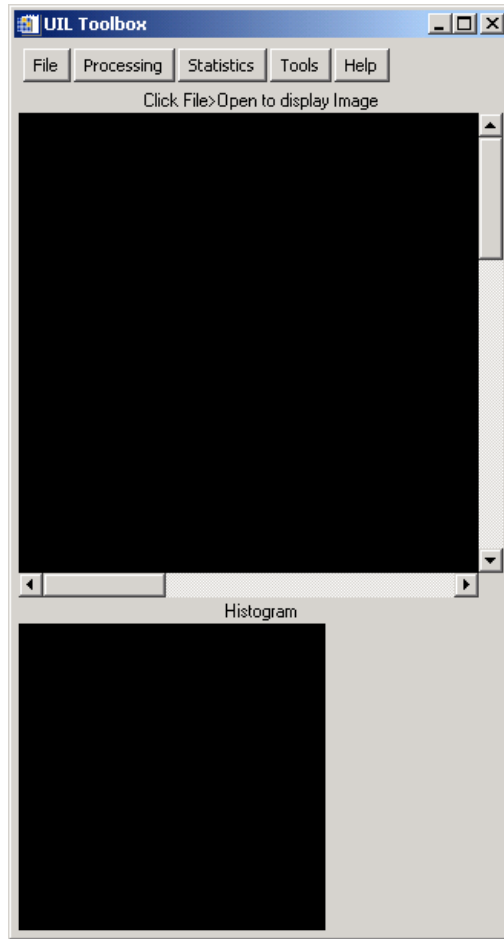


Figure 12. Ultrasound Imaging Lab Toolbox GUI.

This toolbox calculates first-order statistics of the rf data, such as the histogram. It does calculate as well normalized moments and creates a B-scan image that gets displayed in the larger frame of the GUI. Image processing is also performed in this GUI. Some of the images created are shown in the next section.

Frequency domain analysis is performed on the raw data looking for spectral signatures of the different structures.

For this study we chose to analyze the integrated backscatter, a spectral feature. The power in the backscattered signal as a function of frequency can be expressed as

$$|E(f)|^2 = |P(f)|^2 |I(f)|^2 |S(f)|^2 \quad (9)$$

The averaged signal power spectrum,  $|E(f)|^2$ , is shown in Figure 13 below.

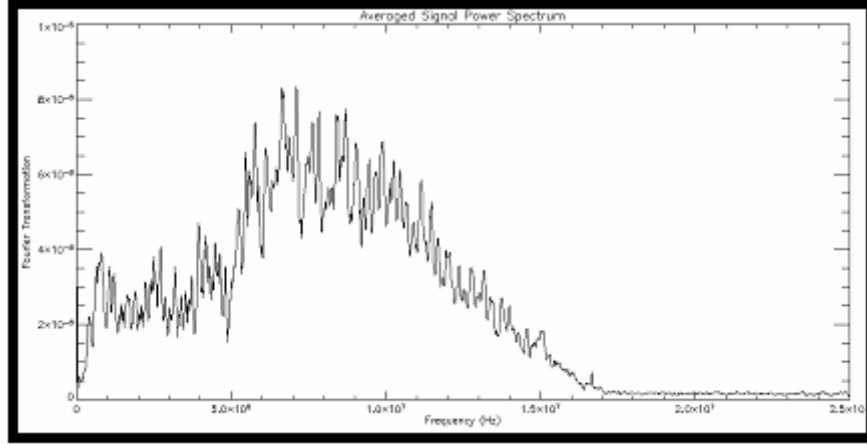


Figure 13. A plot of Averaged Signal Power Spectrum. Amplitude versus frequency.

Where  $P(f)$  denotes the transfer function of the transducer and associated electronics,  $I(f)$  represents an exponential decay factor due to the tissue that includes attenuation and  $S(f)$  is the backscatter transfer function of the tissue volume being interrogated.

The backscattered transfer function of the tissue is a useful relative measure of the efficiency with which ultrasound at different frequencies is backscattered by the tissue volume under investigation. It is independent of the electromechanical properties of the transducer, however it depends on the beam geometry, the distance between the transducer and the tissue volume, and the attenuation of the intermediate tissue.

The frequency dependence of the transducer is removed from the backscattered signal using a reference power spectrum from a planar perfect reflector:

$$|E_{ref}(f)|^2 = |P(f)|^2 R_{ref}^2 \quad (10)$$

Here  $R_{ref}$  is the acoustic amplitude reflection coefficient. Since we are assuming a perfect reflector then  $R_{ref} = 1$ . The reference power spectrum,  $|E_{ref}(f)|^2$ , is shown in Figure 14 below.

