Through-microscope spectroscopic excitation and emission for fluorescence molecular imaging as a tool to guide neurosurgical interventions

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ABSTRACT

In intraoperative microscopy, quantitative fluorescence imaging has proven to be a powerful tool to guide neurosurgical interventions. However, commercial instruments lack detection sensitivity and are designed to image a single fluorescent tracer, usually indocyanine green, protoporphyrin IX or fluorescein. We introduce here a versatile and modular high-sensitivity spectroscopic imaging system that can be seamlessly connected to commercial neurosurgical microscopes and provide surgeons with spectroscopic fluorescence and reflectance images of the surgical field. The system provides an unprecedented spatial and spectral information content by allowing through-microscope, wide-field images to be acquired hyperspectrally at both excitation and fluorescence emission wavelengths. The instrument is capable of exciting and detecting a large number of visible and near-infrared markers, while measuring tissue autofluorescence throughout the optical range. Illumination is achieved with a supercontinuum laser (~400nm to >1000nm) coupled to a laser-line tunable filter with 3 nm spectral resolution. On the detection side, an imaging bundle directs the fluorescent light to a beam splitter, which channels signals through two liquid-crystal tunable filters with sensitivity either in the visible or the NIR, allowing imaging to be achieved between 400nm and 1100nm. Detection of visible light is done with a scientific grade charge-coupled device (CCD) camera, while NIR detection is done with a highly sensitive electron-multiplying CCD camera. Detailed system characterization studies are presented using liquid phantoms mimicking brain tissue to determine the system sensitivity and specificity, its ability to quantify and simultaneously image multiple fluorescent markers, and its capacity the detect near-infrared fluorophores at depth in tissue.