

Chemical Items Used for Preparing Tissue-Mimicking Material of Wall-Less Flow Phantom for Doppler Ultrasound Imaging

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Abstract

The wall-less flow phantoms with recognized acoustic features (attenuation and speed of sound), interior properties, and dimensions of tissue were prepared, calibrated, and characterized of Doppler ultrasound scanning demands tissue-mimicking materials (TMMs). TMM phantoms are commercially available and ready-made for medical ultrasound applications. Furthermore, the commercial TMM phantoms are proper for ultrasound purpose or estimation of diagnostic imaging techniques according to the chemical materials used for its preparation. However, preparing a desirable TMM for wall-less flow phantom using a specific chemical material according to the specific applications is required for different flow. In this review, TMM and wall-less flow phantoms prepared using different chemical materials and methods were described. The chemical materials used in Doppler ultrasound TMM and wall-less flow phantoms fabricated over the previous decades were of high interest in this review.

Keywords: Acoustical properties, tissue-mimicking material, vessel-mimicking material, wall-less flow phantom

INTRODUCTION

Since the 1960s, tissue-mimicking material (TMM) has been utilized for the preparation and characterization of ultrasound imaging. Wall-less flow phantoms are as well utilized to examine the performance of ultrasound device for practicing of sonographers. The achievement of equivalent TMM is a necessary to process for a quality monitor of Doppler ultrasound diagnostic instrument. It is essential that chemical items utilized in the TMM are prepared in a planned method to be nearly equal to the acoustical properties of real tissue with attenuation and speed of sound of 1540 ± 30 m/s, <0.5 dB/cm at MHz, respectively.^[1-3]

Flow phantom is a model of TMM with a vessel-mimicking material (VMM) surrounding it during pumping of blood-mimicking fluid (BMF).^[4-7] The acoustical features of the different ingredients of the flow phantom correspond to the acoustical features of human blood, tissue, and vessel.^[8] As required and identified by the International Electrotechnical Commission (IEC 61685 standard 1999),^[10] it can be applied for a proper BMF and TMM.^[10-12]

However, when the tubing materials are lacking acoustic properties, the deformation of the Doppler spectrum will lead to the refraction at the vessel wall^[13,14] and attenuation.^[15,16] Regarding acoustical and physical properties, the most proper tubing materials are known as C-flex™. The acoustic speed in the tube should be identical (the same ranges to the TMM) to prevent refraction artifacts.^[17] The speed of sound in TMM is usually 1540 m/s.^[17-20] The refraction artifacts can be noticed when using tubes with a high velocity of sound.^[21]

Several researchers^[17,19,22-30] have measured and examined both the acoustic speed and attenuation of the tube (TMM) by pulse echo signal technique. Through comprehensive literature review, the studies measured and calculated the speed of sound and attenuation through the solid (TMM) samples via measuring the time of flight (ToF) or time shift, t , of the signal

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wave pulse from the reflection waves by applying Equations 2.1 and 2.2, respectively.^[23,31,32]

$$SS = \frac{2(l)}{t} \tag{2.1}$$

Where SS is speed of sound of sample, *l* is sample thickness, depth, or distance, *t* is the ToF of the signal wave pulse from the reflection wave.

$$\alpha = \frac{1}{-D} \ln \frac{Ap2}{Ap1} \tag{2.2}$$

Where α is the attenuation coefficient of sample, $-D$ is the difference in distance or depth of sample in mm, Ap1 is the power signal amplitude at frequency *f* and *x*, *y* positions of (reference signal) with no presence sample (amplitude of transmitted signal wave), Ap2 is the power signal amplitude at frequency *f* and *x*, *y* position through the sample (amplitude of received signal wave).

Doppler ultrasound signals were obtained in good form because the attenuation of TMM was suitable (<0.5 dB/cm/MHz) according to the IEC recommendations. Moreover, for this reason, the C-flex tubing like a VMM which has a speed of sound identical to human tissue was not used because the attenuation of C-flex is nearly ten times greater than the tissue.^[9,33] Furthermore, the attenuation of C-flex tube avoids penetrating the ultrasonic beam to the depth and get a Doppler ultrasound signal with the probe under investigation. This type of tube has an attenuation of 58 dB/cm at 8 MHz and velocity of sound of 1557 m/s.^[16,34] However, acoustic features of some tissues are shown in Table 1.

