EndoTOFPET-US - A Miniaturised Calorimeter for Endoscopic Time-of-Flight Positron Emission Tomography

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Abstract. In the scope of the EndoTOFPET-US project, a novel multimodal device for Ultrasound (US) Endoscopy and Positron Emission Tomography (PET) is being developed. The project aims at detecting and quantifying morphologic and functional markers and developing new biomarkers for pancreas and prostate oncology. Exploiting the Time-of-Flight (TOF) information of the gamma rays allows for a more sensitive, more precise and lower radiation-dose imaging and intervention on small internal structures. The detection of the gamma rays is realised with the help of scintillator crystals with Silicon Photomultiplier (SiPM) read-out, aiming at a coincidence time resolution of 200 ps and a spatial resolution of \( \approx 1 \text{ mm} \). For the endoscopic detector, digital SiPMs are utilised for the first time in an instrument planned for clinical applications. The functionality of the instrument as well as the challenges that accompany the high miniaturisation of the endoscopic detector and the asymmetric and variable geometry of the system, are presented. The demands on the system involve the fields of scintillating crystallography, ultra-fast photon detection, highly integrated electronics, system integration as well as image reconstruction.

The single detector components have been fully characterised and are performing up to specifications. Two dedicated ASIC chips have been developed for the project. The first PET images have been acquired with a test setup that consists solely of hardware and software developed within the collaboration and demonstrate that the data acquisition and reconstruction chain is operational. In this talk, the characterisation of the single components and the status of the detector integration and commissioning is presented.

1. Introduction
The EndoTOFPET-US detector is being developed for the evaluation of new biomarkers and for diagnostic interventional imaging [1, 2, 3]. It consists of a miniaturised PET detector head mounted on an ultrasound endoscope as well as an external detector plate being located next to the patient. The detection of the coincident gamma rays is carried out with scintillation crystals read out by silicon photomultipliers. The first endoscopic prototype is being developed for prostate exams whereas the external plate can be utilised for both prostatic and pancreatic exams. This report reviews the design of the detector system and its software and mainly focuses on the latest results of the project.
2. Internal Probe

2.1. Design

The endoscopic detector comes in two different versions, one for the prostate exam and one for the pancreatic exam. The first prototype will be designed for the prostate case. In this case the endoscopic PET detector is mounted on the trans-rectal ultrasound (US) endoscope EUP-U533 from Hitachi. The PET head extension will be clamped onto the endoscope without altering the endoscope itself. The PET head must not exceed a volume of $23 \times 23 \times 40 \text{ mm}^3$ due to anatomical constraints. Due to the immediate proximity of the detector to the organ under study, a high granularity is crucial for an excellent spatial resolution. This is realised by the use of two matrices of $9 \times 18$ LYSO scintillator crystals from Proteus with a size of $0.71 \times 0.71 \times 15 \text{ mm}^3$. They are coupled with optical glue to two boards of multi-channel digital SiPMs (MD-SiPMs). A front-end printed circuit board (PCB) provides a digital output via an interconnection to the data acquisition (DAQ) card. Besides, a water cooling pipe is embedded in the detector housing which is necessary to ensure a low dark count rate (DCR) despite the heat generation by the electronics. A sketch of the US endoscope and the PET extension is depicted in Fig. 1 (left), along with a drawing of the outer plate design.

![Sketch of design](image)

Figure 1: (left) Sketch of the design of the endoscopic ultrasound endoscope with the PET head extension. The inlet shows a zoom of the PET head, depicting the crystal matrices, MD-SiPMs, PCB and cooling pipes. (right) CAD drawing of the current design of the external PET detector plate. The green plate underneath the detector depicts the front-end boards. Above that, two aluminium plates (grey) house the cooling and mechanically fix the printed circuit boards (PCBs) on which the ASICS are mounted. The uppermost structure symbolises the crystal matrices and the SiPM arrays.

