Invited Paper

Wavefront shaping based on three-dimensional optoacoustic feedback

X Luís Deán-Ben, Héctor Estrada, Ali Ozbek and Daniel Razansky *

Institute for Biological and Medical Imaging, Technical University of Munich and Helmholtz Center Munich, Ingolstädter Landstraße 1, 85764 Neuherberg, Germany.

ABSTRACT

Wavefront shaping techniques have recently evolved as a promising tool to control the light distribution in optically-scattering media. These techniques are based on spatially-modulating the phase of an incident light beam to create positive interference (focusing) at specific locations in the speckle pattern of the scattered wavefield. The optimum phase distribution (mask) of the spatial light modulator that allows focusing at the target location(s) is determined iteratively by monitoring the light intensity at such target. In this regard, optoacoustic (photoacoustic) imaging may provide the convenient advantage of simultaneous feedback information on light distribution in an entire region of interest. Herein, we showcase that volumetric optoacoustic images can effectively be used as a feedback mechanism in an iterative optimization algorithm allowing controlling the light distribution after propagation through a scattering sample. Experiments performed with absorbing microparticles distributed in a three-dimensional region showcase the feasibility of enhancing the light intensity at specific points. The advantages provided by optoacoustic imaging in terms of spatial and temporal resolution anticipate new capabilities of wavefront shaping techniques in biomedical optics.

Keywords: Wavefront shaping, Light scattering, Light focusing, Three-dimensional optoacoustic imaging.

1. INTRODUCTION

Focusing and imaging with light is often hampered by scattering in nanoscale refractive-index inhomogeneities in many materials.[1] Of particular importance are biological tissues, where optical techniques arguably represent the most powerful imaging tool,[2] but strong scattering impedes focusing with standard optical elements beyond a few hundred microns.[3]

The feasibility of focusing light through strongly scattering media has been demonstrated by means of wavefront shaping techniques,[4] where the phase of the incident wavefront is spatially modulated to create positive interference at a location in the speckle pattern of the scattered wavefield. Exploiting this effect for imaging implies on the one hand focusing light within (instead of through) a scattering sample and on the other hand measuring a certain optical response at the focus from external locations. As light is scattered on its way to the outside of the object, a relatively poor resolution can be achieved from optical readings,[3] which further reduces the focusing capability due to the large number of optical modes (speckles) per unit volume.[5] A solution to increase the imaging resolution consists in ultrasonically tagging a light source at a given location and holographically recording the phase of the originated wavefront outside the object. This allows, by phase conjugation, to focus a light beam at the ultrasonically-encoded position.[6–8]

The advantages derived from the combination of optical contrast and ultrasound resolution are also behind the success of optoacoustics (photoacoustics) as a biomedical imaging tool.[9–11] In this case, a short-pulsed laser is generally used to excite ultrasound responses within a sample by means of local photoabsorption and non-radiative relaxation. The feasibility of using optoacoustic responses as a feedback mechanism for iteratively optimizing the brightness at a given location (focusing) has been showcased.[12, 13] Also, by measuring the complex linear relations between input and output optical modes, the optoacoustic transmission matrix approach allows more flexibility to control the wavefield shape in one and two dimensions.[14, 15] Wavefront shaping based

*E-mail: dr@tum.de

Novel Biophotonics Techniques and Applications III, edited by Arjen Amelink, I. Alex Vitkin,
Proc. of SPIE-OSA Biomedical Optics, SPIE Vol. 9540, 95400K
CCC code: 1605-7422/15/$18 · doi: 10.1117/12.2183967

