Time-resolved diffuse optical tomography using fast-gated single-photon avalanche diodes

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Abstract: We present the first experimental results of reflectance Diffuse Optical Tomography (DOT) performed with a fast-gated single-photon avalanche diode (SPAD) coupled to a time-correlated single-photon counting system. The Mellin-Laplace transform was employed to process time-resolved data. We compare the performances of the SPAD operated in the gated mode vs. the non-gated mode for the detection and localization of an absorbing inclusion deeply embedded in a turbid medium for 5 and 15 mm interfiber distances. We demonstrate that, for a given acquisition time, the gated mode enables the detection and better localization of deeper absorbing inclusions than the non-gated mode. These results obtained on phantoms demonstrate the efficacy of time-resolved DOT at small interfiber distances. By achieving depth sensitivity with limited acquisition times, the gated mode increases the relevance of reflectance DOT at small interfiber distance for clinical applications.

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References and links


1. Introduction

Diffuse Optical Tomography (DOT) was developed in the 1990’s for medical imaging with potential applications including mammography or functional brain activity monitoring. A few geometries enable transmittance measurements through tissue and therefore yield information on the whole tissue volume. This is the case of mammography with cylindrical or spherical arrangements of sources and detectors around the breast or of brain imaging of premature infants with helmets of optical fibers [1,2]. However, for various reasons, other applications do not allow transmittance measurements. First, the volume of the organ can be too thick and/or the organ too strongly absorbing i.e. the adult brain [3] thus no photons can be collected in transmittance. Second, the access to an organ may be anatomically limited i.e. the prostate [4] and therefore imaging can be performed only in reflectance. In the cases of reflectance-only measurements, the main challenge of DOT is its depth sensitivity. For the widespread category of DOT instruments using continuous wave sources and detection, depth sensitivity is addressed by using large interfiber distances between sources and detectors so that the majority of collected photons probe deep layers of the tissue. However, for some applications, like prostate imaging [5], the anatomy impedes the use of large interfiber distances. In other cases, the use of small interfiber distances can make the diagnostic procedure more practical, enabling the use of optical probes which are more easy-to-handle than helmets or cylinders of optical fibers which require perfect positioning in order to achieve proper image reconstruction (e.g. for brain measurements [6]).

It has been shown that depth sensitivity can be achieved for small or null interfiber distances by using time-resolved measurements. Employing a pulsed light source and collecting photons at different arrival times provides the means to probe different layers in the tissue for a given interfiber distance [7]. In addition, it has been demonstrated that the sensitivity to absorption contrast in depth is higher for null interfiber distance [8]. However, the technical implementation of a small or null interfiber distance approach is challenging because it requires measuring the diffusion curve or temporal point spread function (TPSF) with a large dynamic range since the number of photons which arrive at the detector at first are multiple decades greater in magnitude than the later photons.

Two main instrumental approaches have been developed to perform time-resolved optical measurements. Single-photon detectors like photomultiplier tubes (PMT) coupled to time-correlated single photon counting (TCSPC) electronics allow the simultaneous acquisition of the TPSF with fine time-sampling of a few picoseconds. However, the electronics is limited by a maximum count rate of a tenth of the repetition rate of the pulsed source in order to avoid corrupted statistics and pile-up effects. For measurements at small interfiber distances, the limit count rate is governed by the first photons and very long acquisition times have to be considered in order to obtain a sufficient signal to noise ratio on late photons. Thus, such acquisition times are not compatible with clinical measurements. Another approach consists in time-gated measurements performed by instruments like CCD camera with image intensifiers. The detector is active (ON) for a time period of only a few hundreds of picoseconds and accumulates all photons received over the time gate. This acquisition mode has the advantage of not detecting the first photons and at the same time to collect the latest photons more rapidly. However, it has the drawback of a low time sampling of the TPSF due to the gate width, unless many overlapping windows are acquired, increasing the time needed for measurements. Time-domain acquisition has been already exploited for DOT, operating either with the TCSPC [9–13] or the CCD detection schemes [14,15].

