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Improving visibility in limited-view scenarios with dynamic particle-enhanced optoacoustic tomography

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ABSTRACT

Limited-view artefacts affect most optoacoustic (photoacoustic) imaging systems due to geometrical constraints that impede achieving full tomographic coverage as well as limited light penetration into scattering and absorbing objects. Indeed, it has been theoretically established and experimentally verified that accurate optoacoustic images can only be obtained if the imaged sample is fully enclosed ($> \pi$ angular coverage) by the measuring locations. Since in many cases full angular coverage cannot be achieved, the visibility of structures along certain orientations is hampered. These effects are of particular relevance in the case of hand-held scanners with the imaged volume only accessible from one side. Herein, a new approach termed dynamic particle-enhanced optoacoustic tomography (DPOT) is described for accurate structural imaging in limited-view scenarios. The method is based on the non-linear combination of a sequence of tomographic reconstructions representing sparsely distributed moving particles. Good performance of the method is demonstrated in experiments consisting of dynamic visualization of flow of suspended microspheres in three-dimensions. The method is expected to be applicable for improving accuracy of angiographic optoacoustic imaging in living organisms.

Keywords: Optoacoustic tomography, photoacoustic tomography, limited-view effects, non-linear reconstruction.

1. INTRODUCTION

The speckle-free nature of optoacoustic (photoacoustic) imaging is generally considered an advantage with respect to backscattering-based coherent imaging techniques such as ultrasound or optical coherence tomography, where speckle grains reduce the resolution, hamper distinguishing small features and overall deteriorate image quality.^{1,2} In these techniques, the speckle pattern is associated to the superposition of partial waves corresponding to randomly distributed subresolution scatterers causing phase shifts ranging from 0 to 2π in the incident wave.³ In optoacoustics, pressure waves generated by individual absorbers have equivalent shape with positive and negative parts that cancel out in the A-mode signals except for areas corresponding to object boundaries, where prominent edges are built up by constructive interference.^{4,5} The inner part of an object appears then invisible when stacking A-mode signals in a B-scan.

The same result regarding object visibility is predicted by considering a continuous distribution of optical absorption. In this case, much like in tomographic imaging modalities such as x-ray computed tomography, it is theoretically established that an object must be fully enclosed by measuring locations in order to be accurately reconstructed.⁶ So-called limited-view effects appear in optoacoustic B-scans or in tomographic acquisition geometries with an insufficient angular coverage,^{7,8} being particularly prominent in elongated structures such as blood vessels emitting pressure waves mainly directed along their normal direction.

The visibility of structures affected by limited-view effects can be enabled or enhanced by artificially creating small optoacoustic sources within them. This has been achieved by using a speckled illumination pattern for optoacoustic excitation, where speckle grains represent individual sources.⁹ The imaging feasibility of this approach has been showcased by combining phantom images obtained with multiple speckle patterns having a controlled speckle grain size. However, its applicability inside biological tissues remains challenging due to the

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need to resolve speckle grains with sizes in the order of the optical wavelength. A different approach to create individual sources consists in locally heating a defined spot with focused ultrasound, so that the corresponding local increase in the Grueneisen parameter allows thermally encoding optoacoustic signals.¹⁰ Images can then be obtained by scanning the ultrasound beam, which is generally a slow process. Also, the potential thermal damage *in vivo* must be carefully evaluated. It is important to notice that the superposition of the images rendered with a linear reconstruction method is equivalent to the image reconstructed with the superimposed signals, so that images must be combined in a non-linear manner to guarantee the full visibility of structures.

Herein, we describe an alternative approach termed dynamic particle-enhanced optoacoustic tomography (DPOT) to improve the visibility in limited-view scenarios based on imaging the dynamic distribution of sparsely located particles.¹¹ The size and average separation between particles must be adapted to the system resolution so that they can be individually distinguished in the images. Ideally, the highest possible concentration of particles fulfilling this criterion is desirable, for which a dense granular image similar to a speckle pattern is rendered.

2. MATERIALS AND METHODS

2.1 Visibility in limited-view scenarios

An illustrative example of the limited-view effects on the visibility of structures is showcased in Fig. 1. For an elongated vertical structure (Fig. 1a, red cylinder), optoacoustically generated pressure waves mainly propagate along the horizontal direction (red arrows) and are not efficiently collected e.g. with transducers located above or below this structure. On the other hand, the optoacoustic signals generated by small absorbers (Fig. 1a, blue dots) propagate in all directions (blue arrows) and hence are efficiently collected at any location. Figs. 1b and 1c display the reconstructed image of a numerically-simulated vessel-mimicking structure when considering an array of 91 transducers covering an angle of 90° located below the image.⁵ Figs. 1d shows the actual image of the structure. It is shown that vertical structures are not visible when considering a continuous optical absorption distribution (Figs. 1b) but these areas are visible when only a few particles (150) are located inside the structure (Figs. 1c).