CHEMICALS MATERIALS FOR PREPARATION TISSUE MIMICKING MATERIAL

Sigma silicon carbide

Sigma silicon carbide (SC) is a compound consisting of carbon and silicon. SC powder grains are joined together to form strict ceramics that are mostly used in several applications. Moreover, in this research study, SC was used as a backscatter factor to mimic real-tissue scatter properties.

Sigma aluminum oxide

Aluminum oxide (Al₂O₃) is a chemical construction made of both the aluminum and oxygen. It is called alkoxide, alundum,

or alumina. Furthermore, Al₂O₃ was used in this research study for attenuation and backscatter function to mimic real-tissue properties.^[16] The diameter of Al₂O₃ used was 3.0 and 0.3 μm.

Sigma konjac root glucomannan powder

Konjac powder consists of dietary fiber (water-soluble polysaccharide). It is a food additive utilized as a thickener and an emulsifier. Konjac powder is found in some plant sorts. However, it was used because its acoustically can be distinguished through a range of frequencies between 5 and 60 MHz and has been applied in the structure of a clinical and preclinical flow phantom.^[17,35]

Sigma carrageenan powder for gel preparation

Carrageenan powder is a gel-forming carbohydrate and is proper for emulsions and surfactants. Carrageenan powder melts at high-temperature degree >60°C. Moreover, it was used because it was of the same function of konjac powder which mentioned above (acoustically distinguished through range of frequencies between 5 and 60 MHz).^[17,35]

Sigma potassium chloride

Potassium chloride (Pc) is a mineral binary salt compound composed of potassium and chloride. It is white and odorless with crystal appearance. It is used in medicine or generally as a fertilizer for fertility the TMM.

Sigma glycerol

Glycerol is viscous fluid and mostly used in molecular biology research studies. Glycerol was used in the preparation of BMF and other viscous fluids for investigation of acoustical properties. In addition, the glycerol is an active solvent and is a popular part in pharmaceuticals. Furthermore, it is nontoxic, odorless, and colorless liquid with a sweet taste. The molecular weight of glycerol is 92.1 g/mol and molecular formula is C₃H₈O₃. Furthermore, the glycerol density is 1.25 g/mL. Glycerol is used as a viscous fluids for the investigation of acoustical properties in mixture fluid of BMF used in this research.

Sigma gelatin

Gelatin is a diverse (heterogeneous) mixture of a large molecular mass of the water-soluble proteins. It exists in collagen and has a density of about 1.3 g/ml. It is used to improve attachment and strength of many items. Gelatin utilized as a thickener and stabilizer in industrial and engineering applications. It was used in this project as a material to increase the strength of TMM at high flow and to keep the acoustical properties suitable.

Among the earliest TMMs prepared for ultrasound imaging were gelatin-based materials. Gelatin, a homogeneous colloid gel, is primarily derived from collagen in animal tissues. The Madsen group mixed gelatin with varying concentrations of alcohol and uniformly distributed graphite powder, with p-methyl and p-propyl benzoic acid used as preservatives against bacterial invasion.^[36,37] Depending on the concentration of n-propanol in water, a speed of sound between 1520 and 1650 m/s at room temperature could be achieved. By varying the concentration

Table 1: Acoustic features of tissues

Material	Density (g/ml)	Attenuation (dB/cm/MHz)	Speed of sound (m/s)	Source
Water	1	0.0022	1480	-
Blood	1.06	0.2	1584	ICRU 1998
ST	1.043	0.54	1561	Mast 2000
Air	0.0012	-	330	-
Fat	0.95	0.48	1478	Mast 2000
Muscles	1.05	1.09	1547	Mast 2000

ST: Soft tissue

of graphite powder in the gelatin-based compound, therefore, adjusting the scattering coefficient, the attenuation coefficient was varied between 0.2 and 1.5 dB/cm at 1 MHz. These materials were reported to have high stability near-room temperature over a period of 4 months, provided that the samples were stored in a closed container below a layer of distilled water. Reported disadvantages to this technique were instability with temperature variations, susceptibility to microbial invasion, and difficulty in achieving uniform distribution of graphite scatters as the particles settled during cooling.^[38-42]

A summary for each chemical with their purpose for preparing the TMM in this review was shown in Table 2 and Figure 1.