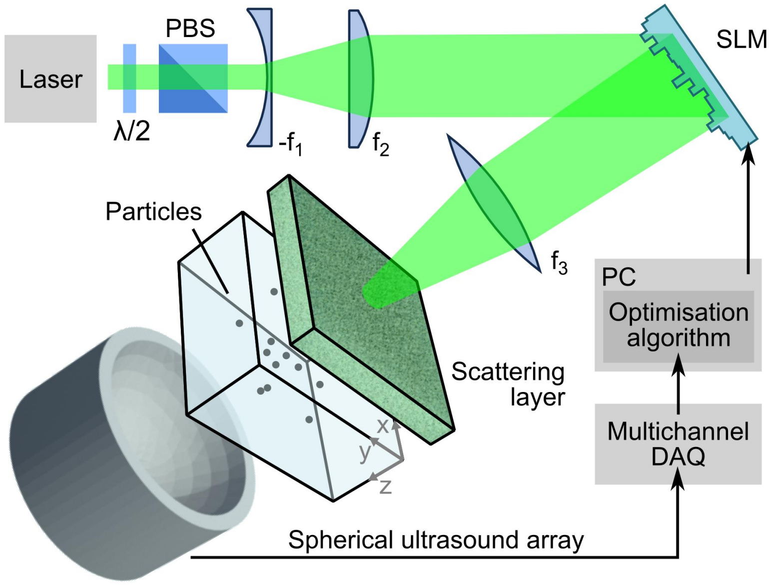

Figure 1. Lay-out of the volumetric optoacoustic wavefront shaping set-up.

on optoacoustic feedback comes with important advantages derived from the fact that there is no need of placing a detector behind the sample. Furthermore, optoacoustic tomographic imaging is unique among optical imaging techniques in the sense that a three-dimensional region can be simultaneously excited. Indeed, recent developments in optoacoustic hardware and parallel reconstruction implementations enable now to acquire and process three-dimensional optoacoustic data at a frame rate determined by the pulse repetition frequency of the laser.[16–18] In this way, wavefront shaping based on three-dimensional optoacoustic feedback (volumetric optoacoustic wavefront shaping) has been recently suggested.[19] Herein we describe the performance of volumetric wavefront shaping for focusing light through scattering objects. Based on the presented results, the potential feasibility to focus light inside biological tissues is discussed.

2. VOLUMETRIC OPTOACOUSTIC WAVEFRONT SHAPING SET-UP

The lay-out of the experimental system described in Ref. 19 is depicted in Fig. 1. Basically, a frequency-doubled Q-switched Nd:YAG laser (Lab-190-30, Spectra-Physics) was used as light excitation source. The laser generates short pulses ($\approx$ 6ns duration) at a wavelength of 532nm and a pulse repetition frequency of 15Hz. The output beam was horizontally polarized by means of a half-wave plate and a polarizing beam splitter and further collimated with a telescopic beam expander. The energy per pulse was set to approximately 4mJ. The collimated beam was reflected in a spatial light modulator (SLM, PLUTO-BB II, Holoeye Photonics AG) and subsequently focused in a light diffuser (Thorlabs DG10-120). The speckle width w of the scattered beam is determined by the width of the illuminated area at the diffuser D as[20]

$$w = \lambda \frac{z}{D}, \tag{1}$$

being λ the laser wavelength and z the distance from the diffuser. The intensity enhancement η that can be achieved by shaping the incident wavefront is given by[5]

$$\eta = \frac{N_{SLM}}{2N_{\mathrm{modes}}}, \tag{2}$$

where N_{SLM} is the number of controlled degrees of freedom (pixels in the SLM) and N_{modes} is the number of optical modes contained within the volume that can be resolved in the wavefront shaping optimization procedure. In our case, the feedback mechanism for the optimization was provided with a three-dimensional optoacoustic