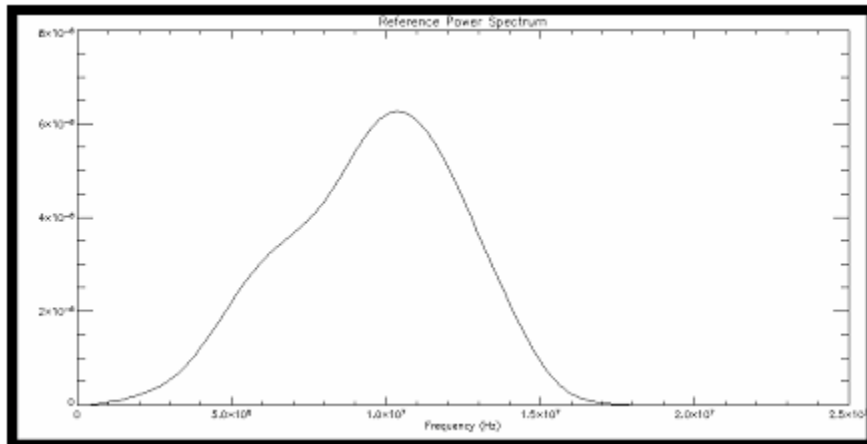


Figure 14. A plot of Reference Power Spectrum. Amplitude versus frequency.

The backscattered transfer function is obtained from measured quantities by normalizing for the frequency dependence of the transducer:

$$|S(f)|^2 = |E(f)|^2 / |E_{ref}(f)|^2 \quad (11)$$

$S(f)$  is known as the apparent backscatter.

The backscatter transfer function is expressed in decibels relative to the reflection from a planar perfect reflector by taking

$$10 \log |S(f)|^2 = 10 \log \left( |E(f)|^2 / |E_{ref}(f)|^2 \right) \quad (12)$$

A convenient index, known as the integrated backscatter, is the frequency mean of the transfer function over the useful bandwidth of the transducer:

$$|IB|^2 = 1/N \sum_{i=1}^N 10 \log |S(f_i)|^2 \quad (13)$$

Where N is the number of frequencies at which the backscatter transfer function was sampled.

The above analysis is carried on using the IDL© GUI shown in Figure 15.

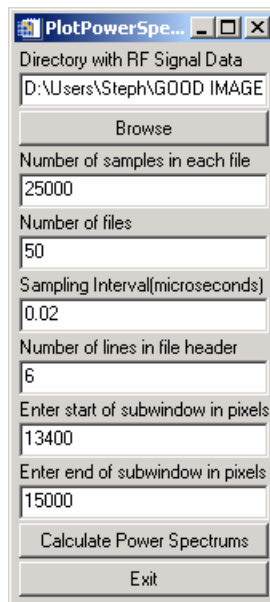


Figure 15. Spectral Analysis GUI.

It should be noted that in order to perform the spectral analysis the RF data were first windowed with a Hanning window to avoid leakage and ringing in the frequency domain.

## 6. Results and Discussion

Figure 16 shows three different B-scan regions from three volunteers. As these images indicate, there are visible tissue structures yet to be characterized. The dark areas on the image correspond to regions where the ultrasound energy is absorbed and the bright areas are where the signal scatters the most.

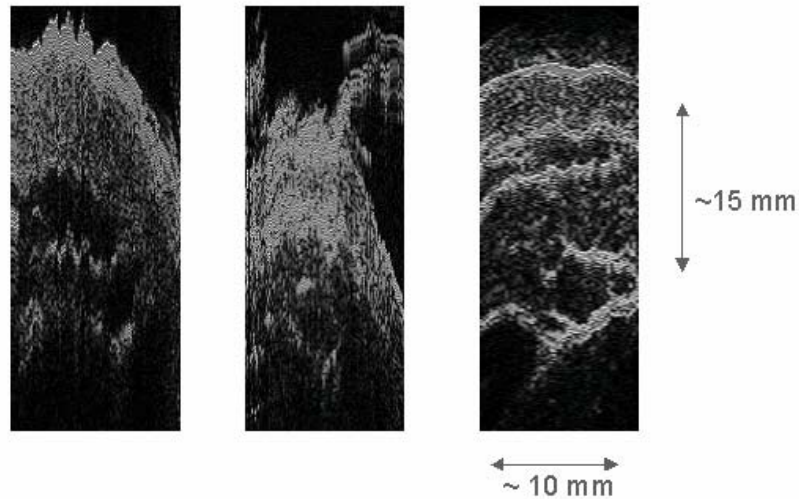


Figure 16. Three different B-mode scans of three volunteers.

