On light sharing TOF-PET modules with depth of interaction and 157 ps FWHM coincidence time resolution

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Abstract

The performance of a light sharing and recirculation mechanism that allows the extraction of depth of interaction (DOI) information is proposed and tested. For these purposes, a dedicated 64-channels readout setup has been developed with intrinsic timing resolution of 16 ps FWHM. Several PET modules have been produced, based on LYSO:Ce scintillators and commercial silicon photomultiplier (SiPM) arrays, with 3 × 3 mm\(^2\) individual SiPM size. The results show the possibility to achieve a timing resolution of 157 ps FWHM, combined with the already demonstrated spatial resolution of 1.5 mm FWHM, DOI resolution of 3 mm FWHM, and energy resolution of 9% FWHM at 511 keV, with 15 mm long crystals of section 1.53 × 1.53 mm\(^2\) and 3.1 × 3.1 mm\(^2\). At the same time, the extraction of the DOI coordinate has been demonstrated not to deteriorate the timing performance of the PET module.

1. Introduction

Positron emission tomography (PET) is a clinical and pre-clinical diagnostic technique based on the simultaneous detection of pairs of 511 keV gamma rays emitted from the annihilation of a positron with an electron (Del Guerra et al 2016). This measurement is usually performed by several rings of crystal scintillators, such as L(Y)SO:Ce or BGO, coupled with photo-detectors, like photomultiplier tubes (PMTs) or silicon photomultipliers (SiPMs). Pre-clinical and organ-dedicated human PET scanners require very high levels of spatial resolutions, typically in the order of 1–2 mm. This is usually achieved by developing detectors based on scintillators with small cross-section, to improve the localization of the gamma interaction point in the radial coordinate. At the same time, the scanners are designed to be close to the region of interest, to minimize the impact of the acollinearity effect.

The need for high sensitivity imposes the use of long scintillators, potentially giving rise to distortions in the reconstructed images due to parallax effects. Various methods to measure the depth of interaction (DOI) of the gamma rays along the main axis of the scintillators have been developed in order to overcome this limitation. Some examples include, among others, phoswich with pulse-shape discrimination schemes (Karp and Daube-Witherspoon 1987, Ziemons et al 2005, Wiener et al 2013), double side readout methods (Bugalho et al 2009, Seifert and Schaart 2015), detectors with light sharing DOI encoding (Miyaoaka et al 1998, Liu et al 2001, Yang et al 2009, Ito et al 2010, 2013), monolithic scintillators (Borghi et al 2016, Marcinkowski et al 2016), phosphor coated scintillators (Berg et al 2016, Kwon et al 2016), sub-surface laser engraving (Uchida et al 2016, Bläckberg et al 2018), double side G-APD cross-strip readout (Kolb et al 2014), and wavelength discrimination (Shimazoe et al 2016). We recently proposed a method to obtain DOI information with high resolution, in the order of 3 mm FWHM, based on a simple light sharing and re-circulation scheme in single side readout and without the need for one-to-one coupling between crystals and
detectors (Pizzichemi et al 2016, Stringhini et al 2016). Due to the limitations of the acquisition setup, at that time
we were not able to investigate fully the timing capabilities of this method, and especially the influence of DOI on
coincidence time resolution (CTR).

Measuring the time of flight (TOF) of gamma rays allows to restrict the point of annihilation of the positrons
to a smaller segment along the lines of response (LORs), which has been demonstrated to sharply increase in the
signal to noise ratio (SNR) of reconstructed images (Conti 2011). The gain in SNR of a TOF PET system, com-
pared to a non-TOF PET one, is directly proportional to the physical dimension of the region of interest under
study and proportional to the CTR. Typical timing resolutions of currently available whole-body PET scanners
are in the order of 215–315 ps FWHM (Miller et al 2015, van Sluis et al 2019). It is clear that smaller objects, like
the ones investigated in pre-clinical imaging or in organ-dedicated PET systems, require even better TOF resolu-
tions to reach the same levels of SNR gain. The first goal of this work is therefore to assess the timing resolution
that can be achieved with the proposed DOI method, in order to determine if it can be successfully adopted for
the development of a new generation of high resolution PET scanners.