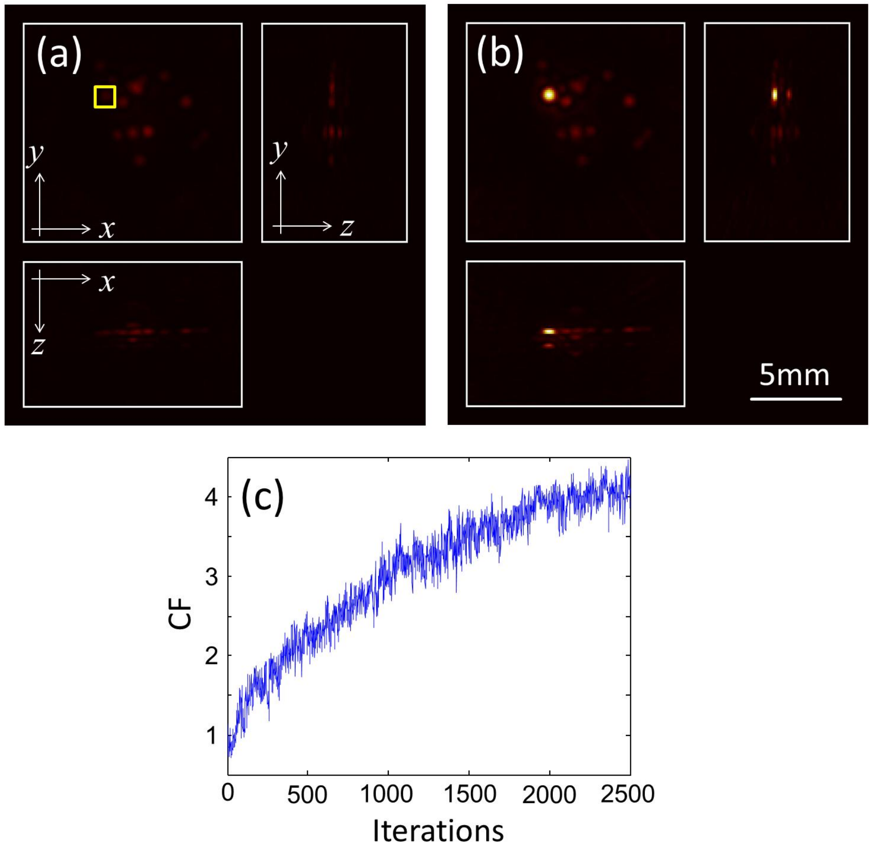

Figure 2. Light focusing at a volume of interest (yellow square) containing a 100μm microsphere. (a) Maximum intensity projections of the three-dimensional optoacoustic image rendered by taking a uniform mask in the SLM (initial iteration). (b) Maximum intensity projections of the three-dimensional optoacoustic image for the optimum mask of the SLM. (c) Cost function as a function of the number of iterations in the genetic algorithm.

imaging system consisting of a 90° spherical array of 256 piezoelectric elements described in detail in.[21] Each element has a central frequency of 4 MHz and -6dB bandwidth of 100%, thus providing nearly isotropic optoacoustic resolution of approximately 200μm.[21] A graphics processing unit (GPU) implementation of back-projection reconstruction allows reconstructing the optical absorption distribution in a volume of approximately 1cm^3 at a faster speed than the time lapse between two laser pulses.[22] Then, the three-dimensional optoacoustic images were used to provide feedback for optimizing the wavefront shape.

An agar phantom containing sparsely distributed absorbing microspheres (Cospheric BKPMS 90-106) with an approximate diameter of 100μm was used to test the performance of the suggested volumetric optoacoustic wavefront shaping approach. The spheres were positioned at a distance of around 60mm from the diffuser, corresponding to a speckle width of approximately 27μm. In order to focus light at a given sphere, we consider as cost function CF the maximum of the optoacoustic image $OA(\mathbf{x})$ in a volume of interest (VOI) around the sphere, i.e.,

$$CF = \max_{\mathrm{VOI}} \{OA(\mathbf{x})\} . \quad (3)$$

The value of the cost function CF was then iteratively maximized by means of a genetic algorithm as described in Ref. 23. The SLM pixels were grouped to form a matrix array of 20x20 elements and the acquired optoacoustic signals were averaged 5 times to minimize the influence of the per-pulse energy oscillations.