Signal analysis is intrinsically linked to the nature of the collected data. When the full TPSF with fine time sampling is available, methods based on moments [16,17] or Mellin-Laplace transforms [18] can be used to reconstruct maps of $\mu_a$ or $\mu_s'$ coefficients in the medium. These methods have the main advantage of requiring limited calculation steps and therefore limited processing time. When the available information is the number of photons...
per gate, maps of $\mu_a$ can be reconstructed by calculating the full TPSF with fine time steps and by integrating them in gates [14,19]. In the case of such gated measurements, other approaches targeting functional applications skip the image reconstruction process and directly analyze the contrast on each time gate for each pair of source and detector. The contrast on the latest gates is then attributed to the contribution of the deepest layers in the medium [20,21].

Recent technological developments on single-photon detectors allow the combination of the advantages of the two instrumental approaches mentioned above. Single-photon avalanche diodes (SPADs) can now be operated in fast-gating mode, meaning that they can switch from the OFF to the ON state in less than 200 ps [22,23]. It was demonstrated that the fast-gated SPADs used with a TCPSC setup enable the acquisition of the full TPSF with a large dynamic range in limited acquisition time and with a time sampling of a few picoseconds [24]. The interest of this setup was shown for tissue spectroscopy [24,25] and for the detection of absorbing heterogeneity in turbid media [26]. However, the use of this approach for DOT has never been demonstrated before, despite great potential of the high-dynamic range gated SPAD acquisition for reflectance DOT requiring short source-detection separation.

In this article we show that the signals acquired with fast-gated SPADs combined with TCSPC enable the reconstruction of maps of $\mu_a$ coefficients in the medium by using analysis methods requiring the full TPSF like the Mellin-Laplace transform. Additionally, we demonstrate that for a given acquisition time, operating the SPADs in the fast-gated mode enables better detection and localization of deeper absorbing inclusions than without gating.

We first describe the experimental setup including a pulsed laser source, a fast-gated SPAD, a TCPSC acquisition board and an optical probe featuring the interfiber or source-detector distances (SD) of 5 and 15 mm. We detail the acquisition protocol designed to compare the performance of the acquisition in non-gated mode and in gated mode. We explain how the acquired signals are pre-processed and the followed scheme for image reconstruction. Finally, we analyze the obtained results for each interfiber distance, demonstrating the potential of the gated approach versus the non-gated one for reflectance DOT.

2. Experiments

2.1 Setup

**Probe and phantom.** The measurements were performed for 6 pairs of sources and detectors positioned as described in Fig. 1(a), with relative distances of 5 and of 15 mm. All sources and detectors were aligned. The 6 measurements were performed sequentially, as our experimental system featured only one source and one detector at a time. We permanently positioned a rigid bar with regular holes separated by 5 mm center to center in order to allow exact repositioning of the sources and detectors at the surface of the medium. Each time the fibers were positioned, we ensured that a proper optical contact was achieved between the phantom and the optical fibers to avoid degrading the measurement with reflections of light from the tip of the fibers.

The measurement was performed in a liquid phantom in which the absorbing inclusion could be easily moved at different depths. This movement was automated with a motorized translation stage. The background of the phantom was made of Intralipid and black ink to reach the following coefficients at 820 nm: $\mu_s = 0.1 \text{ cm}^{-1}$ and $\mu_{s}' = 10 \text{ cm}^{-1}$. The absorbing inclusion was a solid cylinder of 8 mm diameter and 6 cm length made of resin, TiO$_2$ particles and black ink. Its optical properties were $\mu_s = 0.6 \text{ cm}^{-1}$ and $\mu_{s}' = 10 \text{ cm}^{-1}$. During the measurement, the inclusion was always placed at the center of the probe, below S2, at $x = 0$, in parallel to the y axis. The inclusion was only moved along the z axis at different depths (from 10 to 37 mm). This depth is defined as the distance between the surface of the liquid phantom and the center of the inclusion. A one-dimension probe and a cylindrical inclusion were...
chosen to mimic a pseudo two-dimension (2D) configuration, as the employed reconstruction algorithm is currently developed in 2D.