Furthermore, nowadays the direction of research in PET is more and more pointing towards a new frontier
in terms of timing resolution, with the ultimate goal set to 10 ps FWHM CTR (Lecq 2017). The reason for this
can be found in the possibility to access directly the information on the 3D position of the positron annihilation
point, offering novel strategies in the reconstruction or correction algorithms (Defrise et al 2012). Reaching such
a high level of CTR will require a great improvement in the performance of every element of the PET acquisition
chain. At the same time, it is well known that the uncertainty on DOI introduces a bias on timing measurement,
because of the mismatch in the speed of propagation in dense scintillators between gamma rays and optical
photons. The magnitude of this bias has been evaluated in the order of 150–200 ps (Moses and Derenzo 1999,
Shibuya et al 2008) for long (15–20 mm) LYSO:Ce scintillators. There have been several attempts to integrate
the DOI smearing effect on timing into the analytical modeling of CTR in PET detectors (Gundacker et al 2014,
Vinke et al 2014). In particular, it has been demonstrated that while in current LYSO/SiPM detectors the DOI
blur on timing measurements does not significantly affect CTR, its impact would be significant for long, near-
ideal scintillator detectors, preventing the achievement of CTR values below 50 ps FWHM (Toussaint et al 2019).
As a consequence, the goal of 10 ps FWHM timing resolution cannot be reached in PET systems based on long
scintillators without some knowledge on the DOI position of the incoming gamma rays. The computation of
DOI is therefore expected to become mandatory also for whole-body PET scanners. Obviously, this DOI infor-
mation will have to be extracted without affecting the intrinsic CTR of the system. Therefore the second aim of
this work is to demonstrate that the light sharing and re-circulation scheme that we proposed does not degrade
the timing information.

2. Materials and methods

Throughout this paper, we refer in general to a module as a combination of scintillators and photo-detectors. In
section 2.1, a configuration to produce a PET module with DOI capabilities is described, based on depolished
crystals and a light sharing scheme. Subsequently, a procedure to optimize the extraction of timing information
and improve CTR with DOI is proposed in section 2.2. To evaluate the impact on timing resolution of the DOI
extraction method, another module configuration will be presented in section 2.3, similar to the one illustrated
in section 2.1, but based on polished scintillators and without light sharing. This configuration does not allow
for the computation of DOI, but it is known to yield optimal energy and timing resolutions, and will therefore be
used as a reference. Finally, the experimental setup and the procedure followed to evaluate the performance of the
modules under study are presented in sections 2.4 and 2.5.

2.1. DOI modules

DOI information can be extracted in a PET module by coupling an array of \( M \times M \) photo-detectors on one
side of a matrix of \( N \times N \) scintillators, as shown in figure 1. In general, \( N \geq M \), i.e. one or more crystals can be
coupled to the same photo-detector, without affecting the validity of the method. The four lateral surfaces of each
scintillator are depolished, while the two remaining sides are polished. The scintillators are separated from each
other by foils of reflective material. The side of the scintillator array opposite to the photo-detectors is coupled to
a light guide made of glass. For both the scintillators–photodetectors and scintillators–glass interfaces, the optical
coupling is obtained by means of optical grease or transparent adhesive, to maximize optical transmission.
Finally, a foil of reflective material is placed in dry contact on the back of the light guide. When a gamma ray
interacts at a given DOI of a pixel in the scintillator array, the light produced propagates in the crystal and is
eventually emitted both from the scintillator side coupled to the photo-detector and from the opposite one (red
and blue arrows, respectively, in figure 1). Because of the optical depolishing of the lateral surfaces of the crystal,
the ratio of the amount of light emitted by the two ends of the scintillator depends on the gamma interaction
position along the crystal (Vilardi et al 2006, Trummer et al 2009).
Thanks to this light re-circulation scheme, a certain number \( K \) of photo-detectors is hit by the photons generated by the scintillation event. We denote these photo-detectors as \( D_i \), with \( i = 1, 2, \ldots, K \). Their physical position in a \( x - y \) plane parallel to the photo-detector array is expressed in terms of the coordinates \( x_i \) and \( y_i \) of their centers. For each \( D_i \), the amount of light collected by the photo-detector is denoted as \( p_i \), and the measured time of detection as \( t_i \). In what follows, the index \( i = 1 \) always refers to the photo-detector directly coupled to the crystal where the interaction occurred. For each scintillation event, this photo-detector \( D_1 \) can easily be identified, since it is expected to measure the maximum amount of light \( p_1 = p_{\text{max}} \). The total amount of light collected by all the \( K \) photo-detectors can be calculated simply as

\[
P = \sum_{i=1}^{K} p_i. \tag{1}
\]

Given these definitions, it has been demonstrated that for each scintillation event, the quantities

\[
u = \frac{1}{P} \sum_{i=1}^{K} p_i x_i, \quad v = \frac{1}{P} \sum_{i=1}^{K} p_i y_i, \quad w = \frac{p_{\text{max}}}{P} \tag{2}
\]

allow at the same time for the correct identification of the crystal where the gamma interaction occurred, and for the computation of the DOI coordinate with a resolution that has been estimated in the order of 3 mm FWHM. Furthermore, a fast calibration procedure has been proposed and validated (Stringhini et al 2016).

### 2.2. Method for timing optimization

If we consider the DOI module described in section 2.1, a simple estimation on \( t_{\text{in}} \), the time of entrance of the incoming gamma ray in the crystal of interaction, would be provided by \( t_1 \), i.e. the time of detection for the photo-detector \( D_1 \) coupled to the crystal itself. Anyway, because of the light sharing mechanism, only part of the light produced in the scintillation process reaches the photo-detector \( D_1 \). As shown in figure 1, also the photo-detectors adjacent to \( D_1 \) are hit by the optical photons, mainly by the light spreading through the back of the module. As a result, in general the timestamps of these photo-detectors will be seen as delayed with respect to \( t_1 \). Furthermore, it is reasonable to expect that this delay depends on the DOI position, since it is proportional to the difference between the mean path that the optical photons have to travel to reach the photo-detectors. We can therefore state that a relation

\[
g_i(w) = (t_i - t_1)(w) \tag{3}
\]

between the average delay of the \( i \)th photo-detector with respect to \( D_1 \) and the DOI coordinate \( w \) exists, for each \( D_i \). For symmetry, this is valid also in the limit case of \( D_1 \), where of course \( g_1(w) \equiv 0 \).