3. RESULTS

The maximum intensity projections (MIP) of the initial three-dimensional optoacoustic image obtained with a constant phase value in the SLM pixels is displayed in Fig. 2a, showing the volumetric distribution of spheres. The VOI for which the cost function is defined is marked in this figure (yellow square). The equivalent image obtained with a mask in the SLM corresponding to the maximum of the cost function is showcased in Fig. 2b. It is shown that light intensity is maximized for the microsphere enclosed in the selected VOI. The value of the cost function as a function of the number of iterations in the genetic algorithm is displayed in Fig. 2c. Considering elongated speckles of 27μm width, approximiately 14 speckle grains (optical modes) are enclosed in a microsphere, which corresponds to a theoretical enhancement of approximately 14. Speckle decorrelation during the experiment, noise and imperfections of the SLM can however influence the maximum achievable enhancement.[14]

4. DISCUSSION AND CONCLUSIONS

The results showcased indicate the feasibility of controlling a scattered wavefield with optoacoustic resolution in a volumetric (three-dimensional) region. The proof-of-principle experiments performed are still however far from being applicable for imaging within scattering tissues. Indeed, many issues have to be considered for reaching this ultimate goal, particularly for biological tissues *in vivo*. For example, the speckle grain size inside a scattering object is expected to progressively decay to a value in the order of $\lambda/2$. This inevitably substantially increases the number of optical modes in the volume that can be optoacoustically resolved, even if high frequency transducers are used. The number of degrees of freedom in the spatial light modulator must then be accordingly increased for signal enhancement. On the other hand, a potential solution to reduce the number of optical modes can be to include absorbers with small dimensions in the region where light needs to be focused.[24] The coherence of the laser beam also conditions the depth within the scattering sample for which the interference can be produced, which is the basic mechanism for focusing light with this approach.

In vivo imaging is further challenged by motion and consequent speckle decorrelation during the optimization procedure. Fast optimization in the millisecond range is thereby required for successful wavefront shaping. This appears unachievable with the current configuration where the pulse repetition rate of the laser and the refresh rate of the SLM are in the order of tens of Hz. However, the three-dimensional feedback mechanism introduced in this work represents a convenient framework for fast wavefront shaping if the appropriate hardware is developed.

In summary, we expect that volumetric optoacoustic wavefront shaping can help paving the way to the successful application of wavefront shaping techniques to focus light within scattering objects and potentially lead to the development of new imaging approaches for samples of technological and biological relevance.

ACKNOWLEDGMENTS

The research leading to these results partially received funding from the European Research Council under grant agreement ERC-2010-StG-260991.

REFERENCES

[1] Mosk, A. P., Lagendijk, A., Lerosey, G., and Fink, M., "Controlling waves in space and time for imaging and focusing in complex media," *Nature photonics* **6**(5), 283–292 (2012).

[2] Weissleder, R. and Pittet, M. J., "Imaging in the era of molecular oncology," *Nature* **452**(7187), 580–589 (2008).

[3] Ntziachristos, V., "Going deeper than microscopy: the optical imaging frontier in biology," *Nature methods* **7**(8), 603–614 (2010).

[4] Vellekoop, I. M. and Mosk, A. P., "Focusing coherent light through opaque strongly scattering media," *Optics letters* **32**(16), 2309–2311 (2007).

[5] Popoff, S. M., Lerosey, G., Fink, M., Boccara, A. C., and Gigan, S., "Controlling light through optical disordered media: transmission matrix approach," *New Journal of Physics* **13**(12), 123021 (2011).

[6] Xu, X., Liu, H., and Wang, L. V., "Time-reversed ultrasonically encoded optical focusing into scattering media," *Nature photonics* **5**(3), 154–157 (2011).

[7] Si, K., Fiolka, R., and Cui, M., "Fluorescence imaging beyond the ballistic regime by ultrasound-pulse-guided digital phase conjugation," *Nature photonics* **6**(10), 657–661 (2012).

