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Novel Approaches to Photon Detection and Timing for 7-Wavelength Time Domain Optical Mammography

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Abstract

An 8-channel Silicon Photomultiplier probe and a Time-to-Digital Converter are used to build a higher-throughput, cheaper and compact detection chain for time-resolved optical mammography as compared with conventional PhotoMultiplier Tubes and Time-Correlated Single-Photon Counting boards, still providing comparable performance in the estimation of optical properties, but with higher optical responsivity.

1. Background and motivation of the work

Photons injected into highly diffusive media, like biological tissues, are scattered by cellular structures and absorbed by macro molecules (e.g., water, haemoglobin, lipids and collagen). Through the study of photon migration (i.e. diffuse optics, DO), it is thus possible to non-invasively assess the chemical composition and microstructure of tissues [1].

Optical mammography (OM) is an application of DO and has been investigated as a valuable method for breast lesion characterization, tumour risk assessment and therapy monitoring exploiting the correlation of tissue optical properties to changes in breast tissue nature [2]–[5]. Over the years, we developed and applied in clinics a time-resolved (TR) 7-wavelength instrument for OM [6]–[10]. In that instrument, photons were collected through a bifurcated fibre bundle connected to two photomultiplier tubes (PMTs), one for detecting light in the visible range (VIS, 635–800 nm) and one for the near-infrared light (NIR, 800–1060 nm). Each PMT was connected to a time-correlated single-photon counting (TCSPC) personal computer (PC) board to reconstruct the photon distribution of the time of flight (DTOF) curve. With such detection chain, during clinical measures, we experienced low signal level, particularly for dense breasts at long wavelength (1060 nm), leading to low signal-to-noise ratio (SNR) that affected data analysis negatively.

In order to improve the SNR, we decided to take advantage of recent results showing how silicon photomultipliers (SiPMs) can substitute PMTs [11] and time-to-digital converters (TDCs) can replace TCSPC boards [12].

SiPMs and PMTs have different temporal shapes of the single-photon time response (SPTR) and it is known that this strongly affects the estimation of the optical parameters (i.e. absorption coefficient, μ_a, and reduced scattering coefficient, μ_s'). Fast leading and trailing edges will enhance the identification of shape changes of the DTOF curve due to light diffusion into tissue, and are thus positive for the optical characterization of tissue.

PMTs have a limited dark count rate (in the order of few hundreds of counts per second, cps) and a sharp and narrow temporal time response down to 30 ps full width at half maximum (FWHM), depending on type (microchannel plate PMTs) and wavelength range (visible) [13] even though spurious pulses (i.e. afterpulsing) can appear up to nanoseconds after the main peak disturbing the acquisition of the weak TCSPC signal. PMTs are bulky, not scalable and expensive inhibiting multi-channel setups, and the high sensibility to magnetic field and excess light illumination make them unsuitable for use out of the laboratory, like in a clinical environment.

An alternative has recently been identified in SiPMs: a matrix of up to a few thousands of Single-Photon Avalanche Diodes (SPADs), whose avalanches are quenched by a resistor also enabling device recovery [14]. SiPMs are robust, cost-effective and compact devices fostering their use in multi-channel applications, while their high quantum efficiency and wide numerical aperture improve light detection efficiency.

One of the major drawbacks is the increased dark count rate (DCR) in the order of hundred thousand cps (kcps). The DCR alone might thus exceed the photon count rate limit of few percent of laser repetition rate imposed by the TCSPC technique to avoid DTOF distortions.

The second drawback is the presence of a long exponential decay in the trailing edge of the SiPM SPTR, starting about two decades below the peak. The slow time constant decay might hide the contribution of late photons that provide the information of tissue absorption. Fig. 1 shows a typical example of the SPTR curve for a PMT and for a SiPM, highlighting the differences described here above.

However, it was recently shown that proper read-out electronics and cooling foster the tailoring of SiPM for TCSPC applications [15]. Moreover, SiPMs also provide higher light harvesting capability than PMTs [16]. Additionally, being compact solid-state devices, SiPMs can be hosted directly on the detection probe, without the need for optical fibres, thus further increasing the light collection thanks to their large numerical aperture [17].

Finally, time-to-digital converters (TDCs) can often allow increasing the data throughput, i.e. the overall detected photon count rate, with respect to TCSPC boards.