The \( g_i(w) \) relations can be measured directly with a procedure that will be described in section 2.5, where the delay \( (t_i - t_1) \) is plotted, event by event, against \( w \) for each \( D_{i \neq 1} \) after photopeak selection in a given crystal. This allows to build a series of 2D histograms (see for example the one in figure 2), whose profiles provide an experimental measurement of the relations (3). Once these relations are known, for any event of all subsequent
acquisitions it is possible to obtain $K$ independent estimations of $t_1$, simply subtracting from $t_i$ the expected delay from $D_1$, calculated at the $w$ of that specific event

$$t_1^{(i)} = t_i - g_i(w).$$  \hspace{1cm} (4)

These measurements can be combined to get the best estimator of $t_1$, as follows

$$\hat{t}_1 = \frac{\sum_{i=1}^{K} (1/\sigma_i^2) \cdot t_1^{(i)}}{\sum_{i=1}^{K} (1/\sigma_i^2)}$$  \hspace{1cm} (5)

where the weights $\sigma_i$ are obtained from the width of the histograms of the $t_1^{(i)}$ measurements, acquired during calibration, evaluated in the $w$ of the event.

In the same calibration run, the difference between $t_1$ and the timestamps of the photo-detector coupled to an external, fast reference crystal, $t_{\text{ref}}$, plotted against $w$, for several events in the photopeak of a given crystal. A clear correlation is observed, as shown in figure 3, reflecting the impact of the DOI coordinate on timing. From the profile of such scatter plot, it is possible to obtain an experimental measurement of $d(w_0)$, i.e. the average delay expected, as a function of $w$, between $t_1$ and a fixed external reference. For each event localized in the same crystal of any subsequent acquisition, the best time estimator of $t_{\text{in}}$ can be found as

$$\hat{\theta}_{\text{in}} = \hat{t}_1 - [d(w_0) - d(w)]$$  \hspace{1cm} (6)

to correct $\hat{t}_1$ by the difference between the average delay expected at the value of $w$ measured for that event and the average delay that would be measured at a fixed reference DOI position, expressed by $w_0$. The width of the delay histograms constructed using $\hat{\theta}_{\text{in}}$ should therefore represent the best possible CTR achievable by the DOI module under study.

2.3. Reference modules configuration
A PET module configuration without DOI capabilities is also studied in this work. It is based on the typical structure of modules used nowadays in PET scanners, and will be useful for comparison with the DOI module proposed. The structure of a reference module is very similar to the one of a DOI module. The only differences are the use of fully polished scintillators, and the absence of a light guide, as shown in figure 4. As a result, light sharing is extremely reduced and no DOI capabilities are expected. On the other hand, polished scintillators are known to yield the best results in terms of timing and energy resolutions.

2.4. Experimental setup
A total of eight modules have been assembled for testing in this work. As reported in table 1, they are divided in two groups of four DOI modules and four reference modules, assembled following the configurations described in sections 2.1 and 2.3, respectively.

Each module is assigned a unique ID, $X.Y.Z$, where $X$ denotes the module type ($D = $ DOI module, $R =$ reference module), $Y$ the number of scintillators in the LYSO:Ce array, and $Z$ the item number (1 or 2) between identical arrays. All modules are based on LYSO:Ce crystal arrays produced by Crystal Photonics Inc., United States (see figure 5). In particular, the lateral surfaces of each scintillator in the arrays used to assemble DOI modules
are depolished, while each crystal is fully polished in the case of reference modules. Foils of enhanced specular reflector (ESR, by 3M), 70 µm thickness, are inserted between the crystals and build the matrix structure, acting also as a wrapping material. The reflectors are not bonded to the scintillators, and therefore a thin air gap remains between ESR and crystals. The modules are wrapped with a layer of Teflon, to ensure mechanical stability. The arrays are coupled by means of optically clear adhesive (OCA 8172CL, by 3M), 50 µm thickness, to a TSV photo-detector array produced by Hamamatsu, model S13361-3050-AE-04 (see figure 5), made of 16 multipixel photon counters (MPPCs), each with 3 × 3 mm² active area. In DOI modules, a light guide made of glass,
12.8 \times 12.8 \times 1 \text{ mm}^3, is coupled by means of optically clear adhesive (OCA 8146-5, by 3M), 125 \mu m thickness, to the scintillator array, and covered with a foil of ESR in dry contact. In reference modules no light guide is used, and the foil of ESR is placed directly on the scintillator array.