2.2. Multichannel digital Silicon Photomultipliers

The photodetectors of the internal probe are multi-channel digital Silicon photomultipliers (MD-SiPMs) which have been custom developed within the collaboration [4, 5]. The sensor has a size of $7.2 \times 14.4 \text{ mm}^2$ and is composed of $9 \times 18$ MD-SiPMs or clusters, each of which contains of $16 \times 26$ single photon avalanche diode (SPAD) pixels with a size of $30 \times 50 \mu\text{m}^2$. The SPADs are equipped with a one-bit counter which provides the digital count of pixels fired. They are read out column-wise with multiple time-to-digital converters (TDCs) which enables independent photon time-of-arrival measurements. A reasonable trade-off between fill factor and number of time-over-threshold measurements leads to a number of 48 TDCs per column of clusters and a fill factor of 57%. Combining the information of the different timestamps statistically ensures that the lower bound of the theoretically achievable CTR is always reached and thus improves the CTR significantly [6, 7, 8]. Digital SiPMs typically suffer from high dark count rate (DCR) which, however, can be significantly reduced by cooling and by masking noisy pixels.
This behaviour is shown in Fig. 2. As can be seen, a DCR of 41 MHz without masking at a temperature of 20°C and 3 V excess bias can be reduced to 23 MHz with \( \approx 10\% \) masking. The photon detection efficiency (PDE) in this scenario is \( \approx 12\% \). Fig. 2 (right) shows the benefits of additional cooling. The single pixel time resolution of the prototype sensor has been determined to be 120 ± 13 ps FWHM excluding the laser and clock jitter.

The 9 \( \times \) 18 MD-SiPM chip has been fabricated and tested. It features in-situ statistical analysis of the gamma events, real-time noise rejection, a high-speed interface with the DAQ as well as multi-channel timestamping.

Figure 2: Photon detection efficiency (PDE) of the 4 \( \times \) 4 MD-SiPM prototype as a function of the dark count rate (DCR) for different masking levels and for different excess bias voltages (left) and different temperatures (right).

3. External Plate

3.1. Design

The outer detector plate has an area of 23 \( \times \) 23 cm\(^2\) and consists of 4096 LYSO crystals from Crystal Photonics Inc. with a size of 3.5 \( \times \) 3.5 \( \times \) 15 mm\(^3\). The crystals are separated by a 100 \( \mu \)m thick reflector foil from Vikuiti 3M\(^{TM}\). They are coupled to analogue xSiPMs which are discrete through-silicon via (TSV) MPPC arrays from Hamamatsu. Dedicated fast 64-channel application specific integrated circuits (ASICs) are mounted directly on the detector plate in order to optimise the timing properties. Two cooling plates are embedded in the detector housing which consist of aluminium plates with integrated water pipes. The design of the outer plate is sketched in Fig. 1 (right). The frontend system comprises two types of boards, the board housing the ASICs (FEB/A) and the board interfacing to the DAQ (FEB/D). The FEB/A which is housing two 64-channel ASICs has one connector for each MPPC matrix allowing for easy replacement of damaged components and take care of the digitization of MPPC signals. The connectors between the FEB/A daughter boards and the FEB/D motherboard provide connections for input voltages, MPPC bias voltages, clocks, control bus and output links. The current design foresees 2 FEB/D boards mounted on the bottom of 2 cooling plates.

3.2. ASICs

The aim is to develop a front-end TOF ASIC, being able to read out the time stamping and energy measurements. Special requirements are the time binning of 50 ps and a linear input bias range of 0.5 V as well as a low power consumption to minimise cooling. Two dedicated fast ASIC
prototypes have been developed, StiC [9] and TOFPET ASIC [10]. In both cases, the ASICs provide a fine time measurement and a time-over-threshold (ToT) measurement for each input pulse, where the latter one determines the pulse energy. The ASIC inhibits a self-triggering mechanism based on a double-threshold system. For the time measurement, a low threshold is used, whereas a higher threshold accommodates for dark count rejection and ToT measurement. Tab. 1 summarises some key parameters of the two ASICs.

|                         | STiC          | TOFPET-ASIC  |
|-------------------------|---------------|--------------|
| Jitter (at >5pC)        | < 30 ps       | < 25 ps      |
| Input bias lin. range   | 0.7 V         | 0.5 V        |
| TDC time bin width      | 50 ps         | 50 ps        |
| Power consumption       | 19 mW/ch.     | 8 mW/ch.     |
| Output rate             | 160 MBit/s    | 160 MBit/s   |

Table 1: Key parameters of the two ASICs, StiC and TOFPET.

Fig. 3 shows the measured coincidence time resolution (CTR) for the STiC (left) and the TOFPET (right) ASIC. The measurements with the 16-channel STiC chip are performed using a $^{22}$Na source and two $3.1 \times 3.1 \times 15$ mm LYSO crystals coupled to MPPCs. The MPPCs are connected to the STiC chip using differential readout. The energy resolution of the 511 keV peak is $\approx 12\%$. The measured CTR at optimal HV-settings is 220 ps FWHM. The final 64-channel STiC chip has been manufactured and tests are ongoing. The measurements with the 64-channel TOFPET ASIC also use a $^{22}$Na source and two $3.1 \times 3.1 \times 15$ mm LYSO crystals coupled to MPPCs in coincidence. They are connected to the TOFPET chip using single-ended readout. Using a preliminary calibration, the CTR in this case was measured to be 270 ps FWHM, see Fig. 3 (right).

