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Attractive New Technologies for 7-Wavelength Time Domain Optical Mammography

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Abstract: An 8-channel Silicon PhotoMultiplier (SiPM) probe and Time-to-Digital-Converter (TDC) realize a higher-throughput, cheaper and compact detection chain for time-resolved optical mammography than photomultiplier tubes (PMTs) and Time Correlated Single Photon Counting (TCSPC) boards, providing comparable estimate of optical properties with increased optical responsivity.

OCIS codes: (170.6510) Spectroscopy, tissue diagnostics; (170.3830) Mammography; (170.6920) Time-resolved imaging; (170.5280) Photon migration

1. Introduction

Optical mammography has been largely investigated as a method for breast lesion detection and therapy monitoring. It is sensitive to physiological parameters that correlate with the presence and modifications of unhealthy tissue inside the breast. Furthermore, the use of non-ionizing radiation opens to monitoring of patient's therapy response even on a daily basis with no risk for health.

Our group previously developed a 7-wavelength, Time-Resolved (TR) portable instrument for optical mammography [1]. 20 MHz picosecond pulsed diode lasers emitted in the "visible" (VIS at 635 nm, 680 nm, 785 nm) and "near-infrared" (NIR at 905 nm, 930 nm, 975 nm, 1060 nm) spectral ranges. Light pulses at all wavelengths were time-multiplexed and injected into the compressed breast by means of a single optical fiber. The photons transmitted through the breast were collected by a 1-meter-long fiber bundle, with bifurcated distal ends connected to two different photomultiplier tubes (PMTs), for VIS and NIR, respectively. A collecting optics focused the light onto the active area of the two PMTs. Photon timing was achieved by two separate Time Correlated Single Photon Counting (TCSCP) boards. The system was employed in a clinical study on more than 200 patients [2–5]. The main limitations of the instrument were related to the low signal level ($< 5 \times 10^4$ counts/sec), especially for dense breasts and at the 1060 nm wavelength, which in some cases may make data interpretation weaker, affecting the accuracy of the results.

To overcome these limitations and potentially reduce the breast scanning time, here we present novel approaches to the detection of transmitted light and to the acquisition of the Distribution of Times of Flight (DTOF) that have led to a renewed design of the instrument detection and acquisition sections. Additionally, we present a characterization of the new technologies and of the overall instrument performance.

2. System design

Recently it has been proven that in most situations Silicon Photomultipliers (SiPMs) could profitably replace PMTs [6] and multi-channel Time-to-Digital Converters (TDCs) could replace TCSPC PC boards [7] for high throughput data collection. Therefore, we have employed these promising technologies to renew our instrument setup.

SiPMs are silicon-based single-photon detectors composed by an array of hundreds of microcells, each made up of a Single-Photon Avalanche Diode (SPAD) and a resistor for avalanche passive quenching and recovery [8]. They are (i) compact and (ii) cheap devices and several can be hosted into a single size-limited probe to be placed in direct contact with the sample, thus exploiting the SiPM (iii) high numerical aperture to increase light harvesting. With (iv) wide spectral coverage (from 350 nm up to 1100 nm) and (v) high quantum efficiency [6], an increase in signal level at all wavelengths is expected. With these premises our group has developed an 8-channel integrated SiPM probe (3.5 cm x 3.5 cm overall, SiPM model C30742-11, Excelitas Technologies, USA, each with 1 x 1 mm^2 active area, and 51% geometrical fill factor) mounted in place of the collecting fiber bundle and PMTs. A thermo-electric cooler element lowers the device dark count rate from 150 Kcps to 80 Kcps and the use of a dark shield surrounding the probe limits the stray light contribution, creating a probe for TR Diffuse Optics (DO) applications that embeds multiple detectors directly collecting remitted photons from the tissue with no need for fiber optics. The total actual active collection area is 4 mm^2.

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The SiPMs output signals are acquired by a commercial 8-channel TDC (SC-TDC-1000/08 S, Surface Concept, Germany) to reconstruct the DTOF curve. The device has an overall maximum throughput of 40 million counts per second (Mcps), much better than the limit of 5 Mcps of the TCSPC boards used in the previous configuration, at a much lower cost per channel (<1 k€/channel for the TDC, 8 k€/channel for the TCSPC board), giving access to multi-channel parallel acquisition with an overall higher acquirable signal level.

The overall renewed system design and the detection probe are depicted in Fig. 1.

