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Validity and Sensitivity of 2 MHz and 4 MHz Pulsed Wave for Detecting Emboli in Carotid Phantom

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Abstract

Stroke remains a serious medical condition resulting in significant mortality and disability. Early detection using ultrasound technology is a way forward to prevent potential strokes. It has been known that ultrasound transducer of a single crystal with a frequency of around 2 MHz used for embolus detection in the Meddle Cerebral Artery (MCA), but no specific transducer have been validated for embolus detection in Common Carotid Artery (CCA) yet. Our study aims to use carotid phantom to report the sensitivity and specificity of embolus detection of 2 MHz, and 4 MHz PW probes in continuous monitoring of the common carotid artery. Our results show validity and high sensitivity of 2 MHz and 4 MHz pulsed Doppler transducers to detect solid embolic particles up to the size of 200 µm in a phantom of the common carotid artery. 2 MHz probe was more sensitive in detection of 200 µm particles and a symmetric to MCA probe monitoring. Simultaneous monitoring of MCA and CCA with the use of Doppler ultrasound with 2 MHz probe has a potential value to identify the active embolic signal source in patients with acute stroke. The monitoring may help to prevent or predict future acute stroke events thereby preventing potentially life threatening medical condition.

Keywords: Carotid phantom; Carotid artery; Polystyrene microspheres

Introduction

It has long been known that transducer of a single crystal with a frequency of around 2 MHz can be used for embolus detection in the MCA, but no specific transducer has been validated for embolus detection in CCA yet. A few studies have investigated embolus detection in CCA, Spencer et al. used two continuous wave (CW) transducers with different frequencies to monitor the CCA and ICA simultaneously in two patients with prosthetic heart valves. The study showed that the probe with 2.5 MHz frequency was capable of detecting emboli at a rate of 10 to 17 times more than from a probe with 5.0 MHz frequency [1,2]. Stump et al. used 5 MHz Doppler probe for continuous monitoring of the common carotid artery and reported that, for in vitro studies, ultrasound machine with 5 MHz, CW was capable of accurately detecting 193 µ polystyrene microspheres particles with high inter and intra observer reliability. And, in primary clinical use, embolic signals were detected in all patients monitored during cardiopulmonary bypass, whereas, no embolic signals were detected in healthy control subjects. There are no previous study that have investigated detection of emboli in the common carotid artery with pulsed wave (PW) probes. The present study aims to report the sensitivity and specificity of embolus detection of 2 MHz and 4 MHz PW probes in continuous monitoring of the common carotid artery.

Materials and Methods

Carotid flow phantom

To estimate the average diameter and depth of the common carotid artery (CCA), we scanned 10 healthy subjects, 6 males (mean age 33 ± 5 years, body mass index (BMI) 23.4 ± 3) and 4 Females (mean age 30 ± 4 years, BMI 24.3 ± 2.3) (Table 1), using B-mode ultrasound (Philips ATL5000 HDI) with L7-4 linear array probe. The mean CCA diameter was 5.9 ± 0.5 mm and depth was 17 ± 3 mm. Figure 1 shows an example of B-mode image.

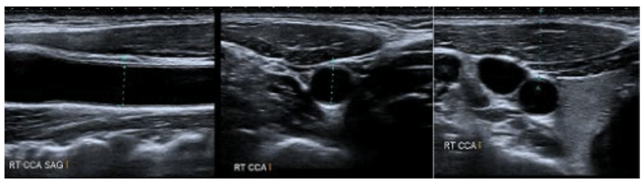

Figure 1: B-mode images of the CCA (A) Diameter in Sagittal views (B) Diameter in transverse view (C)

Based on these measurements, a flow-phantom was constructed using an agar-based tissue-mimicking material (TMM) which has a backscatter similar to soft tissue, attenuation was 0.5 ± 0.03 dB/cm (0.5 db/cm/MHz, soft tissue average), and speed of sound 1541 ± 3 cm/s (1540 cm/s in soft tissue) [3].

The tissue mimicking materials were mixed as it described below

82.97% water, 11.21% glycerol, 0.46% benzalkonium chloride, 0.53% 400 grain SiC powder (Logitec Ltd, Glasgow, UK), 0.94% 3 µm Al_2O_3 powder (Logitec), 3.00% Struers agar (Merck Eurolab, Roskildevej, Denmark)'. The ingredients were mixed in a double boiler, and then heated to 96°C and kept in the boiler at 96°C for 3 hours. The mixture was allowed to cool to 42°C, which then flowed into TMM container.

