

Non-contact optoacoustic imaging by raster scanning a piezoelectric air-coupled transducer

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ABSTRACT

Optoacoustic techniques rely on ultrasound transmission between optical absorbers within tissues and the measurement location. Much like in echography, commonly used piezoelectric transducers require either direct contact with the tissue or through a liquid coupling medium. The contact nature of this detection approach then represents a disadvantage of standard optoacoustic systems with respect to other imaging modalities (including optical techniques) in applications where non-contact imaging is needed, e.g. in open surgeries or when burns or other lesions are present in the skin. Herein, non-contact optoacoustic imaging using raster-scanning of a spherically-focused piezoelectric air-coupled ultrasound transducer is demonstrated. When employing laser fluence levels not exceeding the maximal permissible human exposure, it is shown possible to attain detectable signals from objects as small as 1 mm having absorption properties representative of blood at near-infrared wavelengths with a relatively low number of averages. Optoacoustic images from vessel-mimicking tubes embedded in an agar phantom are further showcased. The initial results indicate that the air-coupled ultrasound detection approach can be potentially made suitable for non-contact biomedical imaging with optoacoustics.

Keywords: Optoacoustic imaging, photoacoustic imaging, raster-scan, non-contact imaging, air coupled transducers.

1. INTRODUCTION

Optical contrast arguably represents the most powerful means to interrogate biological tissues, where different methods based on fluorescence, bioluminescence, absorption or reflection can provide information at the functional and molecular levels.¹ Also, being optical excitation non-ionizing, no strong safety concerns apply in a clinical environment. The spatial distribution of optical properties at depths up to a few centimeters within biological tissues can be imaged with epi- and trans-illumination schemes. However, these methods are generally inadequate due to the ill-posed nature of the mathematical inversion procedure.²⁻⁴ Furthermore, strong scattering in biological tissues severely limits the achievable resolution for depths beyond the diffusive limit of light.⁵

The limitations of pure optical imaging techniques have shifted the research efforts in biomedical optics to the development of optoacoustic (photoacoustic) techniques, which preserve rich optical absorption contrast while providing higher (ultrasound) resolution.⁶⁻⁸ Optoacoustics has enabled novel applications in biomedical research with small animals⁹⁻¹² and especially-designed systems have been recently developed for the clinical translation of this modality.¹³⁻¹⁶ One of the main hardware limitations associated to optoacoustic techniques stems from the fact that ultrasound transmission between optical absorbers within tissues and the measurement location is needed. Thereby, much like in echography, commonly used piezoelectric transducers require either direct contact with the tissue or through a liquid coupling medium. The contact nature of this detection technology represents then a disadvantage of optoacoustics with respect to other imaging modalities (including optical techniques) in applications where non-contact imaging is needed, e.g. in open surgeries or when burns or other lesions are present in the skin.

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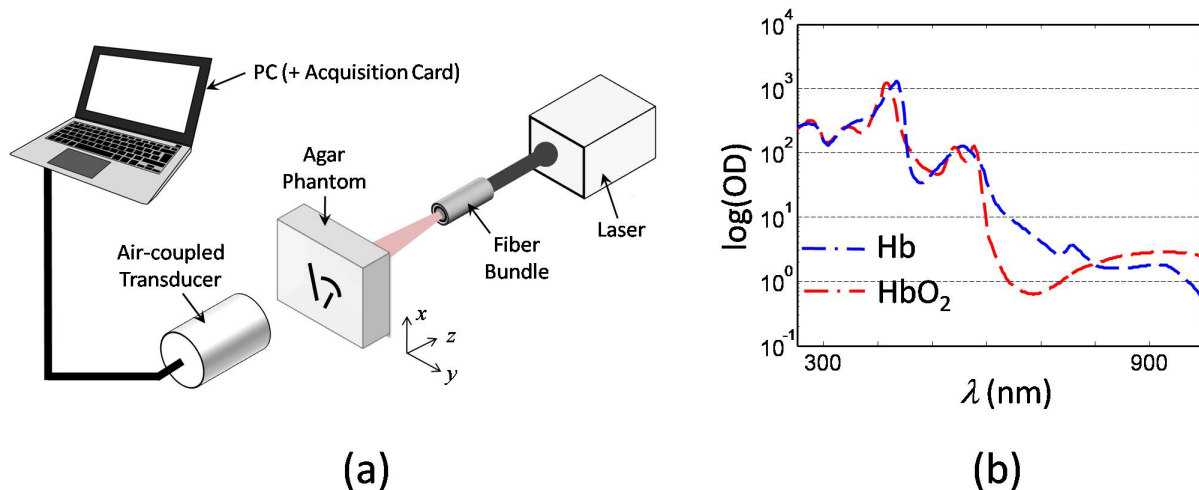