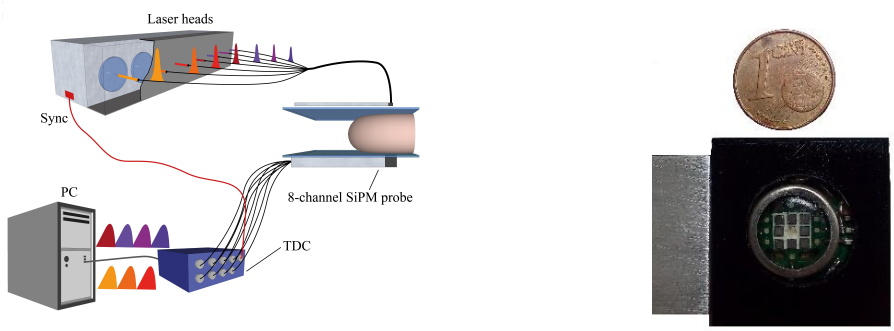

Fig. 1. Left: Upgraded instrument set-up. The laser pulses are sequentially produced at the 7 wavelengths and transmitted light is detected by the 8-channel SiPM probe. Then the TDC generates the time distribution of transmitted photons. Right: Picture of the head of the 8-channel SiPM probe.

3. Responsivity

The responsivity evaluates the overall detection efficiency of the instrument as the fraction of the input illumination transmitted through a calibration phantom at each wavelength [9]. The results, comparing the old detection chain (PMTs and TCSPC boards) and the new one (SiPMs and TDC), are summarized in Fig. 2, and show an increase in responsivity of up to 2-3 orders of magnitude, especially at 785 nm and 1060 nm. The low responsivity at these wavelengths for the previous detection chain was mainly due to the low quantum efficiency of the PMTs at the edge of their respective sensitivity spectral range.

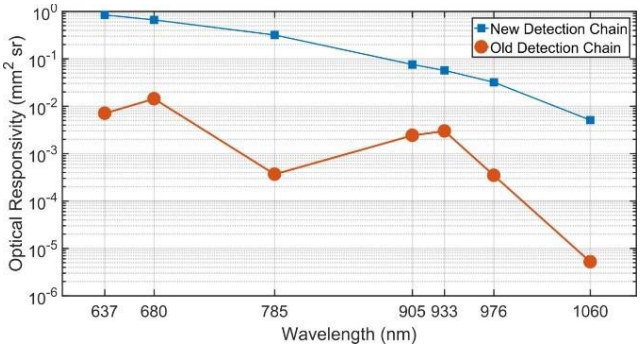

Fig. 2. Responsivity vs wavelength in the old (red circles) and new (blue squares) instrument set-ups.

The overall increase is due to (i) the removal of the collecting bifurcated fiber bundle and related dichroic filter, (ii) the removal of fiber-coupling and PMT's optics related losses, (iii) the use of 8 parallel detectors with (iv) high Numerical Aperture (NA close to 1 in the new setup *vs* ~0.37 in the previous setup), (v) in contact with the inferior glass of the compression unit, and (vi) with a higher quantum efficiency than PMTs (>20% at 600 nm). The higher responsivity is a crucial point in favor of SiPM detectors that potentially gives access to those breast types (dense and thick) at long wavelengths previously discarded or giving raise to low quality measures, due to low signal level. The reported increase is significant especially for the 1060 nm wavelength that is the collagen fingerprint, a constituent whose accumulation is linked to cancer pathogenesis [3].

4. TDC characterization

The TDC provides a digital code of the timing measurement without the use of analog timing electronics typical of TCSPC boards. It is affected by a strong Differential Non Linearity (DNL), up to 0.8 Least Significant Bit (LSB) peak-

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to-peak, where 1 LSB is 82.3 ps. However, two subsequent time bins are built such that the DNL is nearly compensated, thus obtaining a negligible Integral Non Linearity (INL). The DNL degrades the shape of the temporal distribution of the time of flight (DTOF) and therefore a compensation of the non-linearity is needed. The implemented correction algorithm reduces the DNL to 0.1 LSB at maximum, and improves the otherwise indented curve shape by smoothing it. The temporal resolution is lower (~ 150 ps) compared to the TCSPC board (~ 8 ps), yet likely adequate for optical mammography as the modifications of the DTOF curve due to tissue absorption and scattering are higher, in the order of few nanoseconds.

