PhD THESIS DEFENSE: Preclinical and clinical studies in oncology and endocrinology with diffuse light.

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11:00

ICFO Elements Room and online (Teams)

Near-infrared diffuse optical spectroscopy (DOS) techniques are capable of non-invasive measurement of microvascular hemodynamic parameters of deep tissues (>1 cm penetration). One important focus of the field has been applications in oncology, where the characterization of the tumor vasculature could play both a diagnostic and therapeutic role. This is mainly because malignant tissue growth requires the co-option and generation of blood vessels to be supported. Microvessel density, microvascular blood flow and hypoxia have been linked to the progression of the disease, the likelihood of metastasis and patient survival, and can thus guide diagnosis, treatment plans and prognosis.
In this thesis, I have applied DOS methodologies in two projects exploiting hemodynamic information for cancer management. The first one consists in the demonstration of a toolbox

for the optimization of plasmonic photothermal therapy (PPTT) in mice, while the second focuses on the contribution to the clinical diagnosis of thyroid cancer in nodule patients. PPTT uses plasmonic nanoparticles (NPs) that are injected into the body and act as localized sources of heat upon external illumination to induce tumor cell death. Various aspects of the therapy are modulated by the optical and hemodynamic parameters of tumor tissue and can thus be studied with DOS monitoring. Moreover, it enables simultaneous quantification of NP concentration. Such information can improve the understanding and the outcome of the treatment and accelerate its slow progress to the clinics.

To prove this, we conducted experiments using DOS monitoring along PPTT to model the therapy steps and explain the variability among individuals. This was done on patient-derived orthotopic renal cell carcinoma models, injected with gold nanorods and treated with fixed conditions. The hybrid device combined continuous-wave broadband diffuse reflectance (DRS) and diffuse correlation (DCS) spectroscopies. The data was related to the NP accumulation, the temperatures reached during treatment, tumor growth and animal survival. Moreover, we analyzed the underlying mechanisms with simulations and demonstrated the extrapolation of therapy conditions for individual mice. With this, we managed to determine the relevant interactions and prognostic factors to guide the personalization of the therapy in a way that could be readily applied to other PPTT protocols.

The second study was part of the LUCA project, which aimed at implementing an ultrasound-guided hybrid DOS device that could be integrated into the clinical workflow of thyroid cancer screening and provide relevant hemodynamic information to improve diagnostic capabilities. The incidence of thyroid cancer has been on the rise for decades and the low specificity of standard screening methods implies tens of thousands of unnecessary thyroid extraction surgeries are carried out each year just in Europe. Therefore, any improvement in the discrimination between benign and malignant nodules can have a relevant impact on the large scale.

A clinical campaign was carried out with the LUCA device, a state-of-the-art device combining time-resolved spectroscopy (TRS) and DCS around a regular ultrasound transducer. The properties of thyroid, nodules and neck muscles were measured in nodule patients and healthy volunteers. Data from sixty-six subjects allowed to characterize these tissues, study the effect of demographic and anatomical variables and assess their diagnostic capabilities. In this way, we gathered a large reference data set relevant to various medical applications beyond oncology and identified the most promising indicators of malignancy.

With these studies I have shown how the information obtained with DOS has important roles in these particular applications and what are some of the mechanisms behind them. These results can guide the future steps of research endeavors and have implications for the advancement of solutions to these clinical problems.

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