Figure 1. (a) Layout of the experimental setup. (b) Optical density of oxygenated (HbO_2) and deoxygenated (Hb) hemoglobin for a typical concentration of 150 g/l in blood as a function of the optical wavelength.

Detection of optoacoustically-induced ultrasound waves from remote locations is possible with optical methods such as interferometry or beam deflection.^{17,18} These techniques are based on the measurement of surface displacement, so that no further ultrasound propagation is required. However, surface heterogeneities can hamper the applicability of these methods for imaging actual biological tissues. Another technology allowing non-contact ultrasound detection is based on air-coupled transducers. Air-coupled transducers have been designed to overcome the huge acoustic impedance mismatch between air and the ultrasonic sensing element. In the case of low and medium ultrasonic frequencies, micro-membrane capacitance transducers are the best choice.^{19,20} At frequencies higher than 1 MHz, piezoelectric transducers adapted to air by using microporous coupling layers are more convenient as, having good sensitivity, focused apertures and array configurations can be easily made.²¹ The feasibility of detecting optoacoustic signals with air-coupled transducers has been demonstrated,²² although no discussion was provided on the applicability to image actual samples. Herein, we discuss on the feasibility of optoacoustic imaging with focused air-coupled transducers in realistic situations where the light fluence is maintained below safety standards and for an optical absorption equivalent to that of blood, the main endogenous absorber in biological tissues generating optoacoustic contrast.

2. MATERIALS AND METHODS

2.1 Experimental setup

The experimental system employed was described in Ref. 23. The lay-out of the system is depicted in Fig. 1. Basically, a phantom consisting of an agar block containing ink channels with different diameters was imaged. The thickness of the phantom was approximately 1 cm and the ink channels were located at a shallow depth (approximately 500 – 1000 μm) within the phantom, where optical illumination was provided from the opposite side. Specifically, an optical parametric oscillator (OPO)-based laser was used (Innolas Laser GmbH, Krailling, Germany). The light beam was guided through a custom-made fiber bundle (CeramOptec GmbH, Bonn, Germany) and set to a wavelength of 750 nm for optimal power at the sample (12 mJ at the output of the fiber bundle). The output of the bundle was positioned in close proximity to the surface of the phantom, so that the diameter of the light beam at the ink rod was approximately 9 mm, i.e., the energy density was approximately 20 mJ/cm². A spherically-focused air-coupled transducer with 20 mm diameter and 25 mm focal distance was positioned on the opposite side of the fiber bundle in a trans-illumination scheme as depicted in Fig. 1. The transducer has a central frequency of 800 kHz and a –6dB bandwidth of 400 kHz. The phantom was attached to a platform allowing raster-scanning along the x and y directions. The optoacoustic signals were digitized with an embedded acquisition card with 10 MSPS and 12 bit vertical resolution (AlazarTech, ATS9351).