![Diagram](image)

**Fig. 1.** (a) Schematic representation of the probe and phantom. A total of six pairs of sources and detectors are included in the probe with 2 possible interfiber distances: 5 mm for S1D1, S2D1, S2D2 and S3D2 and 15 mm for S1D2 and S3D1. The absorbing inclusion is positioned below S2 and moved at different depths. (b) Experimental setup with a pulsed laser, a variable optical attenuator (VOA), a SPAD and a TCSPC board. An electronic synchronization signal at the output of the laser is sent to the delayer and the TCSPC board.

**Source and optical chain.** A fiber based 4-wave mixing laser (Fianium, UK), provided pulses of 26 ps full width at half maximum at 820 nm at the repetition rate of 40 MHz. A home built variable optical attenuator (VOA) was positioned at the output of the laser in order to control the incident power injected in the excitation fiber (Fig. 1(b)). In order to exploit the measurements at different gate delays, we need to know precisely the values of attenuation provided by the VOA. It was calibrated at the beginning of the measurement and these values were an input for pre-processing the measured signals. After attenuation by the VOA, the laser beam was injected into a 400 µm core optical fiber of 2 m long. The maximum power at the output of the excitation fiber was 55 mW. The diffused light was collected by a 1 mm core fiber 2.1 m long. The length of the fibers was specifically chosen in order to avoid round-trip reflections on the TPSFs.

**SPAD detector.** The fast-gated SPAD module is extensively described in [27]. The opening and closing of the SPAD gate was controlled by a delayer synchronized to the laser source and the output of the SPAD module was connected to a TCSPC board (Becker&Hickl Gmbh, Germany) (Fig. 1(b)). The SPAD module was operated in two different ways. First, in “non-gated” mode the SPAD is ON (i.e. the gate is opened) before the first diffused photons reach the detector and is turned off only after the last photons are collected. In this mode the full TPSF temporally fits in the gate comparable to a measurement performed with a free running detector. With the second “gated” mode the TPSF is acquired portion by portion while the gate of the SPAD is successively delayed. This acquisition mode is performed in order to increase the incident source power without exceeding the maximum count rate associated with the first photons. Whereas the first mode is commonly used for DOT the second “gated” mode is new. The same temporal width of the SPAD gate was used for gated and non-gated acquisitions. A temporal width of 5 ns was chosen so that the TPSFs could fit in the gate for the non-gated measurements, at both interfiber distances.

**2.2 Acquisition protocol**

**Choice of gates.** For non-gated measurements, a gate width of 5 ns was used to contain the full TPSF without falling in the distorted portions of the curve at the opening and closing of the gate.
For gated acquisitions, the first gate was the same as the one chosen for non-gated measurements in order to obtain the full TPSF without distortion. After this first acquisition, the measurements at different gate delays were performed. The choice of the delays is important in order to achieve a good reconstitution of the full TPSF from the different gated measurements. The ideal situation would be to use the minimum number of delays in order to limit the acquisition time. However, the presence of a distorted temporal zone of a few hundreds of picoseconds at the opening of the gate has to be discarded from the analysis (Fig. 2(a)). Once all measurements are rescaled with respect to values of attenuation used during the acquisition, the full TPSF is reconstituted portion by portion from the gated measurements as explained in Fig. 2(b). The principle is simple: the temporal portion of the signal from gate \( n + 1 \) is kept to build the TPSF once it crosses the curve measured in gate \( n \), and so on.