The first two modules in both DOI and reference groups are based on $1.53 \times 1.53 \times 15 \text{ mm}^3$ scintillators and present a 4-to-1 coupling between crystals and photo-detectors (see figure 6, left). These characteristics make them particularly interesting for the study of the possible development of pre-clinical and organ dedicated PET systems. The remaining modules, instead, are more suited for studying the performance of the DOI timing correction method applied to whole-body PET scanners, especially towards the 10 ps FWHM CTR goal, being made of $3.1 \times 3.1 \times 15 \text{ mm}^3$ scintillators, and with 1-to-1 coupling (figure 6, right).

In order to extract the DOI coordinate with the method described in section 2.1, an accurate evaluation of the amount of light hitting each photo-detector is required. This can be achieved by integrating the electrical pulses generated by each photo-detector when hit by the scintillation light. At the same time, evaluating timing and performing the correction procedure proposed in section 2.2 requires parallel multichannel readout with fast electronics. A proper acquisition system has been developed accordingly (see figure 7), based on two identical custom developed front end boards (FEBs) and a combination of CAEN VME digitizers. Each FEB (see figure 8) can host up to two Hamamatsu S13361-3050-AE-04 MPPC arrays, for a total of 32 MPPCs, through two Samtech connectors. Event by event, the signal generated by each photo-detector is split in two parts. One is amplified and fed directly to one channel of a 64ch VME V1740D CAEN module, that digitizes and integrates the pulse shape. The other is routed to one input channel of a NINO-32 amplifier-discriminator board (Anghinolfi et al 2004), that produces a square wave subsequently digitized by one channel of two fast 32ch VME V1742 CAEN modules (LSB 200 ps). The timestamp of the photo-detector is calculated by the crossing of the rising edge of this square wave with a fixed threshold. Upon every trigger event, therefore, a value of the integrated charge deposited and a timestamp is stored for any photo-detector connected to the FEBs. It has to be noted here that the value of integrated charge obtained from each MPPC is corrected to compensate for the well-known saturation effect of SiPMs due to the finite number of microcells present in the photo-detector, with a standard procedure that involves the use of several gamma sources (Otte et al 2005). In particular, each SiPM is coupled to a $4 \times 4$ LYSO:Ce array made of polished scintillators, the measured integrated charge is evaluated for the photopeaks corresponding to the gamma emissions of $^{22}\text{Na}$, $^{137}\text{Cs}$, $^{57}\text{Co}$, $^{60}\text{Co}$ and $^{176}\text{Lu}$ sources, and a calibration curve is derived.

In order to evaluate the timing performance of the acquisition system, the signal of a single Hamamatsu S13360-3050-PE photo-detector (active area $3 \times 3 \text{ mm}^2$), coupled to an individual LYSO:Ce crystal (Crystal Photonics Inc., $1.7 \times 1.7 \times 3.0 \text{ mm}^3$) has been sent by means of a custom adapter to several pairs of channels belonging to the same FEB. The width of the histogram of the difference between the timestamps recorded by the two channels, upon excitation with an external 511 keV source, provides a measurement of the intrinsic timing resolution of the setup. With this method, the average timing resolution of the acquisition system has been evaluated to be 16 ps FWHM, comparable to measurements obtained with a NIN08 board and a fast oscilloscope (Gundacker et al 2016). Since the expected timing performance of the LYSO:Ce modules under test is estimated to be roughly one order of magnitude greater, the contribution to CTR of the acquisition system can be considered negligible and will not be subtracted from the final results.

Although the readout system allows to acquire directly in coincidence two modules, one against the other, in order to properly assess the individual performance of each sample in table 1, and especially to carefully study the validity of the proposed timing correction method, a dedicated experimental setup, based on a single channel external reference detector, common to all modules, has been prepared (see figure 9). One module is connected

**Figure 5.** Scintillator and photo-detector arrays used in this study. All scintillator arrays are made of LYSO:Ce, and produced by Crystal Photonics Inc., United States. In the four on the left, the lateral surfaces of each scintillator is depolished. In the others, all crystal surfaces are fully polished. Arrays on the top raw are made of 64 scintillators, while on the bottom by 16. In the center, one Hamamatsu S13361-3050-AE-04 photo-detector array.
to one of the two FEBs. A single Hamamatsu S13360-3050-PE photo-detector (active area $3 \times 3$ mm$^2$) is plugged via a custom adapter into the opposite FEB, and coupled to an individual LYSO:Ce reference crystal, produced by Crystal Photonics Inc., United States, of dimensions $1.7 \times 1.7 \times 3.0$ mm$^3$. Finally, a $^{22}$Na source is placed between the modules and the reference crystal and the acquisition is performed in coincidence.

