Testing a new surfactant in a widely-used blood mimic for ultrasound flow imaging

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Title: Testing a new surfactant in a widely-used blood mimic for ultrasound flow imaging

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Abstract

Background

A blood mimicking fluid (BMF) developed by Ramnarine et al (1998) has been widely used in flow phantoms for ultrasound flow imaging research, and it has also been cited by IEC 61685 as a reference for making BMF. However, the surfactant material Synperonic N in this BMF recipe is phased out from the European market due to environmental issues. The aim of this study is to test whether Synperonic N can be substituted by biodegradable Synperonic A7 in making BMF for ultrasound flow imaging research.

Methods & materials

A flow phantom was fabricated to test the BMF with Synperonic N and Synperonic A7 as surfactants separately. Doppler images and velocity data were collected using a clinical ultrasound scanner under constant and pulsatile flows; and images and measured velocities were compared.

Results

It was found that both blood mimics can provide exactly the same images under spectral Doppler ultrasound and colour Doppler ultrasound in terms of their image qualities. The maximum velocities under constant flow were measured by the spectral Doppler ultrasound as 0.4714 ± 0.001 m.s^{-1} and 0.4644 ± 0.001 m.s^{-1} for BMF with Synperonic N and BMF with Synperonic A7 respectively. Measured velocities using the two different BMFs were statistically different ($p<0.001$), but this difference was less than 2%.

Conclusion

The Synperonic A7 can be used as a substitute for Synperonic N as a surfactant material in making the BMF for ultrasound flow imaging research.

Introduction

Doppler ultrasound is widely used in clinical practice for diagnosis and assessment of arterial disease[1]. Typically colour flow is used to identify the region of disturbed flow and quantification of blood velocities is performed using spectral Doppler. Those traditional techniques have proven to have limitations such as angle-dependent errors in velocity estimation and limited spatial resolution[2-4]. In recent years, many studies have endeavoured to tackle these problems by introducing new techniques such as vector Doppler[5-7] and there have been attempts to measure other velocity-related quantities such as wall shear rate which may have future diagnostic potential[8, 9].

Validation of flow imaging, both for traditional Doppler techniques and for novel methods, is essential in methods development and before using new techniques in clinical practice. A flow phantom simulates the flow of blood in vessels in the human body using tissue equivalent materials (mimicking the acoustic and mechanical properties of tissue, vessel and blood), and is a common tool for use in validation studies[10, 11]. A blood mimicking fluid (BMF) which mimics the acoustic and viscous properties of blood, and which is relatively easy to manufacture, was reported by Ramnarine et al[12, 13]. This blood mimic has been widely used in the literature (>250 citations on Google Scholar). It is cited by IEC as a reference for making blood mimic for ultrasound research[14]. This BMF uses 5 μm

diameter nylon scattering particles which are suspended in a solution composed of water, glycerol, dextran and surfactant. In the original formulation of the BMF described by Ramnarine et al[12, 13], the orgasol concentration was adjusted to provide blood equivalent backscatter, the glycerol concentration was adjusted to provide the correct acoustic velocity and the dextran concentration was adjusted to provide the correct viscosity. The surfactant Synperonic N is a wetting agent which is responsible for dispersing the particles in the BMF and plays a similar role to detergent in washing of clothes or pots. However Syperonic N was banned for sale in Europe in the year of 2000 due to its long-term adverse effects in the aquatic environment[15]. Although efforts were made to find substitutes for the Synperonic N in the conservation community regarding its cleaning properties on artificially soiled textiles[15], there are no publications that deal with finding a substitute in the manufacturing of BMF for ultrasound flow imaging research.

After the Synperonic N was phased out in the European market, a readily biodegradable product named Synperonic A7 was introduced by Conservation Resources UK Ltd (Abingdon, UK) to replace the Synperonic N. The aim of this study is to evaluate whether BMF made with Synperonic A7 provides similar ultrasound images and velocity data compared to using a BMF made using Synperonic N.

