

THE TAUVIVO TIME-DOMAIN FLUORESCENCE IMAGING SYSTEM FOR THE SIMULTANEOUS IMAGING OF ICG AND TARGETED NIR TRACERS

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Fluorescence-guided surgery imaging systems have mostly been designed to image indocyanine green (ICG), a non-targeted near-infrared (NIR) fluorescent dye which has long been approved for medical use and can be used to monitor blood perfusion or perform sentinel lymph node mapping. ICG has absorption and emission spectra in the so-called 800 nm channel. These longer wavelengths offer deeper tissue penetration than visible-light or 700 nm-channel dyes. Consequently, many of the novel targeted fluorescent tracers are being developed around 800 nm dyes. One notable example is OTL38, a folate-targeting tracer for ovarian and lung cancer which recently received FDA approval. Because of the spectral similarity, this tracer can be imaged with a system designed for ICG. However, since both tracers are in the same spectral channel, they also become indiscernible from each other, possibly resulting in false signals if they were to be used during the same surgical procedure. We propose time-domain fluorescence imaging as a potential solution in such scenarios. While a conventional system images the fluorescent signal intensity in a specific spectral band, a time-domain system can also image the fluorescence lifetime (FLT), a property which quantifies the fluorescence decay speed after excitation. The FLT depends on the molecular structure of the dye and therefore can be used to discern different dyes, even when they emit with strongly overlapping spectra like ICG and OTL38. On the other hand, the FLT also depends on the chemical environment of the dye and potentially also on whether a tracer is bound to its target or not. These properties could help in eliminating non-specific signal originating from unbound tracer or from another tracer being used simultaneously or before. We demonstrate this potential by time-domain imaging of ICG-mimicking vascular and OTL38-mimicking “lung” solid phantoms, both supplied by Quel Imaging. Imaging is performed by a *tauVIVO* (FIG. 1 left), a novel preclinical instrument which we developed for macroscale time-domain imaging of NIR fluorescence. The *tauVIVO* employs pulsed illumination at 775 nm and images fluorescence through a 800 nm – 870 nm bandpass filter with a time-gated camera (*tauCAM*) housing a specialized CAPS¹ image sensor. The system offers fluorescence intensity and rapid FLT estimation at video frame rates with overlays on grayscale video and offers accurate FLT images using phasor or fitting approaches. The FLT imaging reveals distinct lifetimes for the ICG-mimicking (1.35 ns) and OTL38-mimicking (1.95 ns) phantoms making them clearly discernable (FIG. 1 right).

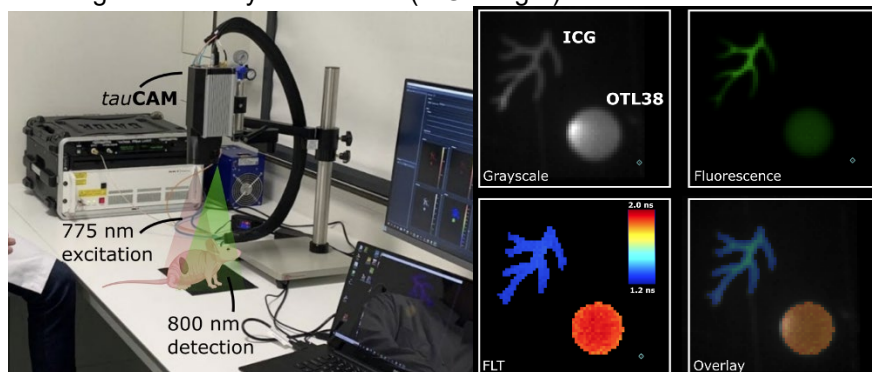


Figure 1 - (left) The *tauVIVO* preclinical imaging instrument (right) The FLT image reveals a difference between the ICG and OTL38 phantom

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