ABSTRACT

Deep Vein Thrombosis (DVT) is caused by blood clots in a deep vein. Doppler ultrasound image is often applied to detecting DVT and evaluating the treatment efficiency of DVT, allowing physicians to observe visible clots and to measure flow velocity of blood flowing in veins. However, during the examinations using Doppler ultrasound, the scatterers properties of clots (e.g., the arrangements and concentration of red blood cells) are very difficult to be reflected so that the diagnostic information is limited.

This study proposes using ultrasound Nakagami imaging to visualize the change in the scatterers properties of clot during clot dissolution. We used a 35MHz single-element transducer and a clinical 7.5MHz array transducer to measure clot samples during their dissolution. By the clot daily information and Nakagami parameter analyzed the specification on the ultrasound signals. The result reveals the Nakagami image is suitable for the blood clot quantitative information.

INTRODUCTION

The vascular diseases are high risk factors for health of human. In general, there are two types of vascular diseases: the first type is cardiovascular disease that happened in the upper body. The most popular symptom is “stroke” which blood clots obstruct at the carotid artery (Hitchcock et al. 2010). Another disease is atherosclerosis that are mainly caused by high degree of cholesterols to decrease the diameter so that blood can’t flow easily.

The second type in the lower body is deep vein thrombosis (DVT), which occur in the lower body. If the disease is not treated earlier, the tiny blood clots may move to heart and lung, causing severe “pulmonary embolism” that can threat patient life. In clinical situation, treating thrombosis is typically performed by using “rt-PA” (Hitchcock & Holland 2010, Hitchcock et al. 2011), but the method of rt-PA effect has some limitation: Age has to be large than 18 years old, and time of stroke should be within three hours. If patient who has transient ischemic attack (TIA) or takes major surgery and anticoagulant drug are not allowed.

Current diagnosis methods include computer tomography that can identify the patient symptom fast, but the injection contrast medium is necessary. However, some patients may have allergy. Furthermore, the radiation exposure is a potential problem. MRI also can diagnosis clot which have no radiation tread, but it is not suitable for every patient who may be afraid of tiny space (claustrophobia). Doppler ultrasound is a comprehensive device which can measure blood
flow for everyone and have no radiation. It offers patients a convenient and comfortable for therapy assess. But, Doppler imaging have defects: no quantitative information associated with the clot structure are provided.

Our purpose of study is trying to use the ultrasound Nakagami image constructed backscattering signals from blood clots to explore the feasibility of evaluating the change in the scatterer properties during clot dissolution. The experimental methods and results are described in the next section.

MATERIALS AND METHODS

Clot preparation
Porcine blood samples were obtained from slaughterhouse. We added the ACD (Acid-citrate-dextrose, including citric acid, sodium citrate dehydrate, glucose) solution into blood immediately. Then, blood samples were stored for one night and put into the centrifuge to centrifuge (2500 rpm for 15 mins) to separate plasma and RBC from blood. Subsequently, we prepare whole blood of 40% hematocrit for simulating the condition of human blood (Huang et al., 2005). The contemporary temperature stir to dissolve completely reduce bubbles production to avoid stratified precipitation.

To induce artificial blood clot, we add calcium chloride with a concentration of 0.5 M into the whole blood. After blood concreting, cutting blood samples to the small cubes corresponding to volumes of about 1 cm³. All samples were stored with saline bath on constant temperature independently.

Figure 1. The procedure of preparing whole blood and including blood clots.

Experimental setup
In our experimental design, we used two ultrasound systems to scan blood clots, including a 35MHz high frequency system and 7.5MHz clinical system.
A high frequency system comprised 35 MHz focused transducer (Asenseor, Taiwan), Pulser / receiver (5900PR, Olympus PANAME TRIS-NDT, USA), analogy-to-digital card (PXI-5152, National instruments, USA), and a personal computer. The low frequency system is a commercial portable ultrasound scanner (Model T3000, Terason, Burlington, MA, USA), with the raw radio-frequency (RF) data digitized at a sampling rate of 30 MHz. The probe is linear array with a central frequency of 7.5 MHz and 128 elements (Model 12L5A, Terason).

**Data analysis**

After image scanning for acquiring raw ultrasound backscattered signals, we weighted each clot using an electronic scale and compared the clot weight with Nakagami imaging and the average Nakagami parameters. The above experimental procedures were performed for eleven days. The Nakagami image is a parametric mapping consisted of the Nakagami parameter of the Nakagami distribution (Tsui & Chang, 2007). the Nakagami distribution is as following (Shankar, 2000):

\[
 f(r) = \frac{2m^{2m}r^{2m-1}}{\Gamma(m)\Omega^m} \exp\left(-\frac{r^2}{\Omega}\right) U(r)
\]  

(1)

\[
 m = \frac{\Gamma(3m)\Omega^m}{E[R^2]^{3m}}
\]  

(2)

and

\[
 \Omega = E[R^2]
\]  

(3)

\(U(.)\):unit step function, \(\Gamma(.)\): gamma function, \(r(.)\): envelope, \(m\):Nakagami parameter and \(\Omega\): scaling parameter. The detail of Nakagami imaging algorithm can be found in the previous study (Tsui & Chang 2007, Tsui et al. 2010).

**RESULTS AND DISCUSSION**

The results of the change in the weight of blood clots as a function of time are shown in figure 3. In average, the weight of clots decreased from 3 to 2 g from day 1 to day 11. This demonstrated that blood clot would dissolve after the formation of blood clot.
The change in the weight of blood clots as a function of time. (a) The first experiment in high frequency. (b) The second experiment in low frequency. Each experiment comprises three clot samples.

The B-mode and Nakagami image as a function of time obtained using 35 MHz and 7.5 MHz transducers are shown in figure 4. The conventional B-mode imaging was difficult to describe the process of clot dissolution. Compared to the B-mode scan, the Nakagami image seems to have the ability to visualize the process of clot dissolution.

To confirm our observation, we calculated the average Nakagami parameter as a function of time, as shown in figure 5. From day 1 to 11, the Nakagami parameter of HF decreased from 1.05 to 0.85, and that of LF reduced from about 0.83 to 0.65, indicating the backscattered statistics tended to vary from post-Rayleigh distribution to pre-Rayleigh distribution when clot dissolved to change the original arrangements of red blood cells. Though the degree of LF decreased not significant which daily parameter has wider range than the HF, it had a trend in the change.
Finally, we performed the comparison between the clot weight and the Nakagami parameter by carrying out linear regression to find the correlation. The correlation coefficients between the clot weight and the average Nakagami parameter for HF and LF were approximately 0.90 and 0.79, respectively. This consequent indicates that the Nakagami image and parameter have potential to reflect the change in the scatterers properties of clot during clot dissolution.

**Figure 5.** The average Nakagami parameters as a function of time measured using HF (a) and LF (b), respectively.

**Figure 6.** The correlation of clot weight and Nakagami parameter. The HF regression which $R=0.9043$ has higher than LF $R=0.7854$. 
CONCLUSION

This study suggests that the Nakagami image can reflect the change in the scatterers properties of blood clot during clot dissolution. The performance of the Nakagami image in monitoring the clot dissolution is better than the conventional B-mode grayscale image.

In the future, the Nakagami image may be used to characterize blood clots to assist in the diagnosis or treatment of DVT and other associated diseases.

REFERENCES