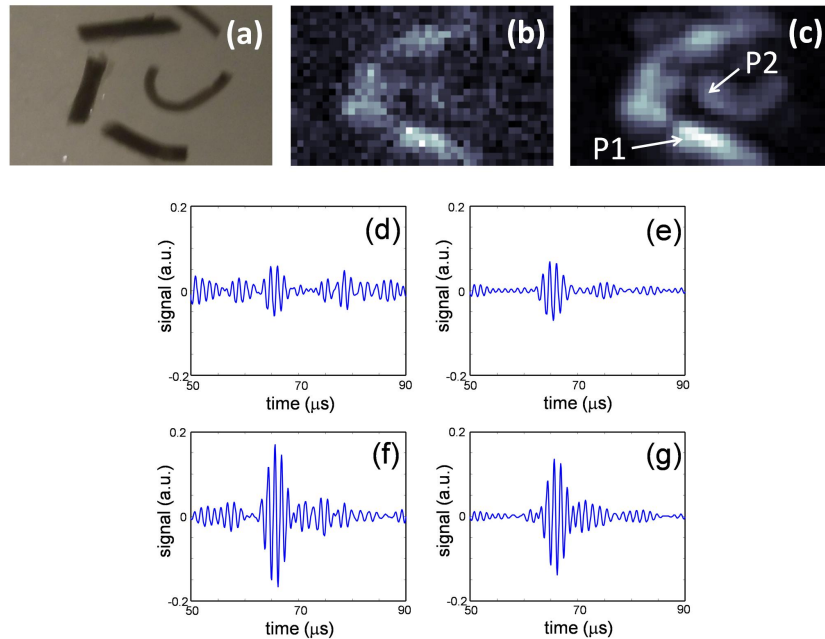


Figure 2. Experimental results. (a) Actual photograph of the phantom. (b) and (c) Optoacoustic image of the phantom obtained by raster-scanning an air-coupled transducer with 10 and 1000 averages respectively. The actual size of the image is $12.3 \times 7.5 \text{ mm}^2$. (d) and (e) Optoacoustic signals for the transducer position P1 marked in (c) for 10 and 1000 averages respectively. (f) and (g) Optoacoustic signals for the transducer position P2 marked in (c) for 10 and 1000 averages respectively.

2.2 Imaging experiment

In order to demonstrate the imaging capability by raster scanning an air-coupled transducer, the phantom was scanned along the x and y directions as mentioned in section 2.1. The phantom contained ink channels with diameters 0.5 and 1 mm and 10 optical density arranged as shown in Fig. 2a. The optical absorption coefficient μ_a (in cm^{-1}) is given by $\mu_a \approx 2.3A/l$, being A the optical density and $l = 10 \text{ mm}$ the length of the cuvette where it is measured. As a reference, the optical absorption coefficient of hemoglobin for a realistic concentration of 150 g/l in blood is displayed in Fig. 1 for different wavelengths. The scanning was performed with a step of 0.3 mm covering a total area of $12.3 \times 7.5 \text{ mm}^2$. The acquired signals were also filter with 600 and 1000 kHz cut-off frequencies. A two dimensional image was formed by considering the peak-to-peak amplitude of the signals in a narrow time window of $12 \mu\text{s}$ around the focal spot for the filtered signals.

3. RESULTS

The resulting images obtained by raster scanning the air-coupled transducer are displayed in Figs. 2b and 2c when considering 10 and 1000 averages respectively. A good correspondence with the actual absorption distribution (Fig. 2a) is observed, with improving image quality as the number of averages is increased. The optoacoustic signals for the two scanning position P1 and P2 marked in Fig. 2c are also shown. Figs. 2d and 2e display the optoacoustic signals for P1 when taking 10 and 1000 averages respectively. A signal-to-noise ratio (SNR) increase is clearly observed for a higher number of averages. On the other hand, Figs. 2f and 2g display the optoacoustic signals for P2 when taking for 10 and 1000 averages respectively. In this case, a sufficiently high SNR is achieved with 10 averages, which indicates the feasibility to image certain structures without substantially increasing the number of averages.

4. DISCUSSION AND CONCLUSIONS

The showcased results demonstrate the basic feasibility to form optoacoustic images by raster scanning air-coupled transducers. The experiments performed are representative of actual biological samples as the energy density was kept below safety exposure limits and the optical absorption coefficient of the structures imaged is in the same order as that of blood. The penetration capability of this methodology in real tissues still needs to be determined. On the one hand, light penetration is maximized by using optical wavelengths in the so-called near-infrared window of light ($\approx 650 - 900$ nm). The optical density of blood is minimized in this range, so that a large number of averages may be required for rendering representative images. On the other hand, the optical density of blood substantially increases for wavelengths in the visible range (400-630nm), reaching values above 1000 cm^{-1} , whereas the safety exposure limit remains at 20 mJ/cm^2 . It was shown that it was possible to detect optoacoustic signals generated by absorbers with a lower absorption coefficient, even with a low number of averages. In this way, in this spectral range it seems feasible to perform a raster scan of superficial structures in a relative short time. The penetration depth however is limited for wavelengths in the visible range and also needs to be further analyzed.

