

HyperProbe consortium: transforming tumour neurosurgery with innovative hyperspectral imaging

Luca Giannoni^a, Anam Toaha^{b,c}, Marta Marradi^{b,c}, Pietro Ricci^{b,c}, Duccio Rossi Degl'Innocenti^d, Ivan Ezhov^e, Charly Caredda^f, Arthur Gautheron^f, Fernand Fort^f, Fabien Schneider^g, Camilla Bonaudo^h, Frédéric Lange^a, Angelos Artemiou^a, Eszter Balázsⁱ, Katharina Krischakⁱ, Peter Gordebekeⁱ, Domenico Alfieri^d, Daniel Rückert^{e,m}, Bruno Montcel^f, Alessandro Della Puppa^h, Thiebaud Picartⁱ, Ilias Tachtsidis^a, and Francesco S. Pavone^{*b,c,n}

^aDepartment of Medical Physics and Biomedical Engineering, University College London, London, UK; ^bDepartment of Physics and Astronomy, University of Florence, Florence, Italy; ^cEuropean Laboratory for Non-Linear Spectroscopy, Sesto Fiorentino, Italy; ^dEmoled S.r.l, Sesto Fiorentino, Italy; ^eKlinikum rechts der Isar, Technischen Universität München, Munich, Germany; ^fUniv Lyon, INSA-Lyon, Université Claude Bernard Lyon 1, UJM-Saint Etienne, CREATIS, Lyon, France; ^gService de Radiologie, Centre Hospitalier Universitaire de Saint Etienne, Université de Lyon, UJM Saint Etienne, Lyon, France; ^hNeurosurgery, Department of Neuroscience, Psychology, Pharmacology and Child Health, University of Florence, Azienda Ospedaliero Universitaria Careggi, Florence, Italy; ⁱService de Neurochirurgie D, Hospices Civils de Lyon, Bron, France; ^lEuropean Institute for Biomedical Imaging Research, Vienna, Austria; ^mImperial College London, London, UK; ⁿNational Institute of Optics, National Research Council, Sesto Fiorentino, Italy.

ABSTRACT

The HyperProbe consortium represents a five-year, multinational initiative funded by the EU, launched in October 2022. Its mission is to pioneer advanced hyperspectral imaging technologies for clinical implementation, with the ultimate goal of significantly improving neuronavigation during glioma surgeries.

Keywords: hyperspectral imaging; neuronavigation; glioma surgery; biomedical optics.

1. INTRODUCTION

Modern imaging technologies, such as MRI, PET, and CT, have revolutionized neurosurgery by enabling surgeons to plan operations and avoid functional brain regions while excising tumors like gliomas. These advances significantly enhance the precision of lesion localization in the central nervous system (CNS) before or during surgery^{1,2}. Additionally, various brain stimulation techniques are utilized intraoperatively depending on the cortical regions involved. Despite these advancements, limitations persist, including varying levels of invasiveness, lack of real-time quantitative data, and reduced specificity and sensitivity. Current imaging methods used in neurosurgery also face challenges. Techniques such as MRI and PET-CT rely on static pre-surgical evaluations, while intraoperative methods like fluorescence imaging often provide low spatial resolution, specificity, and limited information scope³.

To address these limitations, a shift toward a functional-guided neuronavigation approach is necessary. This approach would allow neurosurgeons to make more informed decisions through precise, quantitative, and real-time assessments of intraoperative brain activity. Building on previous research from diverse collaborators, the HyperProbe consortium^{4,5} was established to develop a groundbreaking, contactless, all-optical intraoperative imaging platform based on hyperspectral imaging (HSI)^{6,7,8}. The consortium includes software engineers, physicists, clinicians, and optical and imaging experts.