Methods and materials

Overall design

The blood mimic with Synperonic N ('BMF-N') and the blood mimic with Synperonic A7 ('BMF-A7') were used separately within the same flow phantom, from which spectral Doppler ultrasound and colour Doppler ultrasound data were collected for each blood mimic. The settings in the flow phantom, such as flow rate and transducer location, were kept exactly the same under each situation for the two blood mimics. Both constant and pulsatile flows were tested by a clinical ultrasound scanner (ATL HDI 5000, Bothell, WA, USA). Ultrasound images and measured velocity data from the two types of blood mimic were compared qualitatively and quantitatively.

Flow phantom

The flow phantom from which the ultrasound data was collected is shown in Figure 1. The main components of this flow phantom are tissue mimic, blood vessel mimic, blood mimic and a pump. A pump is used for generating pulsatile or constant flow with similar velocities to those found in human arteries. In the flow phantom used in this study, the blood vessel was mimicked by a 4 mm C-Flex tube (6424-65, Cole-Parmer, UK), and the

tissue was mimicked by an agar-based tissue mimicking material[16]. An inlet length of 8.48 cm was calculated by assuming the mean velocity as 0.5 $m.s^{-1}$ which is slightly higher than the actual velocities in the experiments. In the fabricated flow phantom for this study the inlet length was made as 15 cm to make sure that flow in the insonating area is well-developed. The flow phantom was similar to that described in a previously published paper[11].

When making the BMF-A7, the Synperonic A7 was diluted with water (water: Synperonic A7 = 73:27) and the solution stirred until it turned to clear. This is because Synperonic A7 is a 100% active solution while the original Synperonic N is 27% active. The percentage active is defined by comparing the bleaching power of a solution with the chlorine (one gram of a 100% active bleaching solution has the same bleaching power as one gram of chlorine)

Data acquisition and processing

The ultrasound transducer (L12-5 38) was placed to get the clearest longitudinal view of the blood vessel in the flow phantom (Figure 1) under B-mode imaging, and the location of the transducer was fixed without movement during the whole experiment.

The BMF-N was pumped through the phantom with steady flow. Using spectral Doppler the angle cursor was aligned parallel to the vessel wall, and the sample volume set to 2mm. Detailed parameters about the scanning are shown in Figure 2. Spectral Doppler waveforms from the central part of the vessel were acquired and stored off-line for extraction of maximum velocity envelope. In the HDI 5000 scanner, the data set transferred from Spectral Doppler mode is a binary file with the .XIF extension and an in-house MATLAB toolkit was used to read out its maximum velocity envelope which is 100 points per second[8]. Five to seven seconds of data were stored in the cine loop. The velocity value has a precision of 0.001 $m.s^{-1}$ in the saved envelope data. Colour Doppler images were also acquired under the steady flow. Finally the flow in the phantom was changed to a pulsatile pattern, and spectral Doppler data was collected. In each case data was collected 5 times.

The same procedure was repeated with BMF-A7 flowing in the flow phantom, and data were stored. Settings in the flow phantom were kept exactly the same as they were in the experiment for BMF-N, and the transducer was not moved between the data collections for these two blood mimics.

For the steady flows, the timed collection method was used to measure the actual flow rates in the phantom while collecting ultrasound data with two different BMFs.

The ultrasound images (estimated maximum velocity data and colour images) from scanning of the two blood mimics were compared in terms of general image qualities; overall shape of the Doppler waveform and appearance of speckle for spectral Doppler and colour appearance for colour flow. The presence of clumps of nylon particles might be expected to produce spikes on the Doppler spectrum (similar to those from air bubbles but of lower intensity). The maximum velocity envelope (the spectral outline) is available from the data set transferred from the saved cine loop of each scanning, and their corresponding time-averaged maximum velocities were compared under steady flow between measurements obtained from two BMFs. The standard deviations were estimated from 5 set of time-averaged (5-6 seconds) maximum velocities for each BMF. Statistical testing was performed using an unpaired t-test. For pulsatile flow, the envelopes from the two BMFs were plotted together for comparison.

Results

Spectral Doppler images obtained from both blood mimics are shown in Figure 2 and colour flow images are shown in Figure 3. Visually both spectral Doppler data and colour flow images looked identical for the two BMFs. The speckle pattern present on spectral Doppler and colour flow looked to be similar for the 2 BMFs. There were no obvious

spikes on the Doppler spectrum for either BMF, though occasionally high intensity spikes were seen arising from air bubbles.