Several important next steps from this work are the optimization of the set-up, improvement of the acquisition time and application to image actual biological tissues. Regarding the hardware implementation, an epi-illumination scheme seems to be the next natural step to consider, but other tomographic approaches based on acquiring signals at several locations around the imaging sample may also be studied. On the other hand, optimization of the hardware can also lead to a higher SNR of the collected signals and hence to a lower scanning time. The acquisition time can also be optimized by using transducers arrays, which enable real-time optoacoustic imaging for immersion transducers.^{24,25} Arrays of air-coupled transducers have been developed for non-destructive testing applications^{26,27} and their performance in optoacoustic imaging needs to be analyzed. Finally, although the phantom results anticipate the feasibility to image blood vessels, the applicability for imaging actual tissues needs to be studied. For this, selection of the proper wavelength(s) to guarantee a good trade-off between SNR and imaging depth is an important issue to consider. Also, by imaging at more than one wavelength, it may be possible to determine the blood oxygen saturation. This is important in many clinical applications²⁸ and the non-contact nature of the suggested approach may facilitate the clinical translation of the optoacoustic technology.

In conclusion, optoacoustic imaging with air-coupled transducers in tissue-mimicking phantoms was demonstrated herein. It is anticipated that new optoacoustic systems can be designed with this detection technology, and the important advantages derived from the non-contact nature of this approach are expected to expand the applications of the optoacoustic technology in biological research and clinical practice.

ACKNOWLEDGMENTS

G.A.P. acknowledges the support from the Technical University of Munich University Foundation Fellowship. F.M.E. acknowledges the support from CICYT DPI2013- 46915-C2-1-R Grant. D.R. acknowledges the support from the European Union under Grant Agreement No. ERC-2010-StG-260991.

REFERENCES

- [1] Weissleder, R. and Pittet, M. J., "Imaging in the era of molecular oncology," *Nature* **452**(7187), 580–589 (2008).
- [2] Hansen, P. C. and O’Leary, D. P., "The use of the l-curve in the regularization of discrete ill-posed problems," *SIAM Journal on Scientific Computing* **14**(6), 1487–1503 (1993).
- [3] Gibson, A., Hebden, J., and Arridge, S. R., "Recent advances in diffuse optical imaging," *Physics in medicine and biology* **50**(4), R1 (2005).
- [4] Ntziachristos, V., "Fluorescence molecular imaging," *Annu. Rev. Biomed. Eng.* **8**, 1–33 (2006).
- [5] Ntziachristos, V., "Going deeper than microscopy: the optical imaging frontier in biology," *Nature methods* **7**(8), 603–614 (2010).
- [6] Wang, L. V. and Hu, S., "Photoacoustic tomography: in vivo imaging from organelles to organs," *Science* **335**(6075), 1458–1462 (2012).

