In-vivo And Ex-vivo Detection of Protoporphyrin IX (PpIX) Fluorescence in Experimental Gliomas with a Scanning Fiber Endoscope

Introduction:
At tumor borders, intraoperative protoporphyrin-IX (PpIX) fluorescence signal in gliomas remains suboptimal and inconclusive. Limitations include need for spectrophotometer use, microscope image quantification, confocal endomicroscope detection. We studied PpIX fluorescence detection in an experimental glioblastoma model using a resonant single scanning fiber endoscope (SFE).

Methods:
PpIX signal intensity (SI) was studied in-vitro in GL261 cells; in-vivo and ex-vivo in experimental gliomas (GL261 in mice, n=18) with the SFE and the operative microscope (400nm fluorescence). A video processing algorithm for background signal subtraction was developed. Tissue clearing, whole-brain 3D confocal imaging and histopathology were performed to correlate and validate data.

Results:
Individual glioma cells PpIX fluorescence in-vitro was visible with SFE (SI 214.7 &plusmn; 26.1 AU, background SI 136.6 &plusmn; 6.4 AU; p&lt;0.01; S/B ratio=1.6), but not operative microscope. SFE was used for resection cavity interrogation (tumor SI 183.1 &plusmn; 45.6 AU vs. background 1.7 &plusmn; 1.2 AU; p&lt;0.01; S/B ratio=105.7) and microsurgical removal guidance. In-vivo and ex-vivo SFE had higher S/B ratio and detected significantly weaker PpIX signal than conventional operative microscope. SFE visualized PpIX fluorescence in individual invading tumor areas, atypical and normal microvasculature which correlated with 3D confocal and histopathological data.

Conclusion:
To our knowledge, SFE is the first surgical imaging technology to show the exact PpIX-labeled glioma cells in-vitro and in-vivo. It precisely localized, imaged, and displayed glioma fronts in a relevant animal model at the cellular level. The SFE probe is more sensitive for PpXI fluorescence detection without noticeable photobleaching, and has a higher S/B ratio than a conventional fluorescent operative microscope. SFE may hold significant technological advantage for improvement of fluorescence-guided glioma surgery...

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