The characterization of the modules in terms of timing resolution with this setup requires evaluating and subtracting the contribution to CTR due to the reference detector. This has been measured as follows. First, two identical crystals, each $2 \times 2 \times 5$ mm$^3$ LSO:Ce cod. 0.4% Ca (Agile) and coupled to two single Hamamatsu S13360-3050-PE photo-detectors, have been connected to the two FEBs and acquired in coincidence, upon excitation with a $^{22}$Na source. The FWHM of the resulting delay histogram has been evaluated in 125 ps. This value divided by $\sqrt{2}$ represents the contribution to CTR from one of the two scintillators. Then, the same procedure has been repeated after replacing one of these assembly crystal + photo-detector with the reference one. Subtracting of the previously evaluated contribution of one LSO:Ce cod. 0.4% Ca crystal from the width of the resulting histogram, the contribution to CTR of the reference detector has been evaluated in 88 ps FWHM.

Finally, it has to be remarked here that all the experimental setups described in this section are contained in a light tight box, where temperature is kept constant at 20 °C degrees by means of a dedicated cooling system.

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**Figure 6.** Coupling between crystals (blue) and MPPCs (red), for $X.64.Z$ (left), and $X.16.Z$ (right) modules. The labeling convention for photo-detectors and crystals is also reported.

**Figure 7.** Schematics of the acquisition system developed for this work, based on two custom developed FEBs, one CAEN V1740D and two CAEN V1742 digitizers. Up to 32 photo-detectors can be connected to each FEB. The signal from each photo-detector input is split in two. One side is amplified and fed to the V1740D digitizer, that measures the charge deposited on the photo-detector, by pulse shape integration. The other is routed to the NINO32 chip, producing a square wave that is sent to one of the two V1742 modules for timestamp calculation. For each event, therefore, up to 64 charges and 64 timestamps can be measured in parallel.
2.5. Module characterization procedure

The characterization of each module consists in a calibration run followed by an acquisition that evaluates the timing performance. Both measurements are performed exactly in the same conditions and with the same experimental apparatus, i.e. by means of an external reference crystal as described in section 2.4.

In the calibration run, first a simple charge spectrum of the reference crystal is built and the events outside of the 511 keV photopeak are discarded. Then for the remaining events the values of \((u, v, w)\) coordinates calculated in the module are drawn in a 3D plot. Several accumulation volumes can be identified and separated (see figure 10) by means of a custom clustering algorithm (Stringhini et al 2016). The volumes obtained are used to identify the gamma rays interacting with individual crystals. Events whose \((u, v, w)\) coordinates fall outside of these regions can be interpreted as inter-crystal scatters, i.e. events where a single gamma ray is depositing its energy in more than one crystal. For the purpose of this study, these events are discarded.

When histograms of the total amount of light collected by the photo-detectors, \(P\), are plotted for events confined in each volume, the charge spectrum of each crystal in the module can be reconstructed, as shown for example in figure 11, allowing to determine the ranges of photopeak selection, and at the same time to evaluate the energy resolutions. Once the events in the photopeak of individual crystals are sorted, an accurate calibration curve that allows to reconstruct the physical coordinate of the DOI position from the value of \(w\) can be obtained for each scintillator, as it was demonstrated in a previous work (Stringhini et al 2016). At the same time, also the DOI resolution can be evaluated. Subsequently, a 2D histogram of \((t_1 - t_i)\) versus \(w\) is built for each \(D_{ij}\), like the one shown in figure 2, and the experimental relations \(g_i(w)\) are obtained. Finally, a 2D scatter plot of \(t_1 - t_{ref}\) versus \(w\) is produced, to derive \(d(w)\).

Once the calibration data is available, an acquisition to evaluate CTR is performed. Each event is processed and assigned to a particular crystal in the module, then only the ones simultaneously in the photopeak of both this crystal and the reference one are taken into account. Subsequently, two delay histograms are built. The first,
H_{std} is constructed without taking advantage of the DOI correction, i.e. it is filled with the difference between the timestamp \( t_1 \) of the photo-detector coupled to the crystal of interaction, and \( t_{ref} \), the timestamp of the reference crystal

\[ \Delta t_{std} = t_1 - t_{ref}. \]  

(7)

The second one, \( H_{corr} \), exploits the DOI correction method proposed in section 2.2, by using

\[ \Delta t_{corr} = \theta_{in} - t_{ref}, \]  

(8)

where \( \theta_{in} \) is defined in equation (6). A flow chart to summarize the calibration procedure and the construction of \( H_{std} \) and \( H_{corr} \) is shown in figure 12. The \( H_{std} \) and \( H_{corr} \) distributions are fitted with an exponentially modified Gaussian distribution

\[ G_e(t; \mu, \sigma, \lambda) = \frac{\lambda}{2} \exp \frac{\lambda}{2} (2\mu + \lambda \sigma^2 - 2t) \cdot E \left( \frac{\mu + \lambda \sigma^2 - t}{\sqrt{2\sigma}} \right), \]  

