NOVA I4H – Thesis Proposal

Title:
Optical instrumentation towards the concentration of light in turbid media for phototherapy application.

Objectives:
The propagation of light in turbid media is limited by absorption and scattering phenomena. This has particularly constrained the application of laser radiation in biological tissues since attenuation paths are limited and the capability of focusing inside these media is highly limited beyond its surface.
In the last few years, different approaches are being researched among a few research teams in the world [1-3]. Basically, two optical-based approaches emerged: using photon-activated substances as a "guide" to wavefront correction and the use of Fourier Holography. However, and although the proof of concepts has been done, no application was developed in the promising field of cancer therapy.
In the first mentioned case, the idea is to use a fluorescence substance injected in the zone where the light is to be concentrated and use the emerging scattered signal to inverse the wavefront and thus allow reducing the influence of scattering. An alternative is to use quantum dots instead of fluorescent markers, which may allow working with just one wavelength.
A different approach is to use the concepts of Fourier-domain holography, in which the image obtained on a sensor records the fringes formed by the interference between the scattered light from the point being imaged and a reference light beam. Through numerical reconstruction it might be possible to shape the wavefront so emitted light is unaffected (or less affected) by scattering. Since 2010, a FCUL team is working in phase shaping by developing their own algorithms to simulate phase-shaping and apply them to biological turbid media [4]. Meanwhile, FCT approved funding for a two years R&D project that ended in October 2015 with participation of FCUL, FCT/UNL, Lusófona, INL and FFUC. As result of this research a patent (nº 108994) was already filled and is under evaluation process.
In this context, and following the promising results obtained [5], the main objectives are:
1. Review the possible optical techniques to concentrate light in turbid media, defining pros and cons and their maturity and potential.
2. Identify, implement and test optical instrumentation to wavefront shaping in in vitro and in vivo conditions either to destroy tumors by hyperthermia or drug delivery.
3. Study, implement and apply metrology methods in order to validate the chosen method.
4. Define a road map for in-depth therapeutic destruction of tumors by concentrating light through wavefront shaping methodology or methodologies.

References

[1] I. Vellekoop, et al., Digital optical phase conjugation of fluorescence in turbid tissue, Appl. Phys. Lett. 101, 081108, 2012; doi:10.1063/1.4745775.
[2] C.-L. Hsieh, et al., Digital phase conjugation of second harmonic radiation emitted by nanoparticles in turbid media, Opt. Exp. 18(12) 12283-12290, 2010; doi:10.1364/OE.18.012283.
[3] Y. Pu, D. Psaltis, Seeing through turbidity with harmonic holography, App. Opt. 52(4) 567-578, 2013; doi: 10.1364/AO.52.000567.
[4] R. Gomes, et al., Optical simulation of laser beam phase-shaping focusing optimization in biological tissues, Proc. of SPIE 8785 8785DE-1, 2013; doi: 10.1117/12.2026238.
[5] C. Silva, et al., Bioproduction of gold nanoparticles for photothermal therapy, Therapeutic Delivery, 7(5), pp. 287-304, 2016; doi:10.4155/tde-2015-0011.

Framework:

Research in the field of light propagation in turbulent and turbid media has been developed at the Laboratory of Optics, Lasers and System for several years. This, in conjunction of long experience in light manipulation by optical means has converged with the interest of the Institute of Biophysics and Biomedical Engineering in cancer fight and lead to the creation of a cooperation in the field between these two groups of FCUL. The importance of this theme was recognized by the FCT which funded a project that involved several expertizes and institutions. So, this thesis proposal will complement and evolve the mentioned project and benefit from all the equipment, experience and contacts gathered by it.

Support in other fields of knowledge than the ones of this thesis, if needed to complement the research, will be found in the ongoing funded project.

Tasks:

1. Study the state of the art on the requirements for laser phototherapy and wavefront shaping methods. It should define a relevant scenario, including type of target (e.g. breast cancer), drug delivery systems (e.g. nanocapsules) and required photoactivation energy;
2. Definition of the experimental approach that will be followed in the project. Based on the previous analysis (task 1), it will be defined the method that will be explored taking in account: it's potential in performing as required; it's capability to be implemented and allow the development of an operational device; its novelty;
3. Definition and implementation of the optical instrumentation necessary attain the required light concentration. In this task, it will be projected, implemented and tested the experimental and monitoring setups, as well as and methodologies necessary for the experimental development. This includes the optical apparatus and the command and control of the phase-shaping devices, but also the development of the algorithms to create the wavefronts and the metrology to assess on the performance of the system;
4. Test the method in vitro, in real photoactivation conditions;

5. Disseminate the results (on conferences and publishing papers) besides writing of the thesis.

Venue:
Polo do Lumiar, Estrada do Passo do Lumiar, 22, Edifício D, 1º Andar, 1648-033 Lisboa, Portugal.

This project will take place in Compta-SA, Miraflores, as well as in the Physics Department of FCT-UNL and Laboratory of Optics Laser and Systems of FCUL.

Candidate profile:

The candidate should master optics, biomedical and physical engineering with interest in optical instrumentation and biomedical application. It should capable of manage theoretical formulations, but also be capable of plan, implement and interpret experimental work.

In addition, since this collaboration is between universities and an enterprise, the candidate must be prepared to develop his/her activity in an enterprise environment.

Supervisor

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