Quantitative photoacoustic imaging of simulated carotid plaques in a neck phantom

David Thompson, Wiendelt Steenbergen, Francis Kalloor Joseph


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D.Thompson*, W. Steenbergen, K.J. Francis

Biomedical Photonic Imaging Group, Technical Medical Centre, University of Twente, The Netherlands

ABSTRACT

We present a new curved array-based photoacoustic and ultrasound imaging system, targeted at imaging and characterising atherosclerotic plaques in the carotid artery. The system incorporates an imaging probe with a 256-element ultrasound array as a detector and ultrasound source, a custom fibre bundle with a pair of linear outputs for illumination and a moulded polyvinyl chloride plastisol acoustic interface piece. The initial results presented here focus on an assessment of the imaging depth in a gelatin-based neck-mimicking phantom with channels representing the carotid artery at various depths. We report imaging depths down to 40 mm, which would be an adequate depth for imaging the carotid artery in most patients. Further we present our initial results on unmixing different chromophores embedded in the phantom.

Keywords: photoacoustics, plane wave ultrasound, carotid plaque, atherosclerosis, multi-wavelength photoacoustic imaging

1. INTRODUCTION

Acute ischaemic stroke is the cause of over 10 percent of deaths worldwide. Stroke can be prevented by timely diagnosis and treatment of carotid atherosclerosis, either by medication or operative removal, the latter is known as an endarterectomy. Commonly the decision on whether to treat a stenosis and how is based on whether or not the patient is symptomatic and the level of stenosis. According to Dutch guidelines [1], asymptomatic patients receive medication for stenosis degrees below 70% and are operated when stenosis exceeds 70%. Symptomatic patients are operated once stenosis degree exceeds 50%, while medication is given for anything below that.

Only 20% of the patients with stroke have more than 50% narrowing of the artery (stenosis), however the surgical decision making depends primarily on the degree of stenosis [2]. However, it is becoming clearer and clearer, from histological studies and autopsies, that stenosis degree alone may be an inadequate marker for the need to operate, while plaque composition and morphology can be independent parameters to predict strokes. Endarterectomy currently has a number-needed-to-treat of 6, while the number-needed-to-harm is only 0.3 [3]. An idea that is gaining traction is to focus instead on markers of plaque vulnerability such as the presence of a necrotic lipid core, thin fibrous cap or intraplaque haemorrhaging [4], which may give a better indication of the risk of stroke and thus the need to operate.

One method for better characterisation of plaque composition for the purpose of vulnerability assessment is photoacoustic imaging [5–8]. Photoacoustics holds promise for this application, because the acoustic detection means imaging depths down to several centimeters can be achieved [9–11], while the optical excitation allows the use of multiple wavelength to identify and unmix the various materials present in atherosclerotic plaques [12–14].

This work presents a new set up for photoacoustic and plane wave ultrasound imaging of stenosis in the carotid artery. The average depth of the carotid artery bifurcation is 2-5 cm [15]. Imaging of a gelatin-based tissue mimicking phantom gives an idea of the imaging depths that can be achieved with both modalities. Further, we also present initial results on the spectral unmixing of different photoacoustic sources in neighbouring channels.

*corresponding author: d.thompson@utwente.nl
2. MATERIALS AND METHODS

2.1 Imaging set up

The imaging set up is centred on a custom-built 256-element ultrasound transducer array with a 40 mm radius of curvature and 5 MHz centre frequency (Imasonic SAS, France), shown in Fig. 1(a). For photoacoustic imaging, the illumination is provided by a tunable 10 ns pulsed OPO-laser system (Opolette 532i, Opotek, USA) with pulse energies ranging from 4.5-2.5 mJ in the 680-950 nm wavelength range. Light from the laser is coupled into a fibre bundle (CeramOptec GmbH, Germany), shown on the left side in Fig. 1(b). The fibre bundle has a pair of linear outputs, to ensure uniform illumination, as shown in Fig. 1(b) on the right.

A mould was 3D printed to produce a PVCP interface piece, both shown in Fig. 1(c) to facilitate acoustic coupling between the transducer array and the measurement subject. The sound speed of the interface piece is taken into account when reconstructing images, to prevent any distortions. Figure 1(d) shows the assembled transducer array, fibre bundle outputs and interface piece together in a 3D-printed mount. The fibre bundle outputs are positioned to maximise illumination in the focal region of the transducer array.