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C-flex tubing (Cole-Palmer, IL) with 0.56 cm diameter and 0.08 cm wall thickness were used to simulate the carotid artery. Although, it is known that it causes some distortion of the Doppler waveform, C-flex tube is considered to be as one of the most suitable tubing materials for its acoustical and physical properties which are similar to those of natural arteries. The flow-phantom was incorporated into a closed-circuit with roller pump to simulate the physiological flow in the carotid artery with 1 cardiac cycle/s. The circuit was filled with a solution of water mixed with small amount of blood-mimicking fluid (BMF). Figure 2 shows closed-loop flow-rig, and a camera that was used to record all the particles as they pass through the tubing but before they are detected by the probes. The camera was capable of recording all the particles as they passed through the tube and acted as a gold standard to compare the detection of particles by the probles.

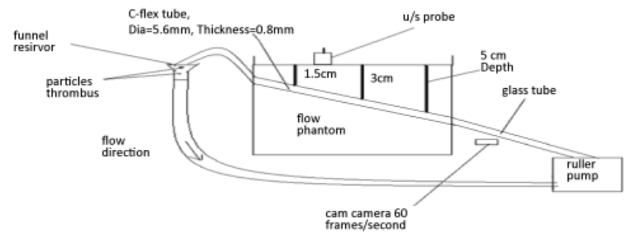

Figure 2: Closed-loop flow-rig used to simulate flow in the carotid artery

Microspheres particles were made from polystyrene divinylbenzene with sizes of 1000 μm. 500 μm, 200 μm and 50 μm (Duke Scientific) were introduced into the closed-flow circuit through the funnel reservoir. The densities of these particles (1050 kg/m^3) were similar to thrombus density (1060 kg/m^3). All the particles with a specific size were recorded by using a web camera at a speed of 60 frames/second; all the introduced particles were clearly seen by the camera except 50 μm particles which were not recognized due to its size. The next step was to record a three minutes video clip for each specific size of the particles (1000 μm, 500 μm, and 200 μm), while simultaneous detecting these particles using a TCD unit with 2 MHz and 4 MHz pulsed wave Doppler transducers. Specially developed software was used to detect and analyse the embolic signals as they passed through the sample volume. The u/s probe was position on the rig where tubing depth was 15 mm which is comparable to the depth of CCA in our volunteers. Next, all the Doppler signals were transferred to the computer with a dedicated software Rtm Data Conversion by [4], which stored all the Doppler signals in the form of rtm, files. By using RtmData Conversion software, Doppler signals were viewed in either the time domain or the frequency domain (Figure 3) shows the front page of the RtmData Conversion software with basic function buttons.

After saving the required Doppler signals in the form of rtm.files, RdRtm Manualv2 software was used to replay the Doppler signals and analyze the embolic signals. Figure 4 shows the front page of RdRtmManualv2 and basic function buttons.

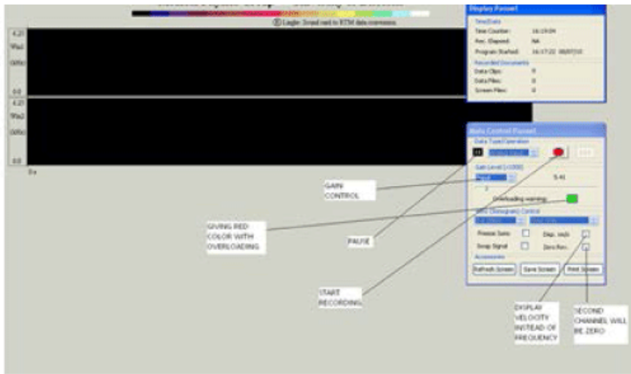

Figure 3: RtmData conversion software with basic function buttons.

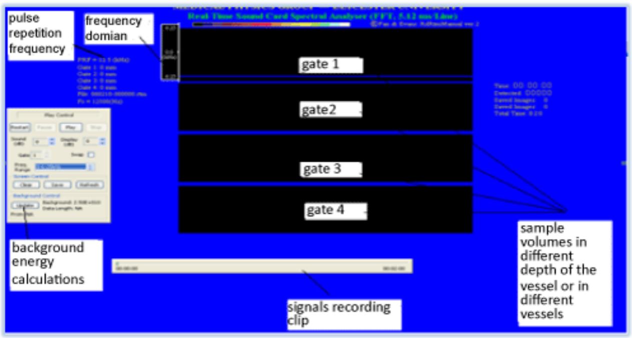

Figure 4: RdRtmManualv2 software with basic function buttons

Results

A three minutes of video clips were recorded for each particle size using the video of emboli entering the phantom. All the particles of 1000, 500, 200 μm diameter were detected and recorded by the camera. It was found that the particles of 1000 μm and 500 μm were detected with 100% sensitivity by 2 MHz and 4 MHz transducers. The 200 μm particles were detected with 94% sensitivity by 2 MHz and 92% sensitivity and high specificity by 4 MHz transducers. Figure 5 shows the number of particles observed by the camera during a 3 minute recording and the number of embolic signal that were detected by TCD. All the signals produced a characteristic chirp, click, or moan in the Doppler audio signal, and were of high intensity and short-duration.