In order to optimize the choice of gates and obtain a smooth reconstitution of the full TPSF, we proceeded as follows. For a given interfiber distance, we performed successive acquisitions of 1 s measurement time with a delay increasing by steps of 100 ps. For each delay, the VOA was automatically set in order to reach the limit count rate of \( 10^6 \) photons per second. This optimal VOA position per delay was stored to be used in the rest of the measurements. This procedure was stopped once the maximum amount of achievable power was reached. Indeed, at this point, no further advantage of time-gating is gained. We applied our TPSF reconstitution method described in Fig. 2(b) to different combinations of the series of gates measured at delay steps of 100 ps in order to determine the minimum necessary gates to reconstitute a smooth TPSF with the largest dynamic range possible.

Finally, 9 gates were used for SD = 15 mm; the source power was increased by a factor of \( 4.6 \times 10^2 \) between the first and the 9th gate. 7 gates were used for SD = 5 mm with a maximum power increase of a factor of \( 4.7 \times 10^3 \). For SD = 15 mm, the power increase with respect to the first gate is smaller than for SD = 5 mm because at this larger interfiber distance, the first gate required more power to reach the maximum count rate. For both interfiber distances, the last gate was measured at the maximum available power that is to say for the smallest attenuation delivered by the VOA. In this condition, we measured a power of 55 mW at the tip of the source fiber.

**Acquisition protocol.** The protocol was designed to compare fairly, for a given acquisition time, the performance obtained with non-gated and with gated acquisitions. For each pair of sources and detectors, series of gated and non-gated measurements were performed for different depths of the inclusion.
Our reconstruction algorithm requires the use of a reference measurement in a known medium in order to take into account the Instrument Response Function (IRF), but no direct measurement of this IRF [28]. In this work, we used the measurement in the phantom without the inclusion as a reference (homogeneous measurement). For practical reasons, the inclusion was not taken out of the tank but moved at 6 cm depth, outside the limits of the optical probe. Instead of performing only one reference acquisition during the measurement, we chose to acquire a reference between two successive acquisitions with the inclusion at different depths (heterogeneous measurements) in order to minimize the time lapse between a reference and its associated heterogeneous measurement, to account for possible drifts (laser power fluctuations, phantom settling, etc.).

For gated acquisitions, we set the gate delay and carried out the measurements for different depths of the inclusion. For each gate and each case (homogeneous and heterogeneous) acquisitions of 1 s were performed and the VOA was positioned to reach a count rate of $10^6$ photons per second. This optimal position of the VOA per gate delay was known from the preliminary measurements performed at delay steps of 100 ps which enabled a rapid positioning of the VOA during the acquisition and decreased the total duration of each measurement.

Non-gated acquisitions were performed within the same acquisition time as used for gated measurements, for fair comparison of both modes. So for example, when 7 gates of 1 s were acquired for the gated measurements at 5 mm interfiber distance, 7 repetitions of 1 s of non-gated measurements were carried out. Thus the two acquisition modes had the same effective photon-counting time. The measurements represented 7 seconds of effective acquisition for each interfiber distance of 5 mm and 9 seconds for each interfiber distance of 15 mm, for each homogeneous and heterogeneous measurement.

3. Signal pre-processing and reconstruction method

3.1 Signal pre-processing

**Non-gated signals.** For a given pair of source and detector and a given measurement, all the repetitions of non-gated measurements were summed, channel by channel. The average offset provoked by the dark count rate (DCR) was then removed to all time channels of all TPSFs.