- [7] Deán-Ben, X. L. and Razansky, D., “Adding fifth dimension to optoacoustic imaging: volumetric time-resolved spectrally enriched tomography,” *Light: Science & Applications* **3**(1), e137 (2014).
- [8] Jathoul, A. P., Laufer, J., Ogunlade, O., Treeby, B., Cox, B., Zhang, E., Johnson, P., Pizzey, A. R., Philip, B., Marafioti, T., et al., “Deep in vivo photoacoustic imaging of mammalian tissues using a tyrosinase-based genetic reporter,” *Nature Photonics* (2015).
- [9] Xia, J. and Wang, L. V., “Small-animal whole-body photoacoustic tomography: a review,” *Biomedical Engineering, IEEE Transactions on* **61**(5), 1380–1389 (2014).
- [10] Deán-Ben, X. L., Ford, S. J., and Razansky, D., “High-frame rate four dimensional optoacoustic tomography enables visualization of cardiovascular dynamics and mouse heart perfusion,” *Scientific reports* **5** (2015).
- [11] Ermolayev, V., Dean-Ben, X. L., Mandal, S., Ntziachristos, V., and Razansky, D., “Simultaneous visualization of tumour oxygenation, neovascularization and contrast agent perfusion by real-time three-dimensional optoacoustic tomography,” *European radiology* , 1–9 (2015).
- [12] Omar, M., Schwarz, M., Soliman, D., Symvoulidis, P., and Ntziachristos, V., “Pushing the optical imaging limits of cancer with multi-frequency-band raster-scan optoacoustic mesoscopy (rsom),” *Neoplasia* **17**(2), 208–214 (2015).
- [13] Deán-Ben, X. L., Fehm, T. F., Gostic, M., and Razansky, D., “Volumetric hand-held optoacoustic angiography as a tool for real-time screening of dense breast,” *Journal of biophotonics* (2015).
- [14] Pang, G. A., Bay, E., Deán-Ben, X. L., and Razansky, D., “Three-dimensional optoacoustic monitoring of lesion formation in real time during radiofrequency catheter ablation,” *Journal of cardiovascular electrophysiology* **26**(3), 339–345 (2015).
- [15] Fehm, T. F., Deán-Ben, X. L., Schaur, P., Sroka, R., and Razansky, D., “Volumetric optoacoustic imaging feedback during endovenous laser therapy—an ex vivo investigation,” *Journal of biophotonics* (2015).
- [16] Singh, M. K. A., Steenbergen, W., and Manohar, S., “Handheld probe-based dual mode ultrasound/photoacoustics for biomedical imaging,” in [*Frontiers in Biophotonics for Translational Medicine*], 209–247, Springer (2016).
- [17] Hochreiner, A., Bauer-Marschallinger, J., Burgholzer, P., Jakoby, B., and Berer, T., “Non-contact photoacoustic imaging using a fiber based interferometer with optical amplification,” *Biomedical optics express* **4**(11), 2322–2331 (2013).
- [18] Khachatryan, E., Maswadi, S., Tsyboulski, D., Barnes, E., Oraevsky, A., Nash, K., and Glickman, R., “Optoacoustic microscopy using laser beam deflection technique,” in [*SPIE BiOS*], 89432T–89432T, International Society for Optics and Photonics (2014).
- [19] Gan, T.-H., Hutchins, D., Billson, D. R., Schindel, D. W., et al., “High-resolution, air-coupled ultrasonic imaging of thin materials,” *Ultrasonics, Ferroelectrics, and Frequency Control, IEEE Transactions on* **50**(11), 1516–1524 (2003).
- [20] Manzanares, A. O. and de Espinosa, F. M., “Air-coupled mumps capacitive micromachined ultrasonic transducers with resonant cavities,” *Ultrasonics* **52**(4), 482–489 (2012).
- [21] Espinosa, D., Montero, F., Gómez, T., Albareda, A., Pérez, R., and Casals, J., “High sensitive piezoelectric transducers for nde air borne applications,” in [*Ultrasonics Symposium, 2000 IEEE*], **2**, 1073–1076, IEEE (2000).
- [22] Kolkman, R. G., Blomme, E., Cool, T., Bilcke, M., van Leeuwen, T. G., Steenbergen, W., Grimbergen, K. A., and den Heeten, G. J., “Feasibility of noncontact piezoelectric detection of photoacoustic signals in tissue-mimicking phantoms,” *Journal of biomedical optics* **15**(5), 055011–055011 (2010).
- [23] Deán-Ben, X. L., Pang, G. A., de Espinosa, F. M., and Razansky, D., “Non-contact optoacoustic imaging with focused air-coupled transducers,” *Applied Physics Letters* **107**(5), 051105 (2015).
- [24] Buehler, A., Deán-Ben, X., Claussen, J., Ntziachristos, V., and Razansky, D., “Three-dimensional optoacoustic tomography at video rate,” *Optics express* **20**(20), 22712–22719 (2012).
- [25] Fehm, T. F., Deán-Ben, X. L., and Razansky, D., “Four dimensional hybrid ultrasound and optoacoustic imaging via passive element optical excitation in a hand-held probe,” *Applied Physics Letters* **105**(17), 173505 (2014).
- [26] Akhnaik, M., Martinez, O., Ullate, L., and de Espinosa, F. M., “64 elements two-dimensional piezoelectric array for 3d imaging,” *Ultrasonics* **40**(1), 139–143 (2002).

- [27] Garcia-Hernandez, M., Chavez, J., Yañez, Y., Kichou, H., Prego-Borges, J., Salazar, J., Turo, A., Espinosa, D., and Montero, F., “Ultrasonic lamb wave nde system using an air coupled concave array transducer,” in [*Ultrasonics Symposium, 2004 IEEE*], **2**, 1282–1285, IEEE (2004).
- [28] Deán-Ben, X. L. and Razansky, D., “Functional optoacoustic human angiography with handheld video rate three dimensional scanner,” *Photoacoustics* **1**(3), 68–73 (2013).