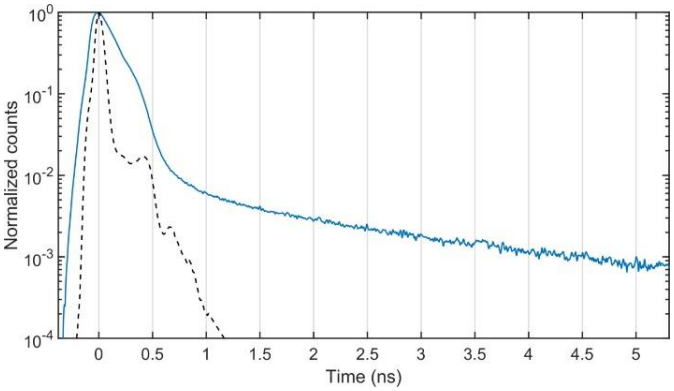

Fig. 1. Typical SPTR curve for a PMT (dashed black line) and for a SiPM (solid blue line).

Thus, here we propose a novel detection chain based on SiPMs and TDC to improve the overall light detection efficiency. The characterization of its performances is also reported.

2. Design of the detection chain

We developed the 8-channel SiPM probe displayed in Fig. 2. As shown, 8 SiPMs dies were assembled one close to the other to build an array. Each SiPM (C30742-11, Excelitas Technologies, Canada) has 1 x 1 mm^2 active area and 51% filling factor, thus forming a 4 mm^2 effective active area macro-pixel detector, with in principle a numerical aperture of 1. A thermoelectric cooler, located below the dies and driven by a microcontroller, guarantees SiPMs temperature stability at about 15°C, thus resulting in a DCR of about 50 kcps. The temperature feedback is provided by a negative temperature coefficient sensor placed in the square hole between dies. The new probe has been used to replace PMTs, optical fibres and focusing optics in the optical mammograph, thus also removing photon losses due to fibre-coupling.

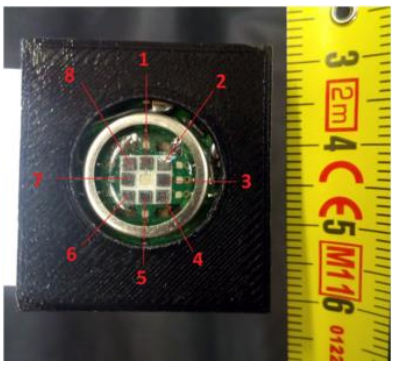

Fig. 2. The developed 8-channel SiPM probe.

The measurement of photon arrival time is achieved by an 8-channel TDC (SC-TDC-1000/08 S, Surface Concept, Germany). The device can reach a total throughput of 5 million cps (Mcps) per channel and its cost is lower than 1 k€ per channel (about one tenth than a classical TCSPC boards).
The TDC has a strong differential non-linearity (DNL) that degrades the shape of the DTOF curve, inhibiting the extraction of the optical parameters. The measured DNL is 80% of the least significant bit (LSB) peak-to-peak, where 1 LSB is on average 82.3 ps. To solve this issue, we implemented a correction algorithm that lowers the DNL to 8% LSB, thus significantly improving the DTOF shape.

3. Characterization of the new detection chain

Following the "basic instrumental performance" (BIP) protocol [18], we measured the optical responsivity of the detection chain (i.e. the overall collection efficiency of diffused light) showing an increase by up to 2-3 orders of magnitude (depending on the wavelength considered) with respect to the use of PMTs and TCSPC boards. This result is mainly due to the parallel use of 8 detectors and to the wide numerical aperture of each one, along with the higher quantum efficiency of the SiPMs (30% at 600 nm, 10% at 800 nm) with respect to the PMTs used in the previous version of the instrument (~8% at 600 nm for R5900U-01-L16 for VIS light and ~2% at 800 nm for H7422P-60 for NIR light, both produced by Hamamatsu Photonics, Japan) over the entire wavelength range of interest. In addition, the TDC low dead time (5.5 ns) as compared to the TCSPC board (125 ns) reduces the dead time count losses, thus improving data throughput.
Due to statistical constraints, the TCSPC technique can properly recover a DTOF curve (with negligible distortion) as long as the detected photon count rate does not exceed few percent of the laser repetition rate. When this limit is overcome, the reconstruction algorithm gives a higher weight to the early photons (i.e. the first arriving photons) with respect to late ones, thus resulting in a distortion of the reconstructed waveform (pile-up distortion [19]) and therefore producing errors in recovering the optical properties of the measured sample.
Using a single detector with either the TDC or the TCSPC board, we measured the pile-up distortion of both acquisition systems by retrieving the optical parameters of a known phantom at different count rate values: 1%, 3%, 5%, 10%, 15%, 20%, 25%, 30%, 35% of the laser repetition rate (set at 10 MHz). The results are shown in Fig. 3: while the TCSPC board introduces a growing error for high count rate levels, the TDC is less sensitive to distortions, thus enabling the use of increased signal level respect to the TCSPC board.