TISSUE-MIMICKING MATERIALS FOR WALL-LESS FLOW PHANTOMS

There are several factors considered with fabrication: a wall-less flow phantom should be suitable with various applications, such as depth, flow waveform (straight, tortuous, oblique), flow rate, and sizes (diameters) of the vessel. For clinical application, the ideal vessel diameters between 3 and 10 mm are recommended and should mimic human vessels. For preclinical uses, the vessel diameters are ideally between 0.5 and 2 mm and should mimic rat and mouse vessels. For clinical application, the highest phantom dimension is ideally between 150 and 300 mm; however, for preclinical application, the range is between 50 and 100 mm. The dimensions of preclinical flow phantom are usually less than that of clinical flow phantom.^[17,43]

Table 2: A brief summary for each chemical with their purpose for preparing the tissue-mimicking materials		
Material name	Manufacture	Main function
Water	Medical Physics Laboratory (USM)	To mimic the water concentration in the tissue
SC (400 grain)	Sigma-Aldrich	To modify the backscatter and allow it to mimic tissue
Aluminum oxide powder 3 μm	Sigma-Aldrich	To affect the attenuation, with a linear dependence as a function of frequency
Aluminum oxide powder 0.3 μm	Sigma-Aldrich	To affect the attenuation, with a linear dependence as a function of frequency
Konjac powder	11 Street Company	To mimic the human/animals tissue
Carrageenan powder for gel preparation (Type I)	Sigma-Aldrich	To mimic the human/animals tissue
Pc	Sigma-Aldrich	Used as a fertilizer for fertility the TMM
Glycerol	Sigma-Aldrich	To provide the required speed of sound

TMM: Tissue-mimicking material, SC: Silicon carbide, Pc: Potassium chloride

VMM is composed of both silicone (polydimethylsiloxane) and elastomer (Sylgard 184). The setup is by integrating a base and a treating factor permitting the mixture to be treated for 7 days at specific temperatures ranging between 25°C and 35°C. Four mixtures of cellulose particles with 50 μm as a scatters with different concentrations by weight (0%, 1%, 3%, and 5%) were added and examined for relevant properties, including the speed of sound, visual appearance, and attenuation with the B-mode ultrasound image. Furthermore, the TMM used a different material mixed with the specific amount by weight such as (SC, Al₂O₃ powder, formaldehyde, high-gel strength agar, glycerol, and distilled water) to obtain a proper backscatter and attenuation properties. The pulse-transmission mechanism used to measure the TMM attenuation coefficients four Sylgard 184 mixtures. All measurement were conducted via single-element unfocussed probe and pulse extend from 2 to 7.5 MHz at room temperature.^[44,45]

There is no tubing material applied to fabricate the wall-less flow phantoms, and the BMF is an immediate link with the TMM. Fabrication of wall-less flow phantoms is necessary to prevent problems that resulted by US deformation through the tube wall.^[15,46] TMM was created by utilizing two hydrogel materials, namely konjac and carrageenan (KC). The KC is composed of two organic materials and was added with water to produce a flexible and strong material. TMM is prepared by mixing SC, Al₂O₃, glycerol, and KC materials. The KC-based TMM had a velocity of sound of 1548 ± 3 m/s and an attenuation (dB/cm) behavior of 0.01024f² + 0.3639f, where f is transferred frequency (MHz).^[35,47]

The wall-less flow phantoms made of metal cores containers with dimensions of 10 cm × 10 cm × 23 cm were mounted in melting temperature of 69°C. Before pouring, the phantom was fixed by reticulated foam and put around the connectors. TMM



