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Development and investigation of the acoustic properties of tissue-mimicking materials for photoacoustic imaging techniques

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***Abstract*—Phantom test devices are used in the development of medical imaging modalities to gain a more complete understanding of the underlying physical processes and to optimize techniques. There are currently no standard photoacoustic imaging (PAI) phantoms, although there is a move towards standardization, notably in a new international consortium (IPASC) focusing on the standardization of PAI techniques and phantoms. The use of gel wax/copolymer in oil materials in PAI is relatively recent with only limited studies carried out, however such materials hold promise for wide-spread adoption as a phantom material due to ease of preparation and extensive component availability. A standardized preparation method for the material has yet to be published. This work describes an investigation of the acoustic properties of various preparations of the bulk material. The final material consisted of 84.49 % mineral oil (light), 12 % Polystyrene-block-poly(ethylene-ran-butylene)-block-polystyrene 3 % low density polyethylene, 0.05 % TiO_2 and 0.46 % Benzalkonium chloride and had stable acoustic properties mimicking fatty soft tissue over 6 months, with a phase velocity of 1464.2 ± 0.4 m s^{-1} and mean attenuation of 4.04 ± 0.2 dB cm^{-1} at 5 MHz.**

Keywords—tissue mimicking material, photoacoustic imaging, acoustic characterization

I. Introduction

Photoacoustic imaging (PAI), which involves the detection of ultrasound signals generated in tissue by the absorption of short laser pulses, has undergone rapid development over the past 20 years. Phantom test objects are an important tool in the development and optimisation of new imaging modalities due to their well-defined properties and structures which may be used to assess modality capability. A wide range of tissue mimicking materials are used in phantom test objects for different imaging techniques (acoustic, optical, MRI). Established techniques based on agar material have been adopted by the standards organization the International Electrotechnical Committee in biomedical Ultrasound [1]; however, for PAI, no such standardized material exists. There has recently been a move towards standardization in PAI most notably with the establishment of the International Photoacoustic Standardization Consortium (IPASC)[2].

For both qualitative and, even more so, quantitative measurements, it is important that certain aspects of the phantom material mimic human tissue. For PAI these characteristics include; the speed of sound, acoustic absorption/attenuation and optical absorption and scattering. Table I (adapted from [3], supplemented with [4]–[8]) shows the approximate ranges for these values in different tissue-types.

TABLE I. Acoustic and optical properties of tissues in the ranges 1 – 10 MHz and 600 – 900 nm respectively [3-8].

Tissue type	Acoustic Properties		Optical Properties	
	Attenuation coefficient (dB cm^{-1})	Phase Velocity (m s^{-1})	Absorption Coefficient (cm^{-1})	Reduced Scattering Coefficient (cm^{-1})
Soft Tissue	0.5–30	1450–1575	0.1–0.5	10–20
Fatty Tissue	1–18	1430–1480	0.05–0.3	3–8
Breast parenchyma	2–25	1460–1520	0.1–0.3	5–15
Blood	0.1–2	~1560	2.0–10.0	10–15
Liver	0.5–0.7	1510–1590	1.15–1.56	22–30
Prostate	0.2	1614	0.05–0.72	1–40
Skin	~ 2–4	~1600	0.05–1.11	2–21
Bone	0.1–2	+2000	0.07–0.09	12–16

Various phantoms and tissue-mimicking materials have been suggested in the literature, water/coupling gel [9][10], hydrogels [11], gelatin [12], PVA [13], PVCP [14][15], silicone [16] gel wax [17] and copolymer in oil (CPO)[18]. Commercial gel wax materials have been used in a number of studies [19] [17] [20]. However, similar to PVCP used previously in phantom studies [3] , the batch to batch variation of commercial gel wax is unknown . Moreover, the exact compositions of the commercial material is proprietary information [17]. It's use may result in variations in acoustic and optical properties of phantoms produced using the same manufacturing process. Similar phantoms have been made using the CPO process for both ultrasound [7], [21] and photoacoustic applications [18], [22], [23]. The advantage of such phantoms is both in the ability to develop a standardized recipe due to the non-proprietary nature of the components and the potential for better control of the various acoustic and optical characteristics using standardized controlled components.

