Early photon optical tomography signal-to-noise ratio improved by almost two orders-of-magnitude by running in the "deadtime" regime

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Optical projection tomography (OPT) is a powerful imaging modality for attaining high resolution absorption and fluorescence imaging in tissue samples and embryos with a diameter of roughly 1 mm. Moving past this 1 mm limit, scattered light becomes the dominant fraction detected, adding significant "blur" to OPT. Time-domain OPT has been used to select out early-arriving photons that have taken a more direct route through the tissue to reduce detection of scattered photons in these larger samples, which are the cause of image domain blur[1]. In addition, it was recently demonstrated by our group that detection of scattered photons could be further depressed by running in a "deadtime" regime where laser repetition rates are selected such that the deadtime incurred by early-arriving photons acts as a shutter to later-arriving scattered photons[2]. By running in this deadtime regime, far greater early photon count rates are achievable than with standard early photon OPT.

In this work, another advantage of this enhanced early photon collection approach is demonstrated: specifically, a significant improvement in signal-to-noise ratio. In single photon counting detectors, the main source of noise is "afterpulsing," which is essentially leftover charge from a detected photon that spuriously results in a second photon count. When the arrival of the photons are time-stamped by the time correlated single photon counting (TCSPC) module , the rate constant governing afterpusling is slow compared to the time-scale of the light pulse detected so it is observed as a background signal with very little time-correlation. This signal is present in all time-gates and so adds noise to the detection of early photons. However, since the afterpusling signal is proportional to the total rate of photon detection, our enhanced early photon approach is uniquely able to have increased early photon counts with no appreciable increase in the afterpulsing since overall count-rate does not change. This is because as the rate of early photon detection goes up, the rate of late-photon detection reduces commensurately, yielding no net change in the overall rate of photons detected.

This hypothesis was tested on a 4 mm diameter tissue-mimicking phantom (μ_a = 0.02 mm^{-1}, μ_s' = 1 mm^{-1}) by ranging the power of a 10 MHz pulse 780-nm laser with pulse spread of < 100 fs (Calmar, USA) and an avalanche photodiode (MPD, Picoquant, Germany) and TCSPC module (HydraHarp, Picoquant, Germany) for light detection. Details of the results are in Fig. 1a, but of note is that we observed more than a 60-times improvement in SNR compared to conventional early photon detection that would have taken 1000-times longer to achieve the same early photon count. A demonstration of the type of resolution possible is in Fig 1b with an image of a 4-mm-thick human breast cancer biopsy where tumor spiculations of less than 100 μm diameter are observable.

[1]Fieramonti, L. *et al. PloS one* (2012).
[2]Sinha, L., *et al. Optics letters* (2016).

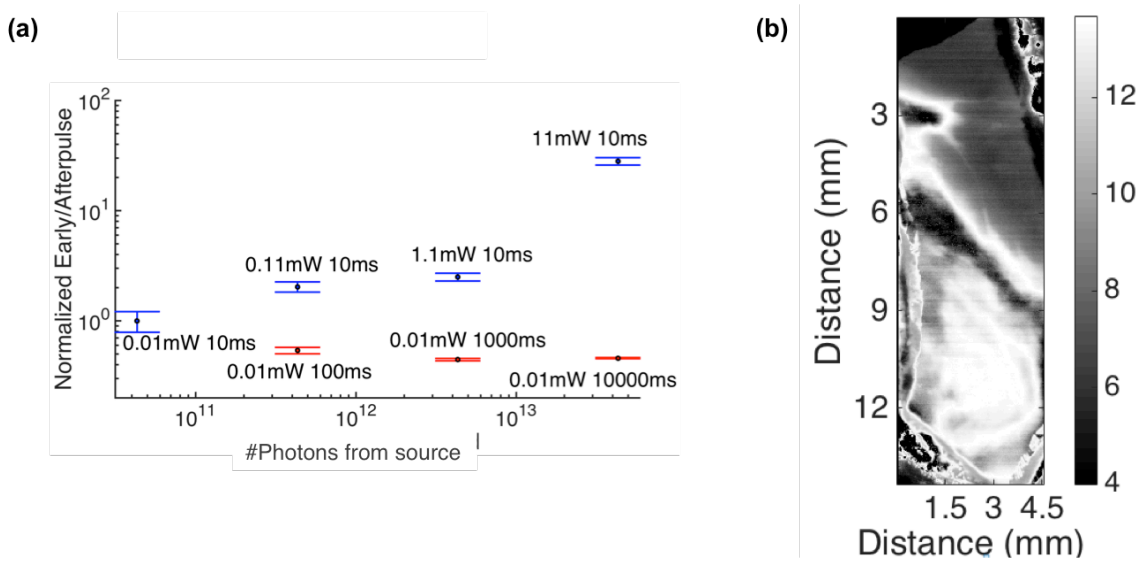

Fig 1. SNR improvement by saturating the detector. (a) The SNR obtained by the number of early photons to the number of afterpulsed photons is shown with different power-acquisition time combination . Even though the early photon counts detected is same when the same number of photons hit the detector but still the afterpulsed photons detected at the detector, which mainly constitutes the background, increases linearly as the acquisition time increases with the same laser power (red curve). However, when the same power-acquisition time combination is achieved with much less acquisition time but by increasing power (equivalent number of photons hit the detector from the source during the acquisition time) such that the detector gets saturated, the curve is no more linear but saturates at higher powers . The blue curve denotes SNR improvement as the detector is saturated while the red one is when the detector runs at conventional mode. (b) The resolution achievable in a 3-5mm thick human breast tissue sample.