**Gated signals.** The pre-processing of gated measurements is more complex than for non-gated ones since: 1) an additional noise source called the memory effect can be present on gated measurements, 2) the full TPSF has to be built from portions measured at different gates. The memory effect is a background noise source when numerous photons impinge the SPAD when it is in the OFF state. This phenomenon is extensively described elsewhere [29]. Whereas we did not observe it for any gate at the interfiber distance of 15 mm, the memory effect became visible at SD = 5 mm for the 4 last measured gates (Fig. 3(b)). We removed the memory effect from each affected gates by selecting a portion to calculate its average level and then subtracting it from all time channels of this gate. This was done separately for homogeneous and heterogeneous measurements as this noise source depends on the number of photons impinging the detector in the OFF state and this number varies depending on the depth of the inclusion. After correcting DCR and memory effect, a rescaling by the attenuation value was done for each gate. The curve was then reconstituted with the method explained in Fig. 2. All the pre-processing steps for gated measurements are summarized in Fig. 3.
Variance. Considering that the measurements are affected by photonic noise only, the variance of each time channel can be estimated by the number of photons measured in this time channel. For non-gated signals, variance is equal to the number of photons per time channel before the DCR correction. With the gated mode, it is necessary to take into account the power increase with which each portion was measured. The variance on the final TPSF is calculated separately for portions extracted from different gates. If the value $D_t$ in the pre-processed TPSF at time $t$ was extracted from gate $G$ measured with a power increase of $F_G$ with respect to the first gate, as $D_t = (1/F_G) \times G_t$, the variance on $D_t$ can be calculated as follows: $\text{Var}(D_t) = (1/F_G)^2 \times \text{Var}(G_t)$. The profiles of the variance curves are depicted in Fig. 4. Each steep change of variance corresponds to a change of gate.

3.2 Tomographic reconstruction method

The reconstruction method is fully described in [18,28]. The image reconstruction is done in 2D within the plane $(x, z)$ of Fig. 1, including the line of sources and detectors, and perpendicular to the absorbing inclusion. The direct problem is solved in 2D with the finite
volume method on a 6 x 5 cm rectangular mesh grid of regular steps of 0.1 cm in the x and z directions. The extrapolated boundary conditions are implemented by enlarging the medium by 1 mm and imposing a null photon density at the extrapolated boundary.

The used datatype is the Mellin-Laplace transform (MLT), enabling time-windowing of the TPSF [16,18] (Eq. (1)):

$$f^{(p,n)} = M^{(p,n)}[f(t)] = \frac{p^n}{n!} \int_0^{\infty} f(t) t^n \exp(-pt) dt$$  \hspace{1cm} (1)

where \( f(t) \) is the TPSF, \( p \) (in ns \(^{-1} \)) is a real positive and \( n \), the order of the MLT, is a positive or null integer. The same “precision” \( p \) was used for all the reconstructed images shown here, and was heuristically set to \( p = 3 \) ns \(^{-1} \). The number of MLT orders included in the reconstruction is optimized for each case, depending on the dynamic range of the TPSFs. Indeed, if this range is small, high orders are corrupted by noise and should not be included in the reconstruction. If the dynamic range increases, more orders can be included and more information on late photons (and therefore on deep layers of the medium) is available.

Our algorithm requires the use of a reference measurement in a known medium for each pair of source and detector in order to take into account the IRF. This reference was acquired in the homogeneous medium without the inclusion between all heterogeneous measurements. Whereas the inverse problem to solve is non-linear, we consider it linear at each iteration of the algorithm, and express it in the matrix form \( Y = WX \) by using the perturbation approach of the diffusion equation. In our case, we link changes in absorption in the medium (matrix \( X \)) to a combination of MLT of the measurements performed in the studied medium and in the reference (matrix \( Y \)) with a sensitivity matrix \( W \). This matrix is obtained by a combination between MLT of Green’s functions estimated in the medium and the reference measurement [28]. To take into account the noise present on high orders of MLT, we added a left preconditioner \( L \) consisting of a diagonal matrix whose diagonal elements estimate the inverse of the standard deviation of each order of the MLT of \( Y \). To increase the weight of pixels far from the probe and favor the reconstruction of deep inclusions, we added a right preconditioner \( R \) based on the squared distance between each pixel and the set of sources and detectors. The final criterion to minimize is then \( \|LWRX' - LY\|^2 \), with \( X = R \cdot X' \).