A standardized preparation method for the material has yet to be put forward in the literature with variations reported in

terms of various aspects of the manufacturing procedure including; heating temperature and timing, ratio of components and use/timing of vacuum and sonication equipment. The aim of this work was to contribute towards the establishment of a standardized photoacoustic material through the development of a non-proprietary CPO material with tissue-like acoustic properties.

II. Methods

A. Components

The materials detailed in Table II were investigated as components of the tissue mimicking material.

TABLE II. Material components investigated

Component	Primary purpose	Manufacturer	CAS number
Mineral Oil (light)	Base oil	330779, Merck	8042-47-5
Polystyrene-block-poly(ethylene-ran-butylene)-block-polystyrene	Base copolymer	200557, Merck	66070-58-4
Glycerol	Phase velocity	158922500, Fisher Scientific	56-81-5
Linseed Oil	Phase velocity	11442834, Fisher Scientific	8001-26-1
Low Density Polyethylene (pellets) (LDPE)	Stiffness and stability	428043, Merck	9002-88-4
Low Density Polyethylene (powder)	Stiffness and stability	43949, Alfa Aesar	9002-88-4
Titanium (IV) oxide, anatase (TiO_2)	Optical scattering	232033, Merck	1317-70-0
Benzalkonium chloride (BC)	Anti-bacterial	26382-0010, Fisher Scientific	8001-54-5

B. Material preparation

Various preparation methods of the material were investigated using these components. The material was predominantly mineral oil based, making up 80–90 % of the material, and included the copolymer polystyrene-block-poly(ethylene-ran-butylene)-block-polystyrene. Initial investigation established an appropriate ratio of copolymer (8–16 %) to oil. The influence of Glycerol and Linseed oil (5–15 %), LDPE (3 and 5 %), and TiO_2 (0.05–0.5 %) on the acoustic properties was then investigated. To ensure uniformity of samples powder constituents were added at the start of the manufacturing process and the solution sonicated before heating to induce polymerization. Benzalkonium chloride (BC) was used as an anti-bacterial agent. The final manufacture technique for the material was as follows. The mineral oil, BC, LDPE and TiO_2 were sonicated for 15 minutes at 50 °C in a 50 Hz ultrasound bath (Series Q, Ultrawave, UK), after which the copolymer was added, and the material was further sonicated for 15 minutes. The material was then placed in an oil bath and heated to at least 135 °C until the copolymer and LDPE were fully dissolved (approximately 1.5 hours). During which the mixture was stirred at 60 rotations per minute using a magnetic stirrer and not permitted to exceed 160 °C at any time. The solution was then poured into glass molds of 60 mm diameter to a height of 5 or 10 mm and placed in a vacuum oven (Stable Temp, Cole-Parmer, UK) at 100°C and evacuated to 30 inches/Hg until all visible bubbles were removed (1.5–2 hours). The samples were then removed and cooled at room temperature. The samples were stored at room temperature.

C. Repeatability and temporal stability

The repeatability of the technique was assessed by manufacturing three batches of four samples of the final material and the acoustic characteristics were compared. The temporal stability of four samples from two batches was investigated over a period of 6 months.

D. Material charactisation

Materials were characterized using the NPL reference materials characterization rig and the four-pulse method described in Ref. [24]. 10 and 5 mm thick, 60 mm diameter samples of each batch of material were prepared for characterization. The attenuation and phase velocity of the samples were acoustically characterized using a broadband pulse through-transmission substitution technique using a 10 MHz center frequency ultrasound transmitter (Force Institute, DK) and a 30 mm active element membrane hydrophone (GEC Marconi, UK) as a receiver.