Figure 6 shows an example of Micro Embolic Signal (MES) detected in the CCA phantom; the signal beneath the sonogram shows the time domain appearance of the MES.

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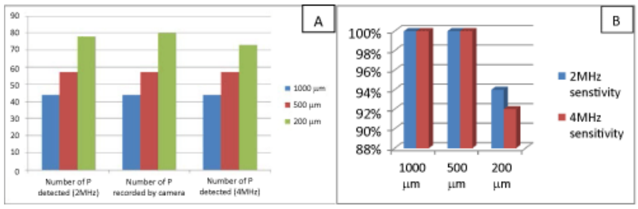

Figure 5: (A) Number of particles that were recorded for three minutes video clip recording and the number of embolic signals that were detected for the same clip. (B) % Sensitivity of embolic signals detection for 2 MHz and 4 MHz probes.

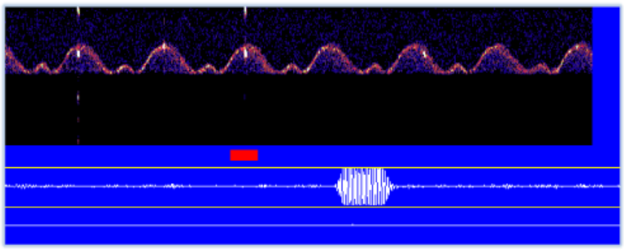

Figure 6: Example of MES detected in CCA flow phantom with time domain display of MES corresponding to the area of sonogram above the red rectangle.

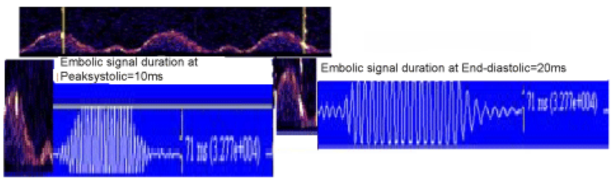

Figure 7: The duration of two embolic signals of 500 µm size, A- at the peak-systolic, B- at the end-diastolic.

Measured embolus-to-blood ratios (MEBR) were calculated for all the particles. The mean MEBR for 1000 µm was 20 ± 2 dB with the 4 MHz probe compared to 23 ± 3 with the 2 MHz probe. The mean MEBR for 500 µm was 19 ± 3 with 4 MHz compared to 23 ± 2 with 2 MHz probe; the mean MEBR for 200 µm was 17 ± 2 with 4 MHz probe compared to 19 ± 2 with 2 MHz probe. Table 1 shows MEBR and signal duration for 1000 µm, 500 µm, 200 µm particles with 2 and 4 MHz probes. Embolic signals that were detected during systole were shorter than those detected in the diastole phase as shown in the Figure 7.

Sex	Participant	Age	BMI
Male	6	33 ± 5	23.4 ± 3
Female	4	30 ± 4	24.3 ± 2.3

Table 1: Demographic Data

Discussion

The result of this study show validity and high sensitivity of 2 MHz and 4 MHz pulsed Doppler transducers to detect solid embolic particles up to the size of 200 µm in a phantom of the common carotid artery. Theoretically, solid emboli cannot be detected unless their diameter is of the order of 80-120 microns [5]. Solid particles of 1000 µm, 500 µm, 200 µm, and 50 µm were used in this study. But due to their small size, images of the 50 µm particles could not be detected. Both 2 MHz and 4 MHz pulsed Doppler transducer easily detected embolic particles of 1000 µm and 500 µm diameter with 100% sensitivity. For 200 µm particles, the 2 MHz transducer showed a detection sensitivity of 94%, compared to 92% by 4 MHz transducer. This finding is consistent with theoretical predictions. In a study of two patients with prosthetic heart valves [1], using 2.5 MHz and 5 MHz CW Doppler probes for simultaneously observing the common carotid artery and the internal carotid artery, it was reported that, 2.5 MHz probes were able to detect the emboli at a rate of 10-17 times more frequently than with a 5 MHz probe. In our study, the 2 MHz probe showed higher sensitivity to smaller particles. All the embolic signals that were detected appeared as a signal of a unidirectional, high-intensity, and of a short-duration, with a characteristic click, chirp and moan that can occur at any point in the cardiac cycle.