(9)

where \( \mu \) is the mean value and \( \sigma \) the standard deviation of the Gaussian component, \( \lambda \) is the rate of the exponential part and \( E \) is the complementary error function. The function \( G_e(t; \mu, \sigma, \lambda) \) does not have any physical meaning and it has been used only to decouple from statistical fluctuations while taking into account possible asymmetries in the histograms. The FWHM is measured directly on the fitted functions, the contribution to CTR of the reference crystal is subtracted and the result multiplied by \( \sqrt{2} \), to obtain the timing resolutions without DOI correction, CTR\textsubscript{std}, and with DOI correction, CTR\textsubscript{corr}, of a system made by

Figure 10. Example illustrating the procedure of crystal separation. First, a 3D histogram of all the events of a calibration run is plotted for a particular module (left). 64 accumulation volumes can be distinguished. To help visualization, here the histogram has been zoomed to a \((u,v)\) area corresponding to the crystals coupled to a single individual MPPC, in this case C2 defined in figure 6 (center). The clustering then performs the separation by starting from a seed defined as the voxel with the highest number of counts \( C_0 \). It then analyses all the nearby voxels, discarding the ones with a number of counts lower then a threshold defined as a fraction of \( C_0 \), and adding the others to the list of seeds. The procedure is then repeated recursively for all the seeds, paying attention to avoid running more then once on the same seed. When no more new seeds are found, the volume represented by the collection of all seeds defines a cluster. These voxels are then removed from the 3D histogram, and the procedure starts again, until 64 clusters are found. The effect of this algorithm on the central plot is shown in the plot on the right, where four regions are clearly separated.

Figure 11. Example of the charge spectrum obtained for one crystal in a test module. In this particular case, the crystal belongs to a \( 8 \times 8 \) crystal matrix coupled with a \( 4 \times 4 \) photo-detector array. The area highlighted in green corresponds to a typical cut for the photopeak range of \( \pm 2\sigma \).
two modules identical to the one under study. Two examples of the delay histograms recorded for one crystal in a $4 \times 4$ and one in a $8 \times 8$ DOI module are shown in figure 13, before and after correction, to give a visual representation of the improvement in CTR.

### 3. Results

For each individual scintillator of every DOI module in table 1, a charge spectrum has been constructed from the values of total light collected, as defined in equation (1). The position of 511 keV photopeak provides an evaluation of the total light collection for the crystal, in units of ADC channels. The energy resolution is evaluated from the FWHM of the photopeak itself. Finally, the timing resolutions, $\text{CTR}_{\text{std}}$ and $\text{CTR}_{\text{corr}}$, have been calculated with the procedure described in section 2.5. The same strategy has been applied to reference modules, with the notable difference that, since no DOI information is available, only $\text{CTR}_{\text{std}}$ can be calculated. Since the two types of array under study, with $8 \times 8$ and $4 \times 4$ scintillators, are interesting for different applications, the results of their characterization are presented in more details in separate sections.

#### 3.1. $8 \times 8$ modules

The average light collection and energy resolution measured for all the crystals in the two $8 \times 8$ DOI modules (D.64.1 and D.64.2) have been evaluated in $(115 \pm 3) \times 10^3$ ADC channels, and $9.9\% \pm 0.2\%$ FWHM. If only the 16 scintillators coupled to the four central MPPCs (i.e. to B2, C2, B3, and C3 in figure 6) are considered, this averages become $(127 \pm 3) \times 10^3$ ADC channels, and $8.9\% \pm 0.2\%$ FWHM. This is expected, since the total amount of light collected by the MPPC array depends on the position of the crystal of interaction with respect to the MPPC array itself, with better light collection the closer the crystal is to the center. Total light collection and energy resolution are clearly anti-correlated, as shown for example in figure 14, for one $8 \times 8$ DOI module. Overall, both light collection and energy resolution values obtained for the DOI modules are very similar to the ones measured for the corresponding reference modules (R.64.1 and R.64.2). In particular, averages of $(118 \pm 3) \times 10^3$ ADC channels and $9.9\% \pm 0.2\%$ FWHM were found for all the 64 scintillators, while $(132 \pm 3) \times 10^3$ ADC channels and $9.0\% \pm 0.2\%$ FWHM for central ones.

The average standard $\text{CTR}_{\text{std}}$ before applying the timing correction method, measured on the two arrays was $307 \pm 3$ ps FWHM for all the scintillators, and $308 \pm 3$ ps FWHM on central scintillators, and it improved to $166 \pm 2$ ps FWHM, and $157 \pm 2$ ps FWHM, respectively, after timing correction (see figure 15). The improvement is therefore in the order of 140 ps, and a slight dependence on the position of the crystal with respect to the MPPC array is observed, similarly to what has been found for energy resolution (see figure 16). The correction method relies on the measurement of the $g_i(w)$ relations defined in equation (3). For the four central MPPCs, eight such relations can be obtained, while only three for the MPPCs in the corners of the array, and five for all the others. As a consequence, the performance of the correction is expected to be better for the crystals coupled to the central MPPCs, as it is experimentally verified. The magnitude of this performance degradation on the borders of the modules is anyway just in the order of a few picoseconds. As a comparison, in reference modules, the average $\text{CTR}_{\text{std}}$ was evaluated in $158 \pm 2$ ps and $154 \pm 2$ ps for all and central scintillators, respectively. A summary of the performance of $8 \times 8$ DOI and reference modules can be found in table 2.