Figure 3: Left: Coincidence time resolution (CTR) for different SiPM bias voltages for the STiC chip. Right: Distribution of the time difference between both modules, i.e. the CTR for the TOFPET chip.

3.3. SiPMs

A mass characterisation of the MPPC arrays has been performed in order to assure the quality of the devices as well as to adjust the operation bias voltage of all individual detector channels to the same gain. For this each MPPC array was characterized under low intensity laser light for 30 different applied bias voltages. For each voltage value a dark run is recorded to extract DCR
and crosstalk. The temperature dependence has been measured to be $\Delta V_{bd}/\Delta T = 70 \text{ mV/K}$ and the measurements have been corrected for that temperature dependency.

A typical single photo-electron spectrum is depicted in Fig. 4 (left). It is acquired by illuminating the MPPC channels with blue laser light, attenuated to low intensity to ensure single-photon detection. The MPPC is mounted on a motherboard incorporating linear amplifiers, high voltage filters and a temperature sensor. The output signal is amplified by a ten times voltage amplifier and read out by a VME-based charge-to-digital converter (QDC) with a resolution of 25 fC per QDC bin. The signal from the MPPC is integrated in a gate with effective length of 100 ns. The distance between the individual peaks of the single photo-electron spectrum is defined as the gain. It is plotted as a function of the applied bias voltage in Fig. 4 (right). From a linear fit, the breakdown voltage is extrapolated as the voltage at which the gain equals to zero. The knowledge of the breakdown voltage is of importance since all channels will operate at a fixed excess bias voltage to assure a homogenous detector response to incoming photons.

![Figure 4](image1)

**Figure 4:** (left) Single photo-electron spectrum (blue) with a multiple Gaussian fit (red asterisks). The red histogram is a spectrum from a dark run from which DCR and cross talk can be extracted. (right) Gain in million electrons as a function of the applied bias voltage as extracted from the single photo-electron spectra. The blue line is a straight line fit on the data points whose errors are negligible on this scale. The breakdown voltage ($V_{bd}$) and gain ($G$) at 1 V overvoltage, obtained from the fit, are given in the inlet.

Fig. 5 (left) shows the difference between the maximum and minimum breakdown voltage per matrix for all 269 MPPC matrices. The mean difference is 140 mV while the maximum difference is smaller than 300 mV for almost every matrix. The deviation is thus below 0.5 V required by the ASICs. In Fig. 5 (right) the DCR for each MPPC channel is shown. The threshold for accepting or rejecting the MPPC array is 3 MHz and the devices above this limit (red entries) have been sent back to the producer.

### 3.4. Crystals

The key parameter of the scintillation crystals is their light yield (LY) since it influences its time resolution. The LY of the external plate crystal matrices is measured with a photomultiplier tube (PMT) and a $^{137}$Cs source. Several response spectra are shown in Fig. 6 (left). In order to account for the differences between a loosely connected PMT and a glued and wrapped SiPM, the resulting LY is corrected for the air gap and the missing glue and wrapping. The average LY amounts to 32320 photons/MeV ±3.5% as can be seen from Fig. 6 (right). The energy resolution is $\approx 13\%$ for the external plate matrices, and similar for the internal probe matrices.
Figure 5: \textit{Left:} Distribution of the maximum difference maximum and minimum breakdown voltage $U_{bd}$ in one array. \textit{Right:} Distribution of the DCR at 0.5 pixels fired at 2.5 V excess bias for all SiPM channels. The red line indicates the threshold of acceptable DCR. Entries marked in red correspond to arrays with at least 1 channel that exceeds this limit.

Figure 6: \textit{Left:} Charge spectra of a $^{137}$Cs source (in arbitrary units) for 5 different matrices. \textit{Right:} Light yield (LY) for 290 crystal matrices.

The gluing of the crystals matrices to the MPPC arrays is performed with the help of an automated alignment setup with additional visual inspection in order to assure the alignment and absence of air bubbles. As an additional quality assurance test, current-voltage (IV) measurements are performed before and after the gluing. After the gluing, the crystals are wrapped with a reflector foil and covered with a thin plastic cap.
3.5. Modules

For the modules (crystal matrices glued to MPPC arrays), the light output, i.e. the number of fired pixels is determined. The experimental setup is similar to the one described in Sec. 3.3 with a $^{22}$Na source instead of a laser being used. Temperature monitoring and correction is applied and every channel is operated at the same gain ($G = 1.25 \cdot 10^6$). The mean energy resolution at 511 keV is $\approx 12.8\%$. The mean number of fired pixels at 511 keV is determined to be $1876 \pm 118$ as can be seen in Fig. 7 (left). The mean spread within one module is $\approx 15\%$.