The mean duration of embolic signals for 1000 µm was 18 ± 3ms, 16 ± 3 ms for 500 µm and 14 ± 5 ms for 200 µm particles using a 4 MHz pulsed probe, whereas in 2 MHz pulsed probe, the mean duration of embolic signals were 16 ± 4 ms for 1000 µm, 33 ± 8 ms for 500 µm and 14 ± 4 ms for 200 µm. It was noticed that the mean duration of embolic signals for 500 µm with 2 MHZ pulsed probe were more than double compared to the rest of emboli signals. To investigate whether this was related to the velocity of the embolus, the velocity of the embolus was calculated based on the Doppler equation and we found no significant difference in the velocity of the embolus compared to other measurements at different sizes [6]. Long duration embolic signals could also be related to the trajectory of the embolus or a difference in the beam position between experiments. The measured embolic blood ratios (MEBR) were calculated. In general, MEBR values were higher with 2 MHz frequency when compared to 4 MHz frequency which is consistent with theoretical predictions. Regarding the correlation of MEBR with embolic size, it was found that there was no remarkable difference in the mean value of MEBR between 500 µm and 1000 µm. Theoretically, MEBR value does not go up irrespective of size in the solid embolus (Figure 8) shows MEBR for 1000 µm, 500 µm, 200 µm with 2 MHz and 4 MHz pulsed probe (Table 2).

Even though 2 MHz is more sensitive with small particles and has a higher EBR, the embolic signal is easily saturated due to ‘cross-talk’ in the electronic and low dynamic range. Figure 9 shows the background of the blood backscatter for 2 MHz and 4 MHz with the same parameters, except the depth of the 4 MHz sample volume was 26 mm, and the depth of the 2 MHz sample volume was 30 mm.

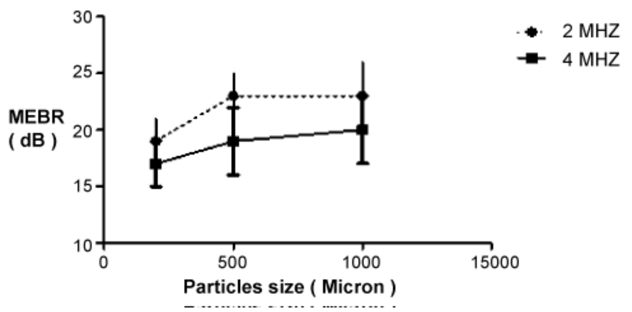

Figure 8: Difference of MEBR at 2 MHz and 4 MHz for solid emboli of 1000 microns, 500 microns and 200 microns diameter.

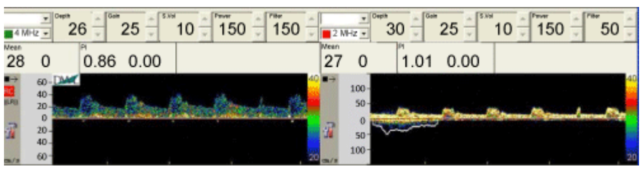

Figure 9: The background of the blood backscatter flowing in the sample Doppler volume of 4 MHz and 2MHz.

Frequency Particle size	4 MHz			2 MHz		
	1000 µm	500 µm	200 µm	1000 µm	500 µm	200 µm
MEB (dB) ± SD	20 ± 3	19 ± 3	17 ± 3	23 ± 3	23 ± 2	19 ± 2
Duration (ms)	18 ± 3	16 ± 3	14 ± 5	16 ± 4	33 ± 8	14 ± 4

Table 2: MEBR and signal duration of the particles with 2 and 4 MHz probes with SD

Theoretically, it is easier to detect an embolus in the middle cerebral artery than in the common carotid artery because of the smaller sample volume (V=π R2L, where V sample volume, R the vessel radius, and L the sample volume length). It is clear from these results that we can also detect emboli in the common carotid arteries with high sensitivity. This can be used to identify the source of emboli by simultaneous monitoring of emboli in the middle cerebral artery and common carotid artery [7]. Monitoring of the CCA has the advantage of avoiding the distortion associated with the temporal bone window.

Conclusion

2 MHz and 4 MHz pulsed probe show high sensitivity in detecting emboli in a CCA phantom. 2 MHz probes were more sensitive to small embolic and this study suggested that it is possible to observe emboli in the CCA and MCA. Use of two probes for embolus detection in the CCA and MCA could help to identify whether the source of emboli is cardiac or from carotid artery disease. The monitoring may help to prevent or predict futures acute stroke events thereby preventing potentially life threatening medical condition.

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