The dead time between two following photon acquisitions for the TCSPC board is 150 ns. This limits the useful acquisition count rate to 5 Mcps, but count losses due to dead time affect the curve shape already at 2 Mcps, causing distortions in the optical parameters retrieval. Instead, the TDC has a 5.5 ns dead time meaning a 185 Mcps maximum count rate, but internal electronics limits the actual count rate to 40 Mcps. Therefore, the TDC is expected to be able to produce the photons distribution curve with reduced count losses and distortions, giving access to a much higher signal level than the TCSPC board. Fig. 3 shows the extracted optical parameters, i.e. the absorption coefficient and scattering coefficient ($\mu_a \approx 0.12$ cm^{-1}, $\mu_s' \approx 8.5$ cm^{-1}) for a known phantom, at different count rate levels using both the TCSPC board (SPC130, Becker&Hickl, Germany) and the TDC, employing the same 8-channel SiPM probe in both cases. The results indicate a positive correlation between the absorption coefficient and the count rate for the TCSPC board due to the "first photon arrived" distortion (that produces a loss of late photons, i.e. photons providing more information on the absorption coefficient [10]). The trend for the TDC is quite flat, indicating that the device is less sensitive to dead time count losses and relative distortions in the experimented count rate range. The trend of the reduced scattering coefficient follows the absorption's one due to positive coupling effect.

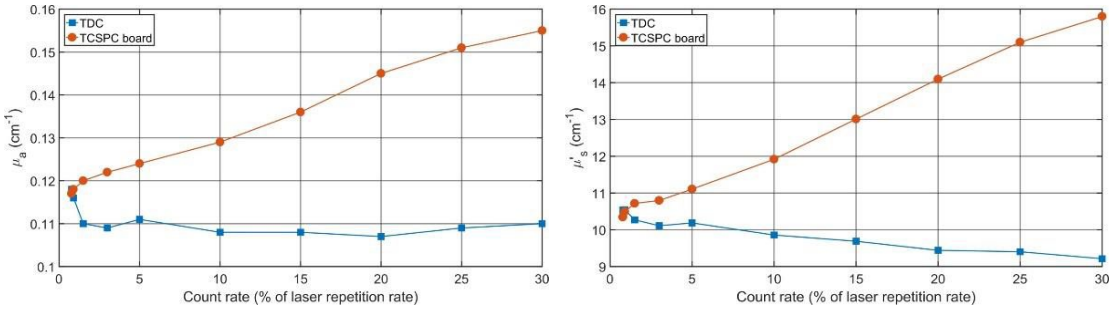

Fig. 3. Left: Absorption coefficient vs count rate using the TDC (blue squares) and TCSPC board (red circles) as acquisition system. In both cases, SiPMs are used as detector and laser repetition rate is 10 MHz. Right: Reduced scattering coefficient vs count rate.

The TDC, with its low dead time, shifts the maximum count rate at which significant curve distortions arise (10% error on estimation) to a much higher value (20%-25% of laser repetition rate) respect to the TCSPC board (5%-10%), giving access to the use of higher signal levels.

5. Performance assessment

We made a preliminary assessment of the performances of the new detection chain, in terms of both accuracy and linearity of the reconstructed optical parameters of 32 solid phantoms with different reduced scattering (μ_s' = 5, 10, 15, 20 cm^{-1}) and absorption properties (from μ_a = 0 cm^{-1} to 0.35 cm^{-1}, in steps of 0.05 cm^{-1}) as foreseen by the MEDPHOT Protocol [11].

The results show that the overall system has good linearity properties for both reconstructed absorption and scattering values. The non-linearity is less than 5% for the absorption coefficient and is around 10% for the scattering.

The accuracy is expressed as the percentage error of the reconstructed optical parameters with respect to conventionally true values. The errors are generally high (>20%), especially for high absorbing media, where the theoretical model starts to fail. However, these results are in line with those obtained with the previous detection chain used in the clinical trials, and therefore make these cheap and compact technologies suitable for actual use.

6. Scan procedure improvement

The PMTs are extremely sensible to excessive light illumination. This aspect forced in the previous set-up to make a pre-scan of the compressed breast aimed at getting the actual scan area size. Still, the scan area for the NIR PMT was smaller

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than the VIS PMT one due to its higher sensibility to excess light illumination near the breast border. SiPMs, instead, are not damaged by excessive light exposure. Hence, there is no need for a pre-scan procedure, thus reducing the overall image acquisition time, and the actual size of the compressed breast can be fully scanned at all the wavelengths.

7. Conclusions

We have upgraded our instrument for optical mammography employing attractive technologies as SiPMs and TDC, aimed at getting a higher signal level, yielding high quality data in a short measurement time. The characterization has shown an increase in the responsivity of the detection chain and comparable performances in the retrieval of the optical parameters. These technologies are therefore a promising alternative to the expensive and bulky previous detection chain, overcoming its main limits. Moreover, their characteristics make them interesting also for other applications where a high throughput, multi-channel acquisition system is needed, like brain activation monitoring or tomography [12–14]. Considering the encouraging results obtained so far, we are planning preliminary sessions of *in-vivo* imaging in view of an upcoming clinical study on the monitoring of neoadjuvant chemotherapy.

8. Acknowledgements

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