#### 3.2. $4 \times 4$ modules

The spatial distribution of light collection and energy resolution measured for one of the two $4 \times 4$ DOI modules (D.16.1 and D.16.2) is shown in figure 17. The distributions of measured timing resolutions before and after timing correction are shown in figure 18, while their spatial distribution can be seen in figure 19. Similarly to
what has been found for $8 \times 8$ modules, light collection, energy resolution and $CTR_{corr}$ are better for crystals coupled to the four central MPPCs.

Average light collection and energy resolution were estimated in $(134 \pm 3) \times 10^3$ ADC channels and $9.5\% \pm 0.2\%$ FWHM, when averaging on all the scintillators of both $4 \times 4$ DOI modules, and $(154 \pm 3) \times 10^3$ ADC channels and $8.8\% \pm 0.2\%$ FWHM when considering only the central channels. In the two $4 \times 4$ reference
modules (R.16.1 and R.16.2), the values of \((139 \pm 3) \times 10^3\) ADC channels and 9.5% ± 0.2% FWHM were found for all crystals, while \((155 \pm 3)\) and 9.0% ± 0.2% FWHM for central crystals.

The average value of CTRs among all the crystals of the two 4 × 4 DOI modules was measured in 233 ± 2 ps FWHM before timing correction, and 165 ± 2 ps FWHM after timing correction. For crystals coupled to central MPPCs, the values were 234 ± 2 ps FWHM and 159 ± 2. For comparison, the average \(\text{CTR}_{\text{std}}\) measured in the two reference modules was 162 ± 2 ps FWHM for all crystals, and 158 ± 2 for the four central ones. A summary of
the performance of $4 \times 4$ DOI and reference modules can be found in table 2, together with the results of $8 \times 8$ modules.

4. Discussion

The results shown in the previous sections are summarized in table 2. The performance of $8 \times 8$ DOI modules is particularly interesting in view of the possible development of a high resolution PET scanner targeted for small animals, or specific organs in human body, where high levels of spatial resolutions are required. The combination of the small cross-section of scintillators (individual area of $1.53 \times 1.53 \text{ mm}^2$) to the already demonstrated DOI resolution of 3 mm FWHM (Stringhini et al 2016), in fact, is considered sufficient to provide an homogeneous spatial resolution at the level of the physical limits imposed by positron range (i.e. in the order of 1.5 mm FWHM for positrons emitted by $^{18}$F-based radio-tracers). The $4 \times 4$ DOI configuration, instead, is more suited for comparison to the case of whole-body PET scanners, where high granularity is not required.

In general, slightly better performances have been found for the crystals coupled to the central MPPCs of the photo-detector array (i.e. B2, B3, C2 and C3 in figure 6), in terms of total light collection, energy resolution, and timing resolution. This difference can be explained, as already mentioned, with the non homogeneous light collection due to the finite dimensions of the $4 \times 4$ MPPC arrays. Anyway, this performance degradation remains very small, even for the crystals in the corners of the modules. Nevertheless, in discussing the results we will focus on the measurements obtained on scintillators coupled to the central MPPCs. The ultimate goal of this research, in fact, is to develop a module structure that can be instrumental to the development of a full PET detector. In such a scanner, several modules would have to be used, to cover a reasonable portion of the solid angle around the region of interest, and reach acceptable levels of sensitivity. The light sharing mechanism at the basis of this work
can easily be allowed between different modules, for example adopting a common light guide, and common optical coupling materials. This would be especially feasible in a flat scanner configuration, where two parallel plates are adopted, like for example in the ClearPEM breast scanner (Bugalho et al 2009), but also in cylindrical PET systems built by repetition of flat sections. As a result, only a few channels on the border of the detector would find themselves in the conditions experienced by the 12 border MPPCs of an Hamamatsu S13361-3050-AE-04 array. In a single module, central MPPCs represents only the 25\% of all the channels. Even in a rather small plate, made for example of 100 DOI modules arranged in a $10 \times 10$ matrix (for a total section of section of about $13 \times 13\text{ cm}^2$, considering some margin), 90\% of the MPPCs would be in the same conditions of the central channels of an individual module. The performance degradation due to border channels, already small in test modules, would be therefore negligible.

The light output has been found to be very similar between DOI and reference modules, both in $4 \times 4$ and $8 \times 8$ arrays. The main factors limiting light extraction are different between the two module structures. In particular, in DOI modules the presence of a light guide is expected to cause some amount of light loss, and at the same time optical photons are more likely to be absorbed by surface imperfections due to depolishing. In reference modules, instead, part of the light emitted upon scintillation is inevitably trapped inside the crystal, as a result of the combination of specular reflection (due to the polished surfaces) and the rectangular parallelepipedous shape of the scintillator. This limitation is not present in DOI modules, where the reflection of optical photons on lateral surfaces is in general not specular, due to the depolished finishing. The results in table 2 demonstrate that these factors on average are balancing out, and in both the $8 \times 8$ and the $4 \times 4$ modules no significant difference has been measured between the light output of DOI and reference configurations. The light output of $8 \times 8$ modules, instead, is in general lower (about 15\%) with respect to $4 \times 4$ modules. This is a known consequence of the higher aspect ratio of small cross-section scintillators, that makes light extraction less efficient, as already reported in literature in the past (Auffray et al 2013). As expected, energy resolution does not degrade between reference and DOI modules, as an effect of the similar light collection. The lower light output of $8 \times 8$ modules does not reflect in a degraded energy resolution, and on average resolutions around 9\% FWHM at 511 keV photopeak have been found in all the configurations tested.