2.2 Phantom

A schematic representation of the neck-mimicking phantom is shown in Fig. 2(a). It consists of a block of 46.5 mg/mL gelatin (Dr. Oetker GmbH, Germany) in demineralised water, containing 0.8 mg/mL TiO$_2$ (Sigma Aldrich, USA), 5 µL/mL India ink and 10 mg/mL CM cellulose (Sigma Aldrich, USA) for optical scattering, optical absorption and acoustic scattering respectively. The block contains 6 cylindrical cavities which can be filled with optically absorbing materials as photoacoustic sources. On one side, 3 channels are placed progressively deeper into the phantom at 25 mm lateral intervals, to allow evaluation of the imaging depth. On the other side 3 channels are placed at a 22 mm depth, closer together to allow simultaneous imaging. This side of the phantom can be used to image multiple absorbing agents for subsequent spectral unmixing.

The first step in preparing the phantom is to soak the gelatin sheets for 5 minutes in demineralised water, after which they are manually squeezed out and added to a beaker containing 700 mL of demineralised water at 40°C. The gelatin-water mixture is stirred using a magnetic stirrer until the gelatin is completely dissolved, which takes approximately 1.5 hours. The CM cellulose is added to the mixture once the gelatin is dissolved, and allowed to mix for 30 minutes. Next, the TiO$_2$ and India ink are added and the mixture continues to stir for a further 1.5 hours to ensure any larger clumps of TiO$_2$ are broken up to achieve a homogeneous mixture.
Figure 2. (a) Schematic of the phantom, showing the positioning of the various channels, (b) phantom mould, based on a plastic food container, with suspended rods to form the channels and (c) the soft tissue mimicking phantom used for imaging with channels filled with India ink.

Once complete, the mixture is poured into the mould shown in Fig. 2(b), a rectangular plastic container with 6 mm diameter metal rods suspended through the lid, which will form the channels. The container is lined with a plastic bag, to facilitate the intact removal of the phantom once complete. The phantom is chilled overnight at 7°C, after which it is firm enough to be unmoulded. It can be seen in Fig. 2(c) that the shallowest channel ended up a little deeper than intended from the phantom design, due to a fabrication inaccuracy in the mould.

3. RESULTS AND DISCUSSION

Figure 3 shows PA images of the three variable-depth channels filled with 0.0023% India ink ($\mu_a = 0.3 \text{ mm}^{-1}$) in water side by side, from the shallowest to the deepest. For the first pair of channels both the near and far boundaries are visible, while for the deepest-lying channel only the upper boundary can be seen, at a depth of 62 mm with a signal-to-noise ratio (SNR) of 3.3. The SNR values of the upper and lower boundaries of the shallowest channel are 5.8 and 3.5 respectively, for the middle channel they are 4.0 and 6.5 respectively.
Figure 4. Plane wave ultrasound images of the progressively deeper channels. All three channels are clearly visible as strongly hypoechoic, with the top and bottom parts of the channel exhibiting stronger signals due to their alignment with the transducer array.

The shallowest 2 channels are clearly visible, at depths of 23 and 28 mm respectively. The decreasing optical fluence due to scattering and absorption and the decreasing sensitivity of the transducer array with depth beyond the focal area makes the third channel more difficult to spot. The near boundary of the third channel, at a depth of 38 mm is just barely visible with a SNR of 1.66.

Figure 4 shows the corresponding plane wave images of the same channels. The images were acquired using 2 plane waves at ±0.3 radians, emitted from the first and last 96 elements of the array respectively. While all three channels can be clearly distinguished there are some differences between them. All three channels are clearly visible as hypoechoic circular structures in a uniformly scattering surrounding. As the signal strength does decrease somewhat with depth, the contrast of the deepest channel relative to the weaker surrounding scattering signals is less than for the first two channels.

Figure 5. (left) Unmixed image of 0.0023% India ink, with an estimated $\mu_a$ of 0.3 mm$^{-1}$, also showing the second channel due to the presence of India ink in the gelatin itself. (centre) Unmixed image of 1.0 $\mu$g/mL ICG in ethanol, estimated $\mu_a$ of 0.023 mg/mL. (right) Blended image of the closely-spaced channels, with the leftmost filled with India Ink in water, the centre with 1.0 $\mu$g/mL ICG in ethanol, the rightmost with olive oil (not visible).

Figure 5 shows 2 spectrally unmixed images by non-negative linear least squares fit to measured spectra, and a blend of the two images. The channels are filled with, from left to right, 0.0023% India ink in water, 1.0
µg/mL indocyanine green (ICG) in 100% ethanol (estimated $\mu_a = 0.023$ mm$^{-1}$) and olive oil. After performing the unmixing, the signals from the olive oil are too weak to be distinguished currently, while the other two materials are clearly separated. The ability to image and spectrally unmix various absorbers with tissue-realistic optical absorption properties is a promising first step towards ex-vivo, and eventually in-vivo, carotid plaque characterisation.

4. CONCLUSION

We have presented a new set up for carotid artery atherosclerosis imaging, including the potential to unmix images to characterise and quantify plaque composition. Phantom images have shown an imaging depth adequate to image the carotid artery using both photoacoustic imaging and plane wave ultrasound.

References