Figure 4 shows the estimated maximum velocity data from each BMF. The Doppler measured maximum velocities (mean±sd) are 0.4714 ± 0.001 $m.s^{-1}$ for BMF-N and 0.4644 ± 0.001 $m.s^{-1}$ for BMF-A7. There was a statistically significant difference in the measured velocities for the two BMFs ($P<0.001$). While this is statistically significant, the difference is 1.5±0.3%; ie. less than 2%.

Flow rates measured by the timed collection methods under steady flow were 139.7±0.61 $ml.min^{-1}$ and 142.1±0.83 $ml.min^{-1}$ with BMF-N and BMF-A7 respectively. The difference is within 2%. If assuming the velocity profile as parabola, these flow rates can be converted into central maximum velocities of 0.371 $m.s^{-1}$ and 0.377 $m.s^{-1}$ for these two BMFs.

Discussions

The visual similarity in spectral Doppler and colour flow for the two BMFs gives very good evidence that the two BMFs produce similar results. The quantitative comparison between maximum velocities while statistically significant demonstrates a difference of only 1.5%. This difference is very small and may be associated with minor changes in pump output.

The implications of this difference in terms of clinical measurements is considered in the remainder of this paragraph. It is well known that measured maximum velocity is angle dependent; an error of ±1^{o} in measured angle at 60^{o} leads to an error of ±3% in estimated maximum velocity as a result of cosine dependence. It is also well known that maximum velocity is over-estimated as a result of geometric spectral broadening with typical errors of 20-40%[17, 18]. This error is proportional to the sine of the angle. If there is a 30% overestimation in maximum velocity at 60^{o} then a ±1^{o} change in angle leads to a ±5% change in estimated maximum velocity. On this basis the 1.5% difference in maximum velocity encountered in this study is unlikely to be significant in comparison to errors encountered in clinical practice and hence can be ignored. Based on these qualitative and quantitative comparisons, it can be concluded that the Synperonic A7 could be a substitute to the Synperonic N in manufacturing the blood mimicking fluid proposed by Ramnarine et al[12].

The physical properties (density, viscosity and particle size) and acoustical properties (velocity, backscatter and attenuation) of the original blood mimic BMF-N were carefully measured by Ramnarine et al[12], and those properties are in good accordance with the IEC requirement. The acoustic properties of BMF-A7 were not measured in the current study. The impact on acoustic properties of the BMF of using Synperonic A7 as a replacement for

Synperonic N will be considered here. For BMF-N 18 ml were used in a batch of 2000ml; so 0.9% by volume. For BMF-A7 4.86 ml were used (diluted to 18 ml with water). The density of Synperonic N, Synperonic A7 and water at room temperature are 1.02 $g.cm^{-3}$, 0.958 $g.cm^{-3}$ and 0.9982 $g.cm^{-3}$ respectively[19-21]. It can then be calculated that the mass of a 2L batch of BMF-N is 1996.79 g (density 0.9983 $g.cm^{-3}$) and of BMF-A7 is 1996.21 g (density 0.9981 $g.cm^{-3}$); a 0.03% difference. If it is assumed that the acoustic properties (speed of sound, attenuation coefficient and backskatter) would be altered by a similar amount (0.03%), then this represents a very small change; eg, speed of sound of 1548 $m.s^{-1}$ for BMF-N[12] would be changed by 0.5 $m.s^{-1}$ for BMF-A7. It is noted that the IEC specification for the speed of sound in the BMF for a standard flow phantom is 1570 ±30 $m.s^{-1}$.The expected change of 0.5 $m.s^{-1}$ is very small in comparison and therefore can be ignored. It has been noted in the literature that when there are large changes in acoustic velocity occur between BMF, vessel mimic and tissue mimic (e.g. use of silicon rubber vessel; velocity 1005 $m.s^{-1}$) this leads to distortion of the received Doppler spectrum[10], however this is not relevant to the small change in acoustic velocity seen in this paper.