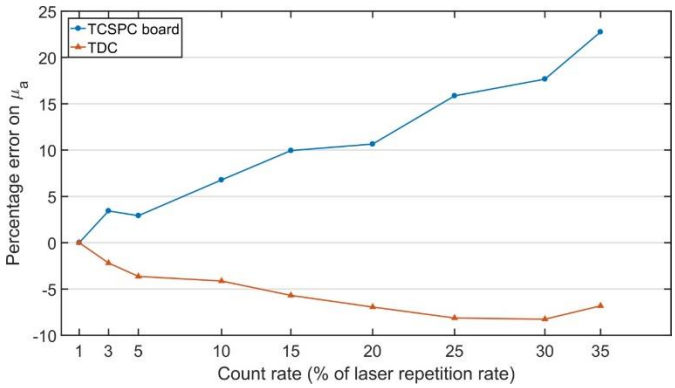

Fig. 3. The error on the estimate of μ_a *vs* detected photon count rate, expressed as percentage of laser repetition rate.

We tested the performances of the new detection chain for the estimate of the optical parameters by applying the MEDPHOT protocol [20]: we reconstructed μ_a and μ_s' of a set of 32 homogenous solid phantoms whose properties cover the range of use in *in vivo* applications. The 32 phantoms are divided into 4 series with growing scattering value (μ_s' =5, 10, 15, 20 cm^{-1}); each set has 8 phantoms with increasing absorption value (μ_a=0, 0.05, 0.1, 0.15, 0.2, 0.25, 0.30, 0.35 cm^{-1}). All measures were performed in transmittance geometry (with 4.5 cm thickness) at 975 nm.
We measured the accuracy of the optical properties estimation comparing the measured value with the nominal value for the phantoms. The results show that the relative error on μ_s' is ~30% while decreases to 20% for μ_a. Even though the accuracy errors are not negligible, they are comparable with those attained with the former detection chain.
We also measured the linearity of the reconstructed optical parameters, thus highlighting possible couplings between absorption and reduced scattering parameters [20].
We observed a high linearity in absorption estimate up to 0.25 cm^{-1}, after which a ~30% integral non-linearity arises (Fig. 4).

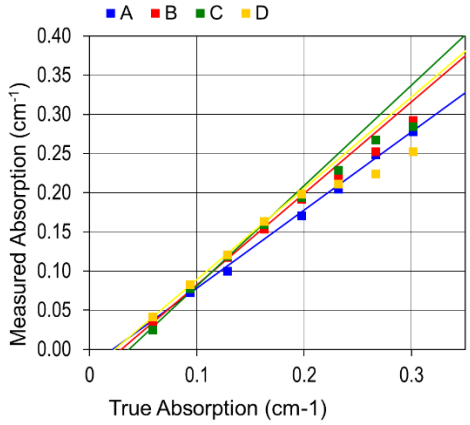

Fig. 4. Linearity plot for the absorption coefficient

The coupling of scattering-to-absorption is negligible for measured μ_a< 0.25 cm^{-1}, but for greater values a positive coupling starts to be observed. The absorption-to-scattering coupling is significant only for measured μ_s' > 8 cm^{-1}.

4. Conclusion

We proposed a complete new detection chain for optical mammography, aimed at increasing the overall signal level, thus improving signal to noise ratio and data robustness. The increased throughput can also lead to a reduction in total time measure.
The new detection chain is based on an 8-channel SiPM probe for photon detection and a multi-channel TDC for photon timing. It realizes a higher throughput (up to 40 Mcps), cheaper, and more compact solution as compared to the bulky and expensive PMTs and TCSPC boards.
The detection chain provides optical responsivity increased by 2-3 orders of magnitude by eliminating optics-related losses and exploiting the high numerical aperture and quantum efficiency of the SiPM. It reaches good performances in the estimation of optical parameters, comparable with the ones of the previous detection chain, as well as high linearity of the estimated optical properties. The TDC can overcome the limits imposed by the TCSPC technique and allows to operate at higher detected photon count rate.
Finally, the employed technologies are suitable for other DO applications where high throughput, multi-channel acquisition is required e.g. brain activation monitoring.
The positive results obtained so far encourage us to plan a preliminary session of *in vivo* breast imaging, looking forward for a clinical study.

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