The algorithm is initialized by a homogeneous map with the estimated value of the background medium (\( \mu_a = 0.1 \text{ cm}^{-1} \)). The solution is then approached by an iterative method, the optical properties of the medium and the sensitivity matrix \( W \) being updated at each step. We consider the stabilization of the depth of the reconstructed absorbing inclusion as convergence, which is reached in less than 10 iterations for all tested cases. All the details of the reconstruction method are documented in [18] for theoretical material on the MLT and in [28] for using this algorithm to process experimental signals.

We ran separate reconstructions including only the pairs of sources and detectors at distances of 5 and 15 mm to evaluate independently the performance of the setup for each interfiber distance.

4. Results

4.1 Dynamic range

Figure 4 shows the pre-processed TPSFs obtained without and with gating for a reference measurement in a homogeneous medium of \( \mu_a = 0.1 \text{ cm}^{-1} \) and \( \mu_s' = 10 \text{ cm}^{-1} \), for SD = 15 mm and SD = 5 mm and underlines the gain in dynamic range with gating. For SD = 15 mm, using gating provides a gain of 2 decades of dynamic range and the measurement of photons with flight times up to 6.6 ns (starting from a \( t_0 \) set before the peak of the TPSF) whereas the maximum was 3.8 ns without gating (Fig. 4) (from the same \( t_0 \)). Gating enables a relatively stable SNR over a large time range whereas the SNR decreases exponentially in time for non-
gated measurements. For SD = 5 mm, we observed an increase of 2 decades with gating, which allowed the detection of photons up to 3.2 ns with respect to 2.2 ns which was achieved without gating.

The interest of the gated mode for detecting deep absorbing inclusions is directly visible on the pre-processed TPSFs (Fig. 5). For SD = 15 mm, whereas it is only possible to distinguish the curves acquired for depths between 10 to 22 mm from others without gating, depths from 10 to 28 mm can clearly be differentiated following gated measurements (Fig. 5(a)). Similar effects are observed for SD = 5 mm (Fig. 5(b)). Moreover, the perfect overlap of all homogeneous measurements at both interfiber distances for non-gated and gated acquisitions confirms that the differences between TPSFs measured for different depths of the inclusion are due to the position of the inclusion and not due to experimental drifts. Figure 5 also shows that the TPSFs reconstructed from gated measurements are not completely smooth but can present steps due to imperfect calibration of the VOA.

The TPSFs of Fig. 5 are used to calculate the MLT and are processed by our DOT reconstruction algorithm in the following section.

![Comparison between non-gated and gated modes on acquired TPSFs, estimated variance and signal to noise ratio (SNR = D / \sqrt{Var(D)})](image)
4.2 Contrasts

The analysis of the contrast on the different orders of MLT is relevant to understand which inclusions should be robustly reconstructed by our algorithm. This contrast is calculated separately for each order of MLT as shown in Eq. (2).

\[
\text{Contrast} = \frac{\text{MLT}_{\text{without inclusion}} - \text{MLT}_{\text{with inclusion}}}{\text{MLT}_{\text{without inclusion}}} \times 100
\]  

Figure 6 shows the obtained contrasts for orders \( n = 1 \) to \( n = 30 \) of the MLT of the TPSFs calculated with \( p = 3 \text{ ns}^{-1} \). These contrasts are depicted only for one pair of source and detector per interfiber distance but the trends described here were similar for all pairs at the same interfiber distance. The error bars were obtained by calculating the contrast when using the references acquired before and after the measurement. Figure 6 demonstrates that for both interfiber distances, whereas the contrast is similar for the first orders, it always reaches higher values for the higher orders of MLT for gated measurements, which suggests that more orders of MLT can be included in the reconstruction algorithm for this acquisition mode.
**SD = 15 mm.** Looking at each individual contrast profile per depth of the inclusion, one can see that contrast is above noise level from 10 mm to 22 mm only for the non-gated mode but for the gated mode, depths of 25, 28 and 31 mm can also be distinguished. This contrast analysis suggests that the detection range in depth can be increased from 22 to 31 mm for SD = 15 mm by using the gated mode.