2. THE HYPERPROBE CONSORTIUM AND ITS OBJECTIVES

Launched on October 1, 2022, the HyperProbe consortium is a five-year initiative funded by the European Innovation Council (EIC) and UK Research and Innovation (UKRI). Key partners include:

1. University of Florence (UNIFI), project coordinator
2. Emoled S.r.l
3. Technical University of Munich (TUM)
4. Université Claude-Bernard Lyon 1 (UCBL)
5. Azienda Ospedaliero-Universitaria Careggi (AOUC)
6. European Institute for Biomedical Imaging Research (EIBIR)
7. Lyon University Hospital (HCL)
8. University College London (UCL)

The project's goals are as follows:

1. Develop the HyperProbe HSI system to map, monitor, and quantify biomarkers for tumor identification and functional brain activity during neurosurgery.
2. Upgrade the HyperProbe system for clinical adaptation and integration into neurosurgical environments.
3. Characterize and validate the HyperProbe system using optically-realistic brain tissue models.
4. Create machine learning (ML) algorithms to process and analyze hyperspectral data.
5. Validate the HyperProbe system in clinical settings by comparing it to existing surgical imaging standards.
6. Conduct feasibility studies to evaluate the HyperProbe's performance during glioma surgeries.

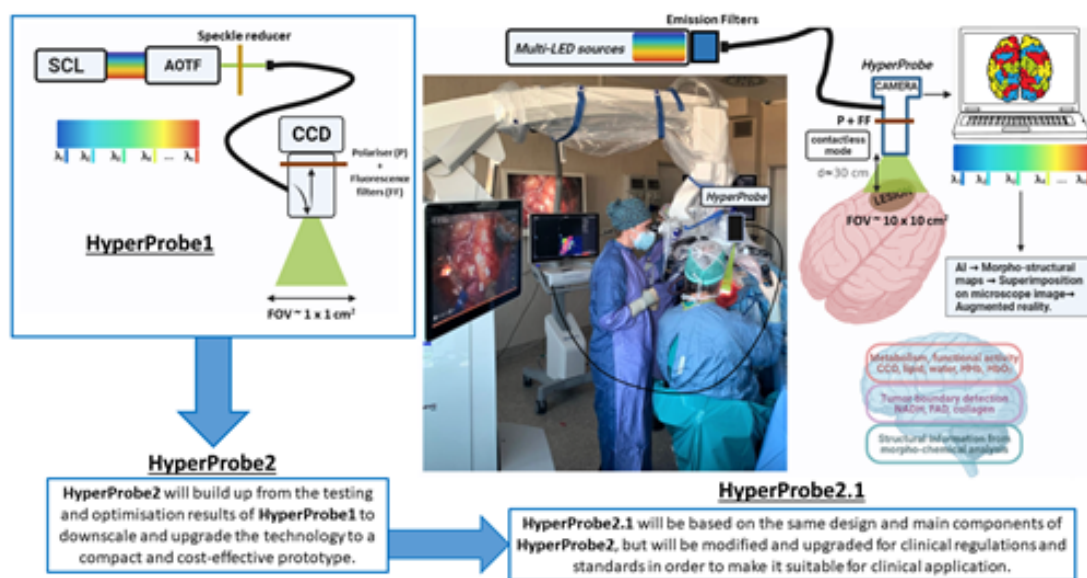


Figure 1. Schematic design of the main HyperProbe devices (HyperProbe 1 and HyperProbe2.1) and the implementation of the final clinical prototype (HyperProbe2.1) in the surgical room.

3. THE HYPERPROBE SOLUTION AND PROGRESS SO FAR

Leveraging the capabilities of HSI, the HyperProbe system can generate two-dimensional images across narrow, contiguous wavelength bands in the electromagnetic spectrum, including near UV-visible (300-700 nm) and near-infrared (700-1100 nm) ranges. By analyzing a tissue's optical signature, it provides detailed quantitative information about its chemical composition and reconstructs 2D optical images of brain tissues. This enables the identification and monitoring of specific biomarkers and offers insights into brain physiology and pathophysiology.

