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Investigation of tissue samples from brain tumor surgery using a combined optical coherence microscopy and fluorescence imaging setup

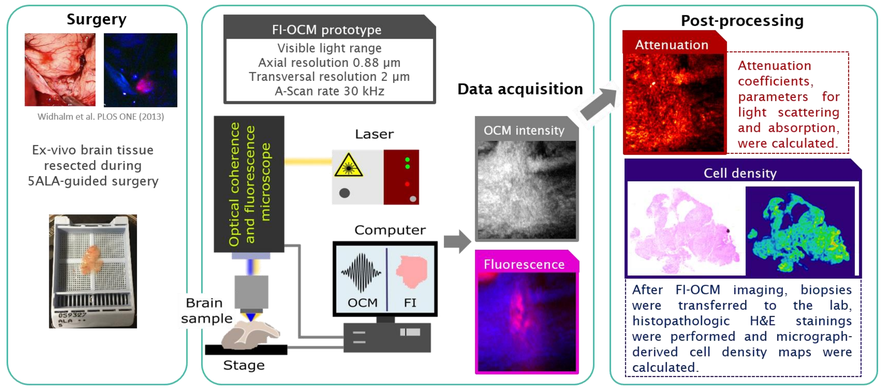
Johanna Gesperger[a,b], Antonia Lichtenegger[a], Thomas Roetzer[b], Pablo Eugui[a], Danielle J. Harper[a], Conrad W. Merkle[a], Marco Augustin[a], Barbara Kiesel[c], Petra A. Mercea[c], Georg Widhalm[c], Adelheid Woehrer[b] and Bernhard Baumann[a]

[a]Center for Medical Physics and Biomedical Engineering, Medical University of Vienna, Austria
[b]Division of Neuropathology and Neurochemistry, Department of Neurology, Medical University of Vienna, Austria
[c]Department of Neurosurgery, Medical University of Vienna, Austria

Background

- **Maximal safe resection is important to prolong the survival of brain tumor patients**.
- The application of **5-aminolevulinc acid (5-ALA), a fluorescent marker,** which is metabolized by tumor cells, is standard to guide tumor resection. Upon illumination with blue light, brain tumors may be visualized by intraoperative real-time fluorescence. However, while 5-ALA is highly sensitive for high grade gliomas, it lacks sensitivity for lower grade gliomas and other brain tumor types, e.g. brain metastases.[1]
- **Optical coherence tomography-based microscopy (OCM)** is an imaging modality that is based on the inherent backscattering of light. Volumetric images can be acquired without labeling in real time.[2] Just recently, OCM has been recognized for neuroimaging applications[3] including the visualization of brain tumors, where the need for additional contrast is urgent.
- Here we present a **combined OCM and fluorescence imaging (FI) prototype** for the *ex vivo* investigation of brain tumor samples resected during 5-ALA-guided surgery.

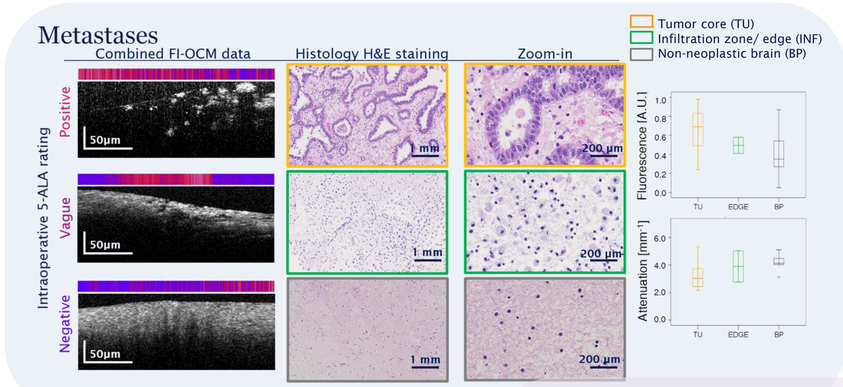
Methods



Tumor entity	Vital tumor core	Infiltration zone/ edge	Non-neoplastic brain parenchyma
Metastasis	6	2	6
Glioblastoma	15	7	8
Lower grade glioma	11	21	2

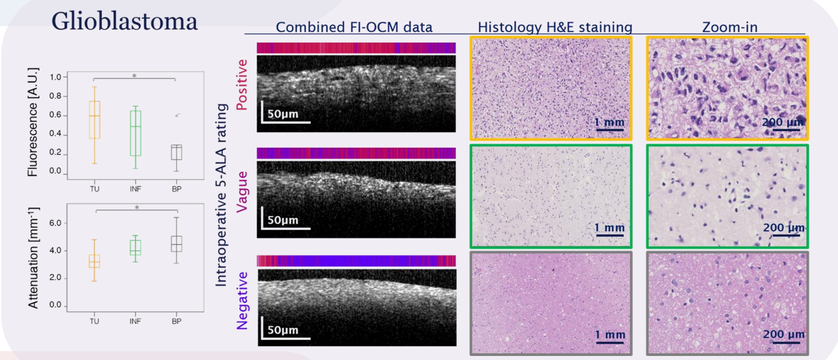
A total of 78 brain tissue biopsies were imaged with our combined FI-OCM setup.[4] Fluorescence intensities were measured, and attenuation coefficients were calculated and correlated against histology-derived cell density maps.[5]

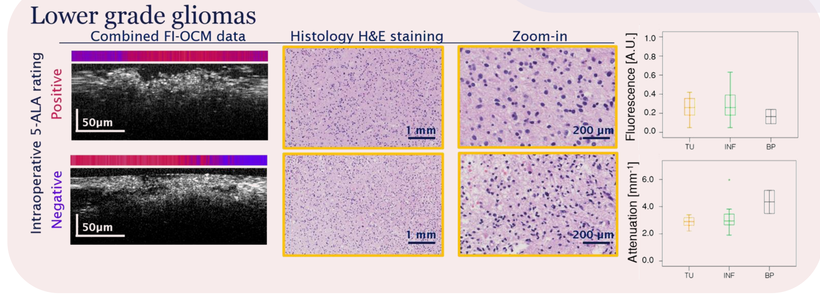
Results



In brain metastases and glioblastoma, the macroscopic 5-ALA fluorescence rating showed a strong correlation to the high-resolution fluorescence. Higher fluorescence intensity was associated with a decreased attenuation coefficient and increased tumor infiltration based on histology.

Lower grade gliomas did not display macroscopic fluorescence in 32/34 cases. Still, sub-visual fluorescence was detected in 11 biopsies with our fluorescence imaging setup. More notably, OCM-based attenuation values decreased with increasing tumor cell content and were of independent predictive value.





Conclusion

Our combined FI-OCM prototype provides additional, clinically relevant contrast, which could be used to improve the resection of tumor margins in patients with brain tumors.

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References

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