It was mentioned in the original Ramnarine's paper that the low-foam property of Synperonic N is important to reduce the problem with bubble formation[12]. In terms of this, the proposed Synperonic A7 (after dilution) showed a similar performance. No obvious

differences between these two BMFs regarding bubble formation were found during the manufacturing procedure and after degassing. Furthermore, bubbles in the BMF would cause big spikes in the PW sonogram but no obvious differences of this can be seen in Figure 2.

Conclusions

It can be concluded that a biodegradable surfactant Synperonic A7 can be used to replace the Synperonic N in the manufacture of the BMF reported by Ramnarine et al [12]. Considering the popularity of the original BMF in the ultrasound imaging community, successfully finding a substitute for the component in the original recipe which is not accessible any more in European market would be important to researchers, at least in Europe, who are interested in this blood mimic.

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Figures

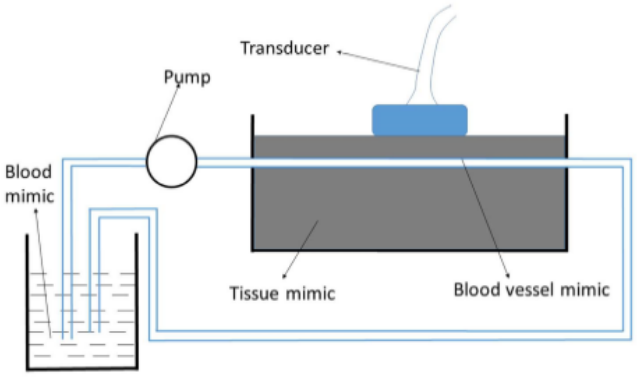


Figure 1. The diagram of the flow phantom

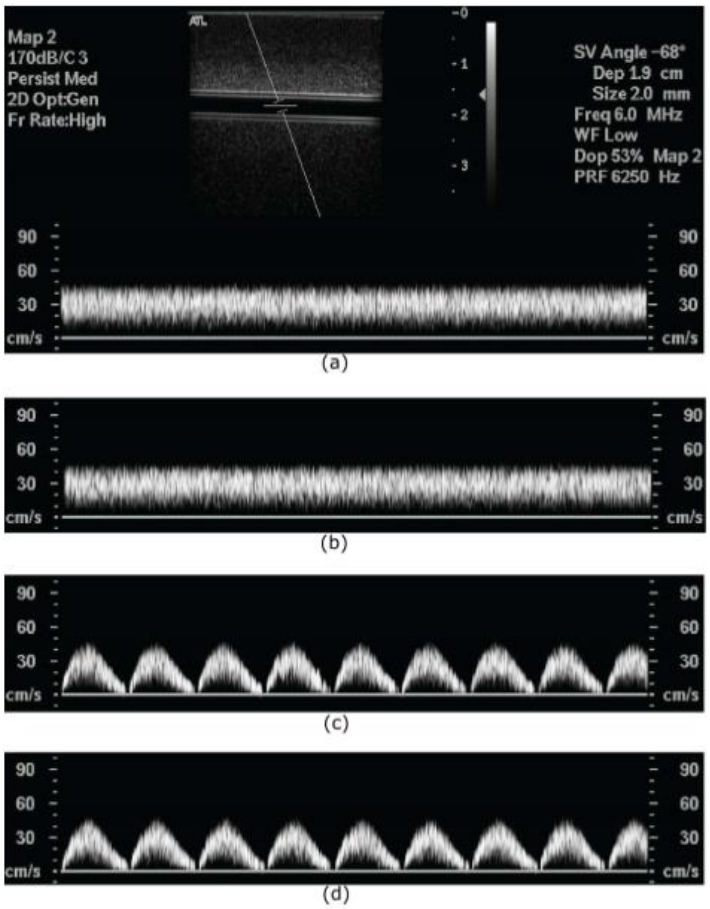
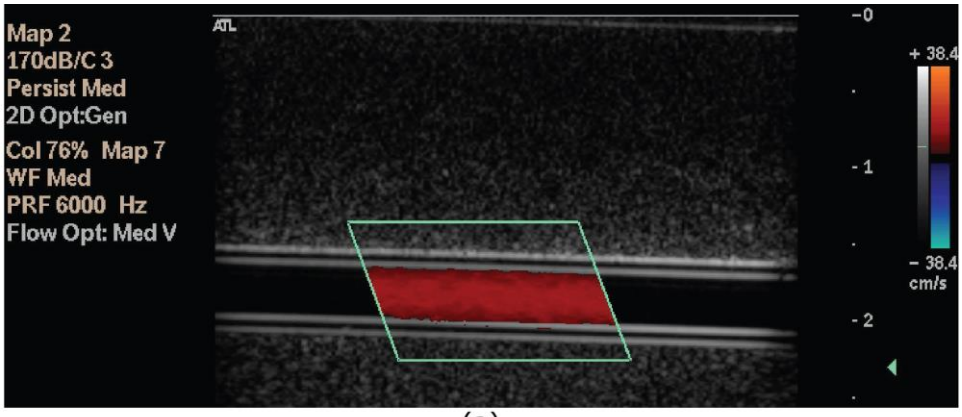
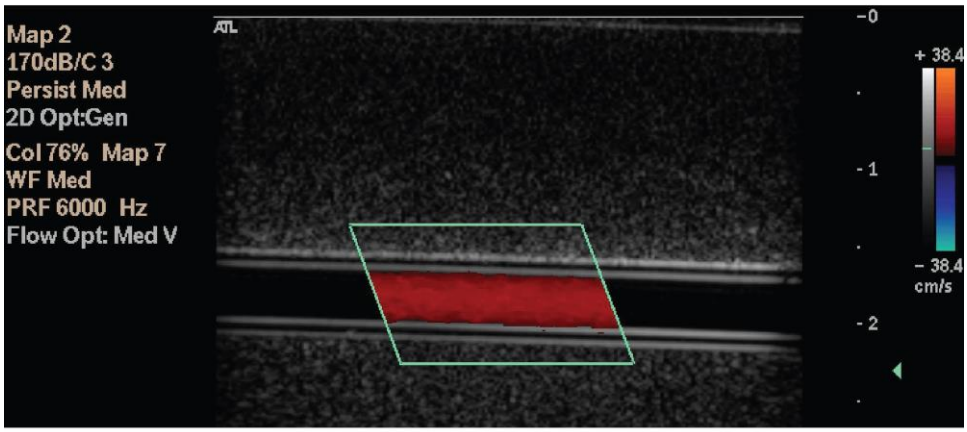