Figure 1: Chemicals items used for tissue-mimicking material flow phantom fabrication: (a) silicon carbide, (b) aluminum oxide, (c) K, (d) C, (e) potassium chloride, (f) glycerol, (g) gelatin

was composed of agar, then poured into the container, and let it set. However, used of agar-based TMM failure was due to leakage the BMF with high flow rate. The problem was solved via the expansion of a new powerful TMM relied on utilization of two types of gels; KC was used instead of agar. The ingredients by (%weight) were konjac powder, carrageenan powder, Al_2O_3 powder 3 μm , Al_2O_3 powder 0.3 μm , H_2O , 400 grains SC powder, glycerol, and Pc, which used to adjusting the temperature of the gel with %weight 1.5%, 1.5%, 0.96%, 0.89%, 84%, 0.54%, 10%, and 0.7%, respectively. Several items were estimated as a portion of the European Commission project which made the TMM.^[22,48] The acoustical properties of TMM were perfect, and it is meeting the requirements of IEC 1685 draft report: At room temperature, it had a velocity of sound of 1550 ± 6 m/s and an attenuation (dB/cm) behavior of 2.81 ± 0.08 with 5 MHz as a frequency. The brand of ultrasound scanner equipment used for examining the flow phantom was named HDI 5000 Philips Medical ultrasound system. The system is provided with linear array transducer L12-5 to scan the flow channels and collect longitudinal imaging of all areas and measurement of flow velocity.^[35,49]

Another wall-less flow phantom was made of 9.52 mm as a vessel diameter. The TMM made of a mixture of 8% glycerol, 3% of very strong agar gel, and 89% of distilled water has the acoustic speed identical to that of soft tissue (ST). The metal rod worked like the mold for the vessel. Vessel lumen preserved in its original form throughout time and the wall less flow phantom was not absorbing water. To prevent drying of the agar gel and potential deformation, the phantom was maintained in a water bath. Experiment research was carried out at room temperature in a horizontal constant flow loop sample. Linear array transducer with 4-MHz (L7-4) was utilized to generate Doppler scan images.^[50]

The great-strength Struers agar is utilized because it produces TMM with more firm and robust, and thus, the likelihood of breakage or tear will decrease when TMM is exposed to the strong high pressure of high flow rates. The primary function of Al_2O_3 powder is to influence the attenuation with a linear proportional of frequency. Furthermore, Al_2O_3 and SC powder adjust the backscatter to mimic tissue. Benzalkonium chloride is used to avoid the development of microorganisms, and glycerol is utilized to supply the required speed of sound. TMM prepared by mixing SC, Al_2O_3 , benzalkonium chloride, glycerol, and KC materials continuously with a magnetic stirring rod. It was then cool to 42°C with keep of stirring and then poured the mixing materials into the test container. The acoustical properties of TMM were perfect, and it is meeting the requirements of IEC 1685 draft report: At room temperature, it had a velocity of sound of 1541 ± 3 m/s and an attenuation (dB/cm) behavior of 0.5 ± 0.03 with nearly 3–10 MHz as a frequency. The VMM made by casting the metallic rod inside the wall-less TMM channel with about 8-mm diameter. The brand of ultrasound scanner equipment which used for examining this flow phantom was named HDI 5000 ATL ultrasound system. This system provided a

linear array transducer to scan the flow channels and doing a measurement of flow velocity.^[16]

CONCLUSION

At present, even though the TMMs are abundant commercially, customized TMM keeps. Many soft TMMs have been described that have compressional acoustical and physical features within the measured range of STs. The backscattering coefficient, nonlinearity parameter, and shear wave speed of sound (in the case of hard tissue substitutes) have rarely been reported.

Several soft TMMs that have different acoustical and physical properties (density, attenuation, and speed of sound) have been explained. The inclusive information steps for the preparation of TMM and wall-less flow phantom items in this review article can be useful to medical and engineering researchers, particularly, in the knowledge to make TMM and wall-less flow phantom proper fabricated for Doppler ultrasound applications. At present, even the TMM are abundant commercially. However, customized TMM keeps having a function, first in the medical Doppler ultrasound research group. The main advantage of TMM is the low-cost and proper elasticity of chemical items.

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Conflicts of interest

There are no conflicts of interest.

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