Currently, a high-performance, laboratory-scale HSI instrument, HyperProbe1, was developed and applied for the characterisation of *ex vivo* fresh glioma biopsies⁹, demonstrating its capability to infer biochemical composition of the tumors by using deep learning unmixing algorithm¹⁰ developed within the framework of the consortium. The system allows users to select specific, narrow wavelengths (up to 79) within the visible and near-infrared spectrum between 510 and 900 nm. The system has now been upgraded to the new HyperProbe1.1, which allows to extend the spectral range to 385-1015 nm (123 wavelength bands), as well as to select different bandwidths of the wavelengths from 5 to 15 nm. Equipped with advanced illumination, spectral separation, light detection, and image reconstruction technologies, HyperProbe1.1 delivers high spatial, temporal, and spectral resolution. Current efforts focus on translating its features into a compact, cost-effective clinical prototype for neurosurgery, referred to as HyperProbe2, and a safety-regulated upgrade, HyperProbe2.1.

Parallel development efforts include:

1. Digital simulation of HSI parameters using Monte Carlo models¹¹ to optimize the instrumentation, as well as the development of realistic and dynamic, tissue optical phantoms for metrological characterisation and validation of the HyperProbe devices.
2. ML-based unmixing algorithms to extract in real-time chromophore concentrations from hyperspectral data, and use them as biomarkers for tumour discrimination and classification¹⁰.
3. Tools for hyperspectral image segmentation and co-registration with other neuronavigational techniques, such as MRI and fluorescence intraoperative microscopy during surgeries.

4. CONCLUSIONS

The HyperProbe project's outcomes promise to transform neurosurgical navigation by introducing accurate, real-time, and quantitative optical methods, enhancing surgical efficacy. Additionally, this initiative could pave the way for broader clinical adoption of hyperspectral imaging technologies across various diagnostic and navigational applications.

REFERENCES

- [1] Sanai, N. and Berger, M., "Surgical oncology for gliomas: the state of the art," *Nat. Rev. Clin. Oncol.* 15, 112–125 (2018).
- [2] Weller, M., van den Bent, M., Preusser, M. et al., "EANO guidelines on the diagnosis and treatment of diffuse gliomas of adulthood," *Nat. Rev. Clin. Oncol.* 18, 170–186 (2021).
- [3] Della Puppa, A., Munari, M., Gardiman, M. P. and Volpin, F. "Combined fluorescence using 5-aminolevulinic acid and fluorescein sodium at glioblastoma border: intraoperative findings and histopathologic data about 3 newly diagnosed consecutive cases," *World Neurosurg.* 122, e856-e863 (2019).
- [4] <https://hyperprobe.eu/>
- [5] <https://cordis.europa.eu/project/id/101071040>
- [6] Lu, G. and Fei, B., "Medical hyperspectral imaging: a review," *J. Biomed Opt.* 19(1):10901 (2014).
- [7] Giannoni, L., Lange, F. and Tachtsidis, I., "Hyperspectral imaging solutions for brain tissue metabolic and hemodynamic monitoring: past, current and future developments," *J. Opt.* 20(4):044009 (2018).
- [8] Wu, Y., Xu, Z., Yang, W., Ning, Z. and Dong, H., "Review on the application of hyperspectral imaging technology of the exposed cortex in cerebral surgery," *Front. Bioeng. Biotechnol.* (10):906728 (2022).
- [9] Giannoni L., Marradi M., Scibilia K., Ezhov I., Bonaudo C., Artemiou A., Toaha A., Lange F., Careda C., Montcel B., Della Puppa A., Tachtsidis I., Rückert D., Pavone F.S, "Transportable hyperspectral imaging setup based on fast, high-density spectral scanning for in situ quantitative biochemical mapping of fresh tissue biopsies," *J. Biomed. Opt.* 29(9):093508 (2024).

- [10] Ezhov I., Scibilia K., Luca Giannoni, Kofler F., Iliash I., Hsieh F., Shit S., Caredda C., Lange F., Montcel B., Tachtsidis I., Rueckert D., "Learnable real-time inference of molecular composition from diffuse spectroscopy of brain tissue," J. Biomed. Opt. 29(9):093509 (2024).
- [11] Caredda C., Lange F., Giannoni L., Ezhov I., Picart T., Guyotat J., Tachtsidis I., Montcel I., "Digital instrument simulator to optimize the development of hyperspectral systems: application for intraoperative functional brain mapping," J. Biomed. Opt. 30(2):023513 (2024).