[8] Judkewitz, B., Wang, Y. M., Horstmeyer, R., Mathy, A., and Yang, C., "Speckle-scale focusing in the diffusive regime with time reversal of variance-encoded light (trove)," *Nature photonics* **7**(4), 300–305 (2013).

[9] Jathoul, A. P., Laufer, J., Ogunlade, O., Treeby, B., Cox, B., Zhang, E., Johnson, P., Pizzey, A. R., Philip, B., Marafioti, T., Lythgoe, M. F., Pedley, B., Pule, M. A., and Beard, P., "Deep in vivo photoacoustic imaging of mammalian tissues using a tyrosinase-based genetic reporter," *Nature Photonics* (2015).

[10] Gottschalk, S., Fehm, T. F., Deán-Ben, X. L., and Razansky, D., "Noninvasive real-time visualization of multiple cerebral hemodynamic parameters in whole mouse brains using five-dimensional optoacoustic tomography," *Journal of Cerebral Blood Flow & Metabolism* **35**(4), 531–535 (2015).

[11] Yao, J., Wang, L., Yang, J. M., Maslov, K. I., Wong, T., Li, L., Huang, C. H., Zou, J., and Wang, L. V., "High-speed label-free functional photoacoustic microscopy of mouse brain in action," *Nature methods* **12**(5), 407–410 (2015).

[12] Kong, F., Silverman, R. H., Liu, L., Chitnis, P. V., Lee, K. K., and Chen, Y. C., "Photoacoustic-guided convergence of light through optically diffusive media," *Optics letters* **36**(11), 2053–2055 (2011).

[13] Caravaca-Aguirre, A. M., Conkey, D. B., Dove, J. D., Ju, H., Murray, T. W., and Piestun, R., "High contrast three-dimensional photoacoustic imaging through scattering media by localized optical fluence enhancement," *Optics express* **21**(22), 26671–26676 (2013).

[14] Chaigne, T., Katz, O., Boccara, A. C., Fink, M., Bossy, E., and Gigan, S., "Controlling light in scattering media non-invasively using the photoacoustic transmission matrix," *Nature Photonics* **8**(1), 58–64 (2014).

[15] Chaigne, T., Gateau, J., Katz, O., Bossy, E., and Gigan, S., "Light focusing and two-dimensional imaging through scattering media using the photoacoustic transmission matrix with an ultrasound array," *Optics letters* **39**(9), 2664–2667 (2014).

[16] 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).

[17] Deán-Ben, X. L., Bay, E., and Razansky, D., "Functional optoacoustic imaging of moving objects using microsecond-delay acquisition of multispectral three-dimensional tomographic data," *Scientific reports* **4** (2014).

[18] 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* (2015). DOI:10.1038/srep10133.

[19] Deán-Ben, X. L., Estrada, H., and Razansky, D., "Shaping volumetric light distribution through turbid media using real-time three-dimensional opto-acoustic feedback," *Optics letters* **40**(4), 443–446 (2015).

[20] Goodman, J. W., [*Speckle phenomena in optics: theory and applications*], vol. 1 (2007).

[21] Deán-Ben, X. L. and Razansky, D., "Portable spherical array probe for volumetric real-time optoacoustic imaging at centimeter-scale depths," *Optics Express* **21**(23), 28062–28071 (2013).

[22] Dean-Ben, X. L., Ozbek, A., and Razansky, D., "Volumetric real-time tracking of peripheral human vasculature with gpu-accelerated three-dimensional optoacoustic tomography," *Medical Imaging, IEEE Transactions on* **32**(11), 2050–2055 (2013).

[23] Conkey, D. B., Brown, A. N., Caravaca-Aguirre, A. M., and Piestun, R., "Genetic algorithm optimization for focusing through turbid media in noisy environments," *Optics express* **20**(5), 4840–4849 (2012).

[24] X L Dean-Ben, H Estrada, A. O. and Razansky, D., "Influence of the absorber dimensions on wavefront shaping based on volumetric optoacoustic feedback," arXiv:1506.03617.