III. Results

A. Copolymer to mineral oil ratio

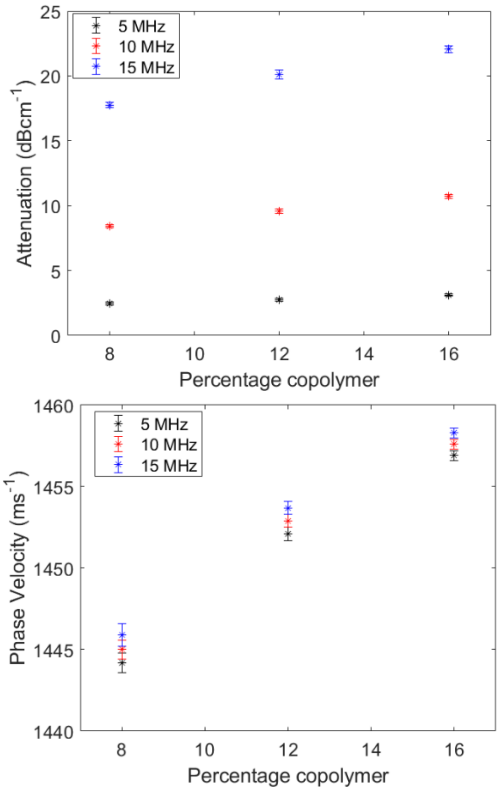

Fig. 1. Attenuation and phase velocity as a function of percentage copolymer at 5, 10 and 15 MHz where the error bars represent the standard error.

The attenuation and phase velocity increased with increased percentage of copolymer in mineral oil (Fig 1.). 16 % was close to the limit for dissolving the material in the mineral oil. To ensure uniformity of all further samples, samples were prepared with 12 % CPO.

B. *Addition of other components to base material*

Glycerol was investigated to increase phase velocity, however, glycerol does not dissolve well in the oil and the turbid samples, such as those seen in the literature[23], were not physically reproducible. The variability of successful manufacture over several attempts ruled out its use in this material. Linseed oil was investigated as a means of increasing the phase velocity. 5 % linseed oil increased the phase velocity from 1452 to 1458 m s^{-1}. However, an increased ratio of linseed oil did not affect the velocity linearly. As the increase was not substantial this was not used in further samples. LDPE was added to increase durability/stability of samples. The material became stiffer with addition of LDPE and both phase velocity and attenuation increased. At 5 % the LDPE was difficult to melt in the solution and the samples were brittle in nature. Originally, the LDPE used was in a pellet form, with a melting point of 160˚C. This was difficult to dissolve in the mineral oil due to the proximity to the evaporation point of the oil. The pellets were replaced with a lower melting point powder form of the material which has a melting point ~135 °C. The material preparation was simplified, and the manufactured samples were visibly more uniform. The phase velocity increased to 1465.5 ± 0.1 ms^{-1}, and the attenuation remained below 1 dB cm^{-1} MHz^{-1} up to 10 MHz. Table 3 shows the attenuation and phase velocity measured at 5 MHz for these samples.

Fig. 2 shows the influence of increased amounts of TiO_2 on the attenuation and phase velocity. There was little effect on the attenuation measured, however, there was a decrease in phase velocity with increased percentage of TiO_2.

TABLE III. ATTENUATION AND PHASE VELOCITY AT 5 MHZ

Material	**Phase Velocity (m s^{-1})**	**Attenuation (dB cm^{-1})**
12 % CPO	1452.1 ± 0.4	2.75 ± 0.11
12 % CPO 5 % Glycerol	1456.7 ± 1.2	3.50 ± 0.14
12 % CPO 15 % Glycerol	1457.0 ± 0.4	3.68 ± 0.04
12 % CPO 5 % linseed oil	1457.9 ± 0.1	2.75 ± 0.01
12 % CPO 10 % linseed oil	1456.9 ± 0.1	2.75 ± 0.01
12 % CPO 15 % linseed oil	1456.5 ± 0.1	2.66 ± 0.01
12 % CPO 3 % LDPE (pellets)	1457.8 ± 0.1	3.72 ± 0.02
12 % CPO 5 % LDPE (pellets)	1463.7 ± 0.1	4.93 ± 0.02
12 % CPO 3 % LDPE (powder)	1465.5 ± 0.1	4.53 ± 0.01