Tissue characterization is a difficult problem because very little is known on tissue-scattering properties. One of the problems is that while measuring tissue properties system effects such as the transducer's spectral characteristics need to be corrected for. On the other hand, at the frequency range used in medical imaging, scattering is a function of frequency.

To better understand tissue function and pathology the creation of an image is not enough, it is necessary to extract information from the pulse-echo data.

Tissue characterization techniques are almost always based on the study of the rf signal, i.e. raw data. These techniques may include basic spectral methods (Fourier analysis), spectral features, integrated backscatter, signal processing, statistical characterization. The ultimate goal of tissue characterization is to use the obtained information to differentiate states of tissue, for example, between healthy and diseased tissue, or to monitor changes in tissue properties in response to medication, or aging, etc.

The experimental analysis performed in this paper calculates the integrated backscatter of the whole signal from the skin, including epidermis, dermis, and probably hair follicles, therefore results represent the global integrated backscatter. These results are presented in Figure 17.

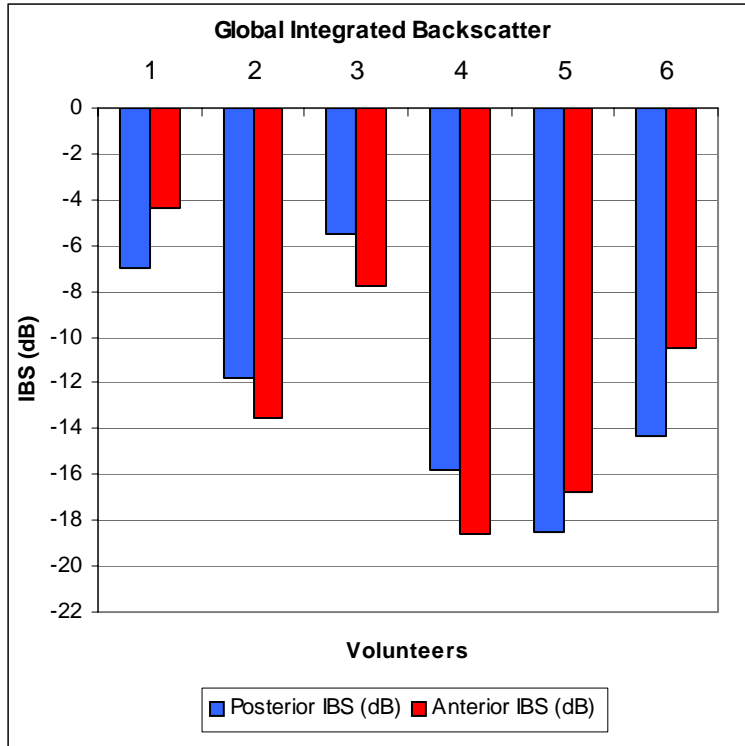


Figure 17. Global Integrated Backscatter versus volunteers.

Statistical methods such as a t-test are applied to quantify statistically significant differences in the backscattered signal.

Table 2. t-test Statistical Results for Posterior and Anterior Data

<b>T-Test Two-Sample Unequal Variance</b>	0.939563	<b>T-Test Paired</b>	0.847127
<b>N Freedom</b>	10		
<b>90% Confidence Level</b>	1.81		

The t-test fails because the result is not above 1.81 for the difference between those two sets of data to be significant.

## **7. Conclusions and Future Work**

Even though there are differences between global integrated backscatter from anterior and posterior regions of the forearm a t-test provided no significant difference in the integrated backscatter. Nevertheless, the authors suggest that the differences are due to the presence of hair follicles, different thickness of skin layers, and presence of blood vessels. However, at 15 MHz it is not possible to resolve the signal from epidermis, dermis, etc. Therefore, it is not possible to extract information from the different tissue structures.

We propose in the future to select shorter windows at different depths to analyze the backscatter from different regions and analyze the need to compensate for attenuation. The integrated backscatter analysis is a valuable tool to discriminate between different skin characteristics. The next step is to repeat this experiment at higher frequencies and conduct a thorough multispectral analysis.

This method can be used to investigate skin water content differences with age. Upon availability of tissue samples from pathology, further studies will include actual assessment of skin pathological conditions.

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