

NIR Raman spectroscopy setup compatible with fluorescence-guided surgery

H. Abbasi ^{*ab}, L.J. Lauwerends ^a, T.C. Bakker Schut ^b, I.P. Santos ^c, P.J. Caspers ^b, J.A.U. Hardillo ^a, S. Koljenović ^d, A.L. Vahrmeijer ^e, R.J. Baatenburg de Jong ^a, S. Keereweer ^a, G.J. Puppels ^{†b}

^a Fluorescence-Guided Surgery Group, Department of Otorhinolaryngology and Head and Neck Surgery, Erasmus MC Cancer Institute, Rotterdam, The Netherlands;

^b Center for Optical Diagnostics and Therapy, Department of Dermatology, Erasmus MC Cancer Institute, Rotterdam, The Netherlands;

^c Molecular Physical-Chemistry R&D Unit, Department of Chemistry, University of Coimbra, Coimbra, Portugal;

^d Department of Pathology, Antwerp University Hospital/ Antwerp University, Antwerp, Belgium;

^e Department of Surgery, Leiden University Medical Center, Leiden, The Netherlands

* h.abbasi@erasmusmc.nl; phone +31 10 704 3117

† g.puppels@erasmusmc.nl; phone +31 10 704 3989

ABSTRACT

Intraoperative near-infrared (NIR) fluorescence imaging using tumor-specific exogenous fluorescent agents provides whole-field images in real-time to assist the surgeon in the complete resection of tumor tissue. Although the method has high sensitivity, the specificity can sometimes be lower than expected. Raman spectroscopy can differentiate between tumor and healthy tissue with high specificity based on their molecular composition. Therefore, a combination of these modalities can be advantageous. A complication that must be addressed is that the NIR spectral region is favored by both techniques for intraoperative tissue analysis. When fluorescence and Raman emissions spectrally overlap, it becomes challenging or impossible to detect the Raman signal. Therefore, these techniques were traditionally considered mutually exclusive for clinical implementation. Here, a Raman spectroscopy setup capable of recording high-quality Raman spectra from tissue containing NIR exogenous fluorescent agents is described. In this setup, an optimal wavelength interval for Raman excitation is identified, which avoids both excitation of fluorescent agent and Raman signal self-absorption by the tissue. This combined novel setup could pave the way for clinical trials benefiting from the complementary value of intraoperative NIR fluorescence imaging and Raman spectroscopy to avoid positive margins in cancer surgery [1,2].

Keywords: Raman scattering, Fluorescence imaging, Image-guided surgery, Multimodal optical diagnostics

REFERENCES

- [1] Lauwerends, L.J., et al., "The complementary value of intraoperative fluorescence imaging and Raman spectroscopy for cancer surgery: combining the incompatibles" *Eur J Nucl Med Mol Imaging* 49, 2364–2376 (2022).
- [2] Abbasi, H., et al., "Development of a near-infrared Raman spectroscopy setup compatible with fluorescence-guided surgery", *Analyst* 148, 2676–2682 (2023).