PhD subject / sujet de thèse (2024)

Title: Combined Raman spectroscopy and full-field optical coherence tomography applied in oncology

Titre : Combinaison de la spectroscopie Raman et de la OCT en plein champ appliquée en oncologie

PhD supervisor(s)/ directeur de thèse :

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Attachment to a program (if applicable):

Summary:

A number of non-invasive optical diagnostic techniques have been used for cancer detection, such as fluorescence microscopy, Raman spectroscopy (1-6), conventional optical coherence tomography (OCT) and reflectance spectrometry. None of these techniques excels at both diagnosis and margin assessment.

Of all the non-invasive optical techniques, FFOCT is one of the most promising for margin detection and also provides morphological information (7-10), while Raman spectroscopy is the most promising technique not only for distinguishing cancerous from benign tumors, but also for identifying cancer types. Co-localized measurements with a combination of OCT and Raman will increase sensitivity and selectivity compared with these two techniques used separately.

The aim of the project is to produce label-free images for optimal resection of tumor tissue during surgery. Simultaneously, Raman analyzes the area scanned by FFOCT to correlate biochemical changes in the tissue due to the tumor's specific molecular fingerprint.

Raman spectroscopy, as a non-destructive, label-free optical instrument based on vibrational spectroscopy, is effective for identifying endogenous intracellular biomolecules and detecting structural and compositional changes in cellular or tissue components.

The combination of confocal Raman microscopy and FFOCT facilitates the study of biomolecular processes at the single-cell level. FFOCT images, although of high resolution, are sometimes complex to interpret in the case of pathologies with ambiguous morphological features, or early-stage pathologies showing only a few structural changes. Confocal Raman microscopy could provide additional information on the biochemical composition of samples, enabling them to be classified. The correlation of morphological and biochemical results would enable better characterization of the tissue and its pathologies.

The aim of this thesis is to combine two imaging techniques, Raman spectroscopy and full-field OCT (FFOCT), to provide surgeons with a new tool for rapid, quantitative evaluation of tumor margins during surgery. Correct assessment of tumor margins during surgery is an essential prognostic factor in avoiding re-operation and the development of metastases.

Initially using a commercial high-resolution confocal Raman microscope, a database of different cancer tissues will be provided, but for a more tailored clinical application and coupled to FFOCT, specific Raman

peaks (as photonic biomarkers) will be applied. The correlation of morphological and biochemical results will enable better characterization of the tissue and its pathologies.

Workplan

The thesis is divided into five steps

1- Establish a technical feasibility of this morpho/chemical imaging technique to characterize the chemical structure and morphological property of cancer tissue as well as healthy margins as control.

2- Compare the obtained results of combined methods of caner tissue (verified by gold standard method) versus healthy tissue and identify any differences that could be applied on the diagnosis in difficult cases.

3- Development of image analysis protocols (chemical and morphological maps from spectra recorded as a function of the position in the microtomic section) and chemometric studies. These protocols will use quantitative image analysis methods using spectral imaging, to do the characterization of samples.

4- Development of statistical tools necessary for the exploitation of these maps within the framework of the study.

5- Evaluation of the potential of hyperspectral Raman imaging coupled FFOCT to clarify the nature of the disease and possibly its pathophysiology and on the other hand for the further development of early diagnostic instruments.

Calendrier	
Creation of bank of Raman data - Identification of vibrational signatures evaluating cancer involvement status of tissue - Using Confocal Raman Laser 532nm microscopy measurements of partner's samples from Strasbourg cancer research teams (glioblastoma, pancreas, breast, upper aero-digestive tract, liver) - Analysis of PCA, LDA, KMCA data and functional characterization of molecules identified as photonic biomarkers for cancer tissues	**1st Year**
Couplage FFOCT- Raman - Installation design, development of recording data and image-data analysis	**2nd Year**
Data analysis - Data analysis and comparison with histological data to validate results	**3rd Year**

References:

1. Salehi, H., Ramoji, A., Mougari, S. et al. Specific intracellular signature of SARS-CoV-2 infection using confocal Raman microscopy. Commun Chem 5, 85, 2022
2. Rauwel. E, Salehi.H et al. Assessing Cobalt Metal Nanoparticles Uptake by Cancer Cells Using Live Raman Spectroscopy. Int J Nanomedicine. 2020 Sep 24;15:7051-7062
3. Gilka.M*, Salehi.H* et al. Simultaneous label-free live imaging of cell nucleus and luminescent nanodiamonds. Sci Rep. 2020, 10, 9791
4. Hamideh Salehi*, Siham Al-Arag*, Elodie Middendorp, Csilla Gergely, Frederic Cuisinier, Valerie Orti Dental Pulp Stem Cells used to deliver the anticancer drug Paclitaxel Stem Cell Research & Therapy 9:103, 2018
5. H. Salehi, L. Derely, A.-G. Vegh, J.-C. Durand, C. Gergely, C. Larroque, M.-A. Fauroux and F. J. G. Cuisinier. Label-free detection of anticancer drug paclitaxel in living cells by Confocal Raman Microscopy. Appl. Phys. Let, 102 , 113701, 2013.
6. H. Salehi , E. Middendorp, C. Gergely, F. J. G. Cuisinier. Confocal Raman data analysis to comparison of apoptotic and non-apoptotic MCF-7 cells caused by anticancer drug paclitaxel. J Biomed Opt.18(5), 056010, 2013.
7. Seromenho, E. M., Marmin, A., Facca, S., Bahlouli, N., Perrin, S., & Nahas, A. (2022). Single-shot off-axis full-field optical coherence tomography. Applied Physics Letters, 121(11).
8. Marmin, A., Catheline, S., & Nahas, A. (2020). Full-field passive elastography using digital holography. Optics Letters, 45(11), 2965-2968.
9. Thouvenin, O., Apelian, C., Nahas, A., Fink, M., & Boccara, C. (2017). Full-field optical coherence tomography as a diagnosis tool: recent progress with multimodal imaging. Applied Sciences, 7(3), 236.
10. Nahas, A., Bauer, M., Roux, S., & Boccara, A. C. (2013). 3D static elastography at the micrometer scale using Full Field OCT. Biomedical optics express, 4(10), 2138-2149.