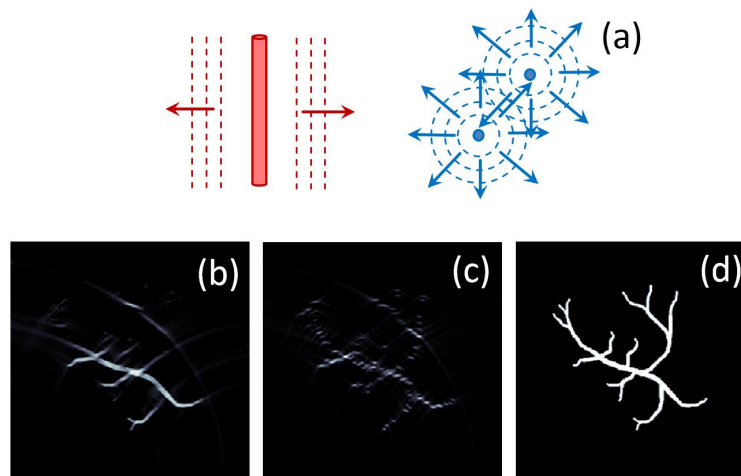


Figure 1. Limited-view effects on the visibility of structures. (a) Main propagation direction of the optoacoustic waves generated by a cylindrical structure (red cylinder) and by small absorbers (blue dots). (b) Reconstructed image of a numerically-simulated vessel-mimicking structure filled with a continuous absorption distribution when considering an array of 91 transducers covering an angle of 90° located below the image. (c) Reconstructed image of the same structure when filled with 150 absorbing particles. (d) Actual image of the structure.

2.2 Dynamic particle-enhanced optoacoustic tomography

As shown in section 2.1, a relatively sparse distribution of particles remains visible under limited-view conditions. Taking this into account, dynamic particle-enhanced optoacoustic tomography (DPOT) is based on a combination of multiple images of flowing particles. The combination of reconstructed images can however not be done by simple superposition. Indeed, even though all particles are visible, limited-view artefacts in tomographic reconstructions are manifested as negative shadows, which cancel out positive absorption values in a similar manner as speckle grains are removed in time-resolved optoacoustic signals.⁵ Full visibility of the structures of interest can only be achieved with a non-linear combination of the reconstructed images. Herein, negative absorption values are removed by means of a non-negative constrained model-based reconstruction algorithm.¹² With this approach, the optical absorption in the region of interest for the i -th particle distribution, expressed in a vector form $\mathbf{H}_i$, is estimated by solving the following least square problem

$$\mathbf{H}_i = \operatorname{argmin}_{\mathbf{H} \geq 0} \|\mathbf{p}_m - \mathbf{A}\mathbf{H}\|^2, \quad (1)$$

being $\mathbf{p}_m$ a vector that represents the measured signals and $\mathbf{A}$ is the model-matrix associated to the discrete optoacoustic forward model. The non-negative constrain $\mathbf{H} \geq 0$ introduces a non-linearity in the reconstruction which is exploited in DPOT. The image of the object $\mathbf{H}$ is eventually rendered by superposing the tomographic reconstructions corresponding to multiple particle distributions as

$$\mathbf{H} = \sum_i \mathbf{H}_i. \quad (2)$$

2.3 Imaging experiment

The experimental performance of DPOT was tested by dynamically imaging the flow of suspended particles. For this, we made use of the unique capabilities of a recently-developed real-time three-dimensional optoacoustic imaging platform allowing image acquisition at rates up to 100 frames per second.^{13,14} Basically, a spherical array of piezocomposite elements covering an angle of 90° with 40 mm radius was used to simultaneously collect 256 optoacoustic signals. While this tomographic configuration can substantially improve optoacoustic imaging performance with respect to linear or planar arrays, limited-view effects still affect the images. 20 μm polyethylene microspheres (Cospheric BKPMS 20-27) suspended in ethanol were injected in a polyethylene tubing with $\approx 200 \mu\text{m}$ inner diameter. The wavelength of the laser was set to 720 nm and the pulse repetition frequency was set to 10 Hz. The three-dimensional optoacoustic model used for tomographic reconstructions is described in Ref. 15.

3. RESULTS

The results of the imaging experiment are depicted in Fig. 2. Specifically, Fig. 2a and Fig. 2b show the images obtained by superimposing multiple tomographic reconstructions obtained with unconstrained and non-negative constrained inversion, respectively. The lateral maximum intensity projections (MIPs) of the three-dimensional images are shown. The spherical array is located in the left part of the images. It is shown that, if no constrain is applied, the linear superposition of images builds up into an image affected by limited-view effects, in a similar manner as for a continuous absorption distribution. On the other hand, the visibility of the tubing is significantly enhanced by superimposing the images reconstructed with non-negative constrained inversion.