**SD = 5 mm.** The contrast profiles indicate that the increase in depth range is even more pronounced for SD = 5 mm. Whereas measurements at depths from 10 to 16 mm are above the noise level from non-gated acquisitions, depths from 10 to 28 mm can be detected with gating. For SD = 5 mm, the contrast profiles for high orders for gated acquisitions differ from those obtained at SD = 15 mm: we do not observe a steep decrease of contrast and no increase of error bars. We hypothesize that this phenomenon is due to the presence of the memory effect. A better understanding and correction of the memory effect could improve the analysis of measurements at short interfiber distances.

### 4.3 Image reconstruction

Following the reconstruction scheme summarized in Subsection 3.2 we separately ran reconstructions for all pairs of sources and detectors at each interfiber distance and obtained 2D maps of the absorption coefficients in the plane (x, z). The number of MLT orders included in the analysis was adapted for each interfiber distance and each acquisition mode to optimize results. For each depth and for each mode, two reconstructions were carried out separately with the references acquired before and after the heterogeneous measurement in order to evaluate the sensitivity of the results to photonic noise. Figures 7 and 8 show the obtained results only for the references acquired before the heterogeneous measurements for SD = 15 mm and SD = 5 mm.

**SD = 15 mm.** Reconstructed images of Fig. 7 corroborate the contrast analysis of Subsection 4.2. At SD = 15 mm with the non-gated mode, the inclusion can be detected down to 22 mm only. For deeper positions, the images obtained are dependent on photonic noise, which results in different images according to the choice of the reference (images not shown here). With the gated mode, the inclusion can be robustly detected down to 31 mm. Therefore, by operating the SPAD in the gated mode, the detection range increases in depth by nearly

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**Fig. 6.** Contrast on MLT orders (p = 3 ns⁻¹, orders n = 1 to n = 30) depending on the depth of the absorbing inclusion for non-gated and gated modes, (a) SD = 15 mm (S1D2), (b) SD = 5 mm (S2D1).

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**SD = 5 mm.** The contrast profiles indicate that the increase in depth range is even more pronounced for SD = 5 mm. Whereas measurements at depths from 10 to 16 mm are above the noise level from non-gated acquisitions, depths from 10 to 28 mm can be detected with gating. For SD = 5 mm, the contrast profiles for high orders for gated acquisitions differ from those obtained at SD = 15 mm: we do not observe a steep decrease of contrast and no increase of error bars. We hypothesize that this phenomenon is due to the presence of the memory effect. A better understanding and correction of the memory effect could improve the analysis of measurements at short interfiber distances.
50%. Results for the depths of 34 and 37 mm are not shown as the images reflect photonic noise for both acquisition modes.

**SD = 5mm.** Without gating, the inclusion can be reconstructed only down to 16 mm. Images obtained for deeper positions, from 19 to 25 mm, reflect only the photonic noise (Fig. 8). On the contrary, the gated mode enables to detect the inclusion down to 25 mm, which represents an increase of around 65% in the depth range detection. Images for depths between 28 and 37 mm are not shown as they only reflect photonic noise.

**Gated versus non-gated.** Figure 9 summarizes the comparison between the non-gated and gated acquisitions for the criteria of the reconstructed depth. As stated before, for both interfiber distances, it is clear that the gated mode has a considerable increased detection range in depth. Additionally, the gated mode has also improved the depth localization within this range. For SD = 15 mm, the reconstructed depth range increases from 20 mm to 25 mm (Fig. 9(a)). For SD = 5 mm, it enlarges from 15 mm to 25 mm, which represents an increase of 65% (Fig. 9(b)).