Figure 7: Left: Distribution of the light output for 511 keV photons in number of fired pixels for all module channels. Right: Distribution of the coincidence time resolution (CTR).

Besides, the coincidence time resolution (CTR) is measured for all modules. For this, the time resolution of each module is measured in coincidence with a reference module. It has been determined with the time-over-threshold method with an ultra-fast amplifier-discriminator chip (NINO)[11] and a time-to-digital converter. Fig. 7 (right) shows the distribution of the CTR for all channels. From this, a mean CTR of $239.5 \pm 10$ ps can be extracted.

4. DAQ & software environment

4.1. DAQ

The data acquisition (DAQ) backend is implemented in a PCI-e board interfacing directly to the DAQ computer. It includes a powerful Virtex FPGA suitable to implement the trigger and data acquisition firmware. Four high speed links to the external plate and up to two links to the endoscopic probe are available on board. Links for control and configuration of the frontend systems are also implemented, as well as central distribution of clock and sync signals. The firmware needed to move data from the external plate ASIC up to the data acquisition computer has been developed and fully tested. The DAQ firmware to communicate with the endoscopic probe system was developed and has been successfully tested. In order to control the communication between the multiple imaging and tracking devices, CAMPCom, a lightweight and portable communication framework for multimodal image-guided therapy [12, 13] has been developed within the project. The communication framework involves the full monitoring and quality control of all processes and enables the slow control. Moreover, a graphical user interface for the medical doctor including the visualisation of the PET/US image is available.
4.2. Tracking
The external plate will be held and thus tracked mechanically by a moveable and lockable arm. It will be additionally tracked by optical tracking system. The expected accuracy is $\approx 0.5$ mm and $0.5^\circ$. The transrectal endoscope will be tracked optically as well. Electromagnetic tracking is not able to provide the required tracking accuracy below 1 mm.

4.3. Image reconstruction
A dedicated image reconstruction based on the ML-EM algorithm has been developed within the project and accounts for the limited field of view and the freehand nature of the acquisition that results in an undefined and continuously changing volume of interest [14]. In order to solve the massively parallel problem of inverting huge matrices the computation is performed on powerful graphic processing units (GPUs). They enable a speedup by a factor of $O(10)$ with respect to conventional central processing unit (CPU) computation, providing an on-line reconstructed image within the order of minutes.

5. Detector integration
As a first proof of principle, the functionality of the full data acquisition, readout and analysis chain is tested with only a few detector channels in coincidence. The 16-channel prototype chip STiC2 was used to read out eight channels of two detector modules. The two detector modules are rotated by 180 degrees in 30 distinct steps around two $^{22}$Na sources with a distance of $\approx 1$ cm. 50k events have been acquired per detector pose. Coincidence events are found by selecting only events from the photopeak and applying a coincidence time window of 2 ns. In Fig. 8 the measurement setup is shown on the left and the reconstructed image of the two-point source can be seen on the right hand side. The reconstructed spatial resolution of the image is $\approx 3 - 4$ mm which is expected since the image quality is driven by the low number of channels and the crystal size of 3.5 mm. It however gives a first proof of principle that the complete acquisition, readout and image reconstruction chain is operational.

![Figure 8: Left: Setup for the coincidence measurements Right: Reconstructed image of the two point sources.](image)

6. Conclusion & Outlook
The EndoTOFPET-US project is a very challenging project due to the extreme miniaturisation of the endoscopic detector, the high demands on the timing characteristics of crystals, SiPMs and ASICs as well as the required reconstructed spatial image resolution of 1 mm. Quality assurance
measurements of the MPPCs and crystals have been performed and its key parameters such as breakdown voltage, gain, DCR and light yield have been extracted. All detector modules have been assembled and fully characterised. It was shown that the measured coincidence time resolution is close to design goal of 200 ps. Two dedicated ASICs have been developed within the project and are shown to perform up to specifications.

The final decision on the choice of the ASIC will be based on measurements to be made with the 64-channel chips fully connected to the detector modules. After the mechanical integration, integration tests of the full firmware reading simultaneously the external plate ASICs and the probe SPAD will be performed. Then, the tracking system will be integrated and the fully operating detector system, including DAQ, reconstruction, PET-US fusion etc will be validated. According to the schedule pre-clinical tests are supposed to start in autumn of 2014.

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