4. DISCUSSION AND CONCLUSIONS

The importance of the presented results stems from the fact that accurate angiographic imaging can potentially be achieved in the diffuse regime of light for samples not accessible tomographically. This is particularly important for the optoacoustic clinical translation, where recent efforts are being directed.^{16–18} Other large animal models are also only accessible from one side due to the limited penetration of light into tissues, typically millimeters to centimeters in the so-called near-infrared window of light (650–900 nm). *In vivo* imaging with full angular coverage is in any case hampered by mechanical constraints and the need to immerse a living organism in a liquid

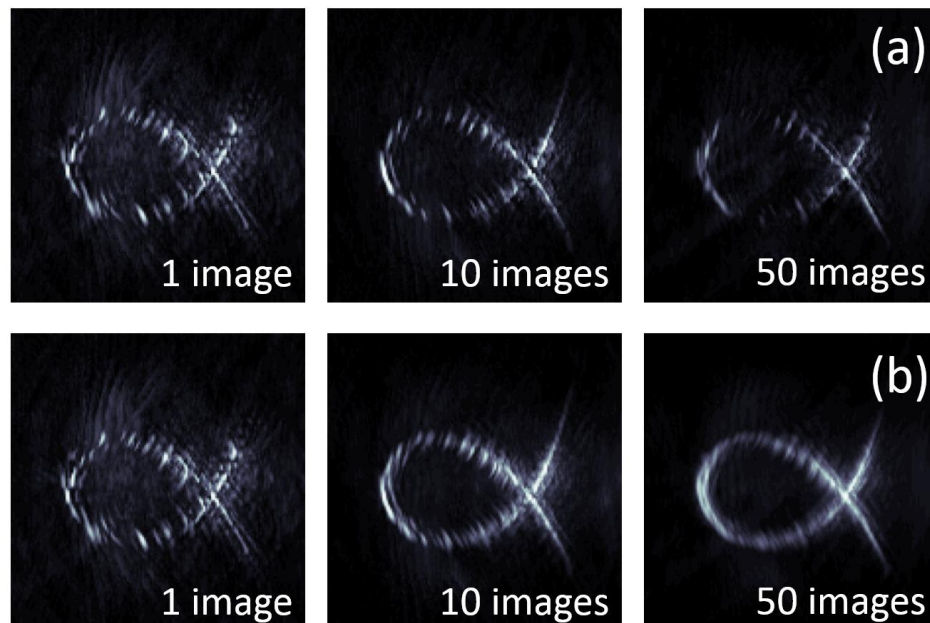


Figure 2. Lateral maximum intensity projections of the images obtained by superimposing multiple frames acquired during the flow of particles for tomographic reconstruction performed with unconstrained model-based inversion (a) and tomographic reconstruction performed with non-negative constrained model-based inversion (b).

coupling medium,¹⁹ so limited-view effects are generally affecting optoacoustic images. For a good performance of DPOT, proper biocompatible particles must however be selected so that they generate a sufficiently strong signal to be imaged separately. Being able to detect the signal generated by individual absorbing particles is also relevant for other purposes. For example, it has recently been shown that the light intensity distribution through scattering samples can be controlled via optoacoustic feedback,^{20–22} and the particles employed for generating optoacoustic signals determine the light intensity enhancement that can be achieved.²³ The signals of individual absorbers can also be used to estimate the flow velocity with Doppler optoacoustic methods,^{24,25} which can also be done with the methodology described herein by tracking individual particles in a sequence of images.

Future steps must be directed towards improving the spatio-temporal resolution of the optoacoustic imaging system used for DPOT, where spherical arrays with higher bandwidth have been suggested.¹⁴ On the one hand, the temporal resolution of the system is reduced by the number of images that need to be combined. Herein, it has been shown that approximately 50 images can yield satisfactory results, and a lower number of images may be sufficient for a denser distribution of particles. On the other hand, the spatial resolution of the system is also essential to image densely distributed small particles, and the development of a high-resolution real-time three-dimensional optoacoustic imaging system is an important next step. The sensitivity of the optoacoustic system is also an important issue to consider along with the development of efficient particles. Indeed, the number of acquisitions required for a good performance of DPOT is further determined by the signal-to-noise ratio (SNR) of individual images. The sensitivity may be increased by unmixing spectrally-distinctive particles with multispectral acquisitions, for which a short delay between pulses at different wavelengths is needed to avoid motion artefacts.²⁶ Ideally, a system with sufficient resolution and sensitivity to distinguish individual cells would be desirable, as it can potentially enable the applicability of DPOT with endogenous contrast.

In conclusion, DPOT allows improving the visibility of structures affected by limited-view artefacts in the diffusive regime of light. Accurate angiographic imaging for depths of millimeters to centimeters within living samples is then possible provided individual particles can be separately detected. As limited view effects are unavoidable in most optoacoustic systems, DPOT is expected to play an important role for optoacoustic image enhancement.

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