However, our algorithm does not exactly accurately retrieve the real position in depth. For SD = 15 mm, the depth is underestimated when the inclusion is deeper than 25 mm. Such behavior has already been observed on simulations [28]. For SD = 5 mm, the depth of the most superficial inclusions is overestimated. In the reconstruction algorithm, other preconditioners should be explored to improve the proper localization over the full detection range. Finally, for gated and non-gated measurements, the deeper the inclusion, the larger the reconstructed inclusion and the greater the underestimated mean $\mu_a$ in the inclusion (Fig. 7 and Fig. 8). A more exhaustive work should be carried out to improve the quantification potential of this method in the future.

![Fig. 7. Reconstructed maps of $\mu_a$ at iteration 15 for each depth of the inclusion, for non-gated and gated modes including all pairs of source and detector at SD = 15 mm (S1D2 and S3D1). The red dotted circle depicts the true position and size of the absorbing inclusion. At each depth of the inclusion, the scale in $\mu_a$ is the same for the non-gated and gated mode.](image)
Fig. 8. Reconstructed maps of $\mu_a$ at iteration 15 for each depth of the inclusion, for non-gated and gated measurements including all pairs of source and detector at SD = 5 mm (S1D1, S2D1, S2D2 and S3D2). The red dotted circle depicts the true position and size of the absorbing inclusion. At each depth of the inclusion, the scale in $\mu_a$ is the same for the non-gated and gated mode.

Fig. 9. Reconstructed depth versus true depth for the non-gated and gated modes, (a) SD = 15 mm, (b) SD = 5 mm.

5. Discussion

Depth sensitivity is one of the main features of time-domain near infrared spectroscopy. This capability was already explored using both single [30] and multi-distance measurements [31]. Time gated instruments can improve this intrinsic features of time-domain techniques [32,33]. Differently from the previous works here a time-gated instrument based on a solid state detector, thus able to efficiently reject early photons, was employed giving the possibility to increase the injected power, reduce the interfiber distance and consequently improve the achievable signal to noise ratio.

The proposed experimental setup with a fast-gated SPAD and the associated protocol has provided signals which could be successfully processed with a DOT reconstruction algorithm requiring the knowledge of the full TPSF. Even if the pre-processed TPSFs were not
completely smooth, similar trends on contrast as those expected from simulations could be observed and relevant maps of $\mu_a$ could be reconstructed. However, we have observed that the obtained maps of $\mu_a$ change slightly depending on the portions of gates kept to build the final TPSF (not shown here). Another error factor relies in the correction of the memory effect. We have presented a correction based on the estimation of an average level of memory effect per gate. Other corrections, like exponential regression could be used. More experiments should be carried out to effectively define the optimal correction method. Another point to improve for processing gated signals deals with exploiting the distorted zone present at the opening of the gate. Indeed, using this portion would enable the use of fewer gates because less overlap between the gates would be necessary, which would decrease acquisition time and increase the useful collected signal. Finally, the gated mode could be improved if more source power or better detection efficiency could be achieved. While increase in power is restricted by safety regulations when dealing with in vivo measurements, improved detection could be implemented by using SPADs with larger active areas or multiple SPADs. Indeed, the development of large area or arrays of gated SPADs is technically feasible, and great improvements can be expected in the future.

6. Conclusion

We have demonstrated the feasibility of DOT on phantoms at short interfiber distance using time-gated SPAD acquisition. DOT algorithms requiring the full TPSF, like methods based on the Mellin-Laplace transform, can provide relevant maps of absorption coefficients. For the two interfiber distances of 5 and 15 mm, we showed that gated acquisitions not only enable an increase in the detection range in depth as compared to non-gated acquisition and previous work [33,34], but also enlarge the depth range within which the algorithm can localize a single absorbing inclusion. This approach can be one solution to image deeper biological tissues with optical probes in a limited acquisition time which would be compatible with medical diagnostics.

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