Figure 2. The images from PW Doppler ultrasound. (a) Constant flow with BMF-N; (b) Constant flow with blood mimic BMF-A7; (c) Pulsatile flow with BMF-N; (d) Pulsatile flow with BMF-A7.



(a)



(b)

Figure 3. Images for colour Doppler under constant flow. (a) With BMF-N; (b) with BMF-A7.

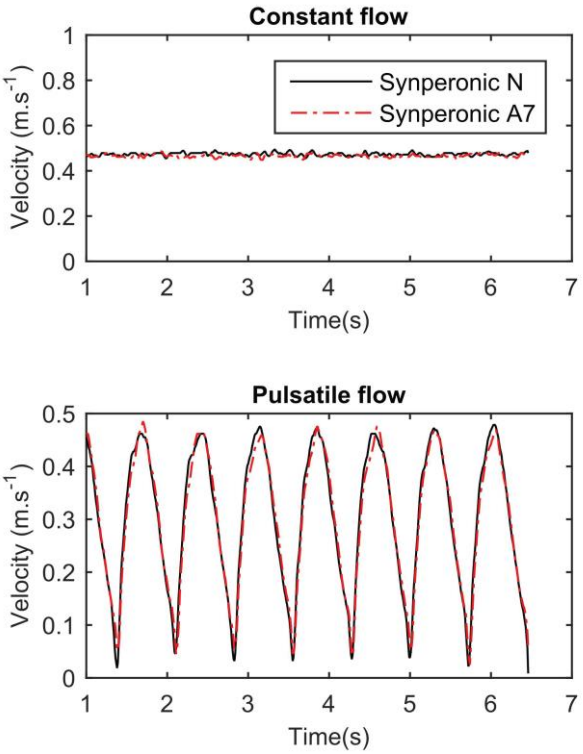


Figure 4. Maximum velocities from both blood mimics.