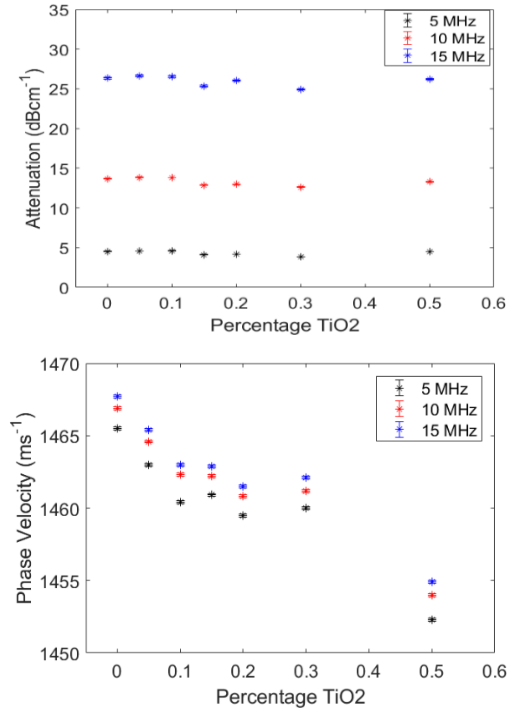

Fig. 2. *Attenuation and phase velocity as a function of percentage of TiO_2 at 5, 10 and 15 MHz.*

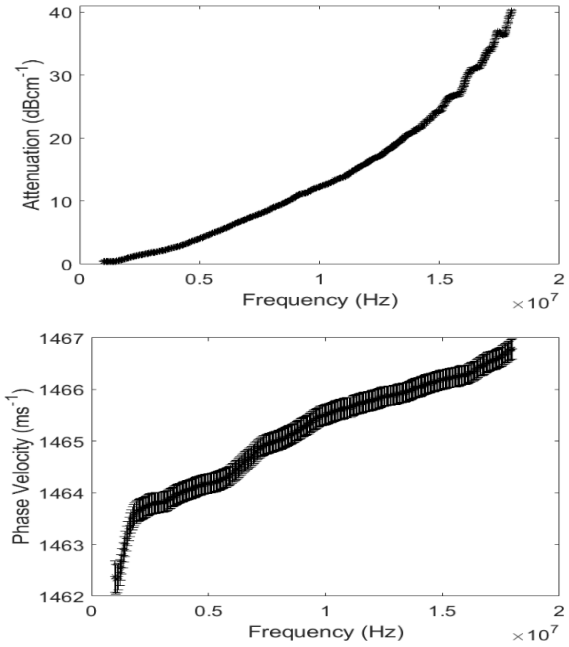

Fig. 3. *Attenuation and phase velocity as a function of frequency for the selected repeatability material (84.49 % mineral oil, 12 % copolymer, 3 % LDPE, 0.05 % TiO_2, 0.46 % BC). The curve represents the results from 3 batches with 4 samples per batch.*

C. *Repeatability of established protocol*

Through manufacturing and characterizing three independent batches the repeatability of the material was found to be very good (Fig. 3). Samples were sufficiently similar in attenuation and phase velocity with a mean phase velocity of

1464.2 ± 0.4 m s^{-1} and mean attenuation of 4.04 ± 0.2 dB cm^{-1} at 5 MHz.

D. *Temporal Stability*

The acoustic properties measured over a period of six months were found to be stable with a mean phase velocity of 1464.4 ± 0.4 m s^{-1} and mean attenuation of 4.3 ± 0.3 dB cm^{-1} at 5 MHz at 20 °C. Due to ambient temperature differences measurements were made at 3 different temperatures, the results indicated a temperature dependence of the material that requires characterization. The phase velocity data has been corrected assuming values from Onda's Acoustic tables of reference (–3.6 ms^{-1} per degree Celsius)[25].

IV. Discussion & Conclusion

This work has established a preparation method for a CPO based tissue mimicking material using CAS registered chemical components which is uniform, reproducible and has anatomically relevant acoustic properties. Variations including glycerol were unsuccessful due to difficulty in achieving uniform reproducible samples. Linseed oil did not appreciably increase the velocity of the material. Increasing amounts of TiO_2, a common optical scatterer, decreased the phase velocity and had little effect on the attenuation. The final material established was 12 % copolymer in oil 3 % LDPE, 0.05 % TiO_2 and 0.46 % BC. The attenuation was suitable for mimicking soft-tissues and was lower than that reported for other PAI materials. The phase velocity was close to that of fatty soft-tissue, such as breast tissue, a common application of PAI. The acoustic properties of the material were stable over a period of six months. The acoustic properties, ease of fabrication and extensive availability of the components from standard chemical suppliers suggest that this material may be suitable for use in a standardized phantom for PAI. Future work will include optimization of the optical properties of the material using a range of chromophores to mimic soft tissues.

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