Excellent levels of performance have been measured in term of timing resolution in both reference and DOI modules, and a consistent improvement in CTR, similar to the one shown in figure 13, has been found for all the scintillators in each DOI module upon application of the timing correction method described in section 2.2. In order to ensure the correctness of the procedure adopted to estimate the timing resolution, and especially to validate the absolute values of CTR $\sim 160$ ps FWHM presented in table 2, a coincidence acquisition was performed between the two reference modules R.16.1 and R.16.2. The purpose is to measure directly the width of delay histograms acquired in coincidence between arrays, without the need to estimate it after the subtraction of the contribution of the external reference detector. The experimental setup is the same described in figure 9, but with one reference module plugged into each FEB, while the $^{22}$Na source is placed approximately halfway.

**Figure 20.** Example of delay histogram recorded between two scintillators from different $4 \times 4$ reference modules, when a $^{22}$Na source is place approximately halfway between the modules (blue), when the source is moved 3 cm towards the right (red), and 3 cm towards the left (green). The full width at half maximum of the distributions are reported on the figure, together with the distance between the centroids.
between them. For each pair of crystals, one for each module, events with simultaneous 511 keV depositions are selected and a delay histogram is built. An example is represented by the blue histogram in figure 20. The average CTR measured on such histograms, for all the possible pairs of scintillators among the four central ones of both the modules, was evaluated in \(160 \pm 2\) ps FWHM. This value is compatible with the ones reported in table 2, and demonstrate the quantitative correctness of the procedure to estimate the timing resolution of the modules. Furthermore, we repeated the same measurement displacing the \(^{22}\text{Na}\) source by 3 cm along the line connecting the two modules, first in one direction, then in the opposite one. The centroid of the delay histograms moved accordingly by \(\sim 200\) ps, as expected (green and red histograms in figure 20). The peaks can be clearly separated, giving a visual confirmation of the resolving power achieved with the setup.

A general degradation of CTR when passing from reference to DOI modules has been found, if the non-corrected, standard CTR\(_{\text{std}}\) is considered, i.e. when the resolution is calculated only on the basis of the signal of the photo-detector \(D_1\) coupled to the crystal of interaction. This is expected, since while almost all the light reaches this photo-detector in the case of reference modules, a consistent portion (in general between 40\% and 60\%) is shared to the neighboring channels in DOI modules. The degradation of CTR\(_{\text{corr}}\) is more consistent in the case of \(8 \times 8\) modules, where the higher aspect ratio results in a larger mean number of interactions for the optical photons with the lateral surfaces of the scintillators, before having a chance to be extracted. This, combined with the modification to the directions of photons introduced by the depolishing, increases the spread in the travel path of the photons, deteriorating the timing performance. When the entire information carried by the optical photons is taken into account, however, by means of the proposed timing correction method, the CTR is recovered, and an average CTR\(_{\text{corr}}\) of \(159 \pm 2\) ps FWHM and \(157 \pm 2\) ps FWHM is reached with \(4 \times 4\) and \(8 \times 8\) DOI modules, respectively. Both values are compatible with the ones obtained with reference modules.

5. Conclusions

We developed a 64-channels readout setup with excellent timing resolution, to test the performance of a DOI extraction method, previously proposed by our group, based on light sharing. At the same time, we proposed and tested a method to improve the CTR in this configuration, by combining the timestamps extracted by the individual detector channels with the use of the DOI information. The results obtained demonstrate that it is possible to achieve a timing resolution below 160 ps FWHM in a structure based on 15 mm long LYSO:Ce scintillators, while simultaneously providing a spatial resolution of 1.5 mm FWHM, a DOI resolution of 3 mm FWHM, and an energy resolution of 9\% FWHM, as already demonstrated in previous works. These levels of performance, coupled to the inherent simplicity of the module structure, and the relatively low production costs due to the single side readout, make this method particularly attractive for the development of a high resolution PET scanner. Furthermore, the values of CTR obtained after timing correction on all tested samples, demonstrate that this configuration allows to extract DOI information without intrinsically degrading the timing performance, with respect to a standard module of the same crystal dimensions but without DOI capability. The light sharing scheme presented in section 2.1, combined with the method described in section 2.2, could represents therefore a viable solution to overcome the physical limitations of CTR due to the mismatch of speed between gamma rays and optical photons in dense scintillators.

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