POsition-sensitive SiPMs Compact and Scalable Beta-Camera (POSiCS)

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ABSTRACT

POSICS proposed a new approach for imaging in Radio-Guided Surgery (RGS). The camera is extremely versatile and can be used as beta or gamma imaging camera, depending on the configuration used, achieving a millimetre spatial resolution in reconstructing tumours with size ranging from few millimetres to centimetres with an acquisition time of tenths of seconds and at a depth up greater than 3 centimetres when detecting gammas. The system is quite compact and features a new sensor technology which can be readout with few channels even if highly segmented.

Keywords: RGS; Gamma camera; Beta camera; position-sensitive detector.

1. INTRODUCTION.

The use of gamma detection technology has nowadays established as a discipline within the practice of Radio-Guided Surgery (RGS) revolutionizing the surgical management of many tumours, improving the effectiveness of the treatment as well as the patient life quality after surgery.
Less explored, instead, is the direct detection of beta (e^+/e^-) emission by radiotracer. This is due to their absorption and decay in traversing the tissue, limiting its application to superficial tumours. However, in this application can be very beneficial allowing to reach a very high definition of the tumour margins for its precise resection, limiting the impact on patient life after treatment.

The goal of POSICS project is to prove the feasibility of a handled imaging device (camera), which can work as beta or gamma camera by simply changing the front part to target a large number of medical applications.

We targeted in our simulation studies 2 extreme cases: The Radio-Guided Surgery of superficial brain tumours as Gliomas which is based on the use of beta detection, and the identification of Sentinel Lymph Nodes (SLN), which can be detected in outpatient treatment based on gamma detection. While the former application requires a much longer path to go to a real product, the second one seems to be more interesting both for the larger number of potential applications, and therefore a wider market, and because the clinical trial and the certifications, needed to go on the market, can be easier and faster, being an outpatient treatment.

The camera developed in the POSICS project has many relevant features than makes it extremely interesting:

- good spatial resolution (we targeted 1 mm, but it can even go below in specific applications)
- innovative sensor technology, which allows a large number of pixels to be readout with few channels
- high scalability, by assembling together the single sensor to create larger tiles to cover a larger area, with limited increment of the number of channels.

The simulation studies confirm that a sub-millimetric spatial resolution can achieved in beta detection even with a single sensitive layer with the use of standard *Fluorodeoxyglucose (FDG-18)* radioactive tracer (radiotracer). Even more impressive is its capability, when used as gamma camera, to spot and define SLN of about 1 cm in radius at a depth greater than 3.5 cm inside the body with the use of *Technetium-99^m* as radiotracer.

2. STATE OF THE ART.

The Radio Guided surgery (RGS) has major impact on the surgical management of cancer treatment as it provides in real-time vital information, as the location and extent of disease, therefore allowing to minimize the surgical invasiveness of many procedures, both diagnostic and therapeutic, thus improving cancer patient life quality. The principle is to use a radioactive material is embedded in some molecules, creating the so-called radiotracer, which is administered to a patient.

The tumours, given their high metabolic activity, accumulates more radiotracer in their tissue than the ordinary ones. A particle detection system can identify a tumour by spotting the area of higher radiotracer activity.

Numerous handheld intraoperative radiation detection probe systems have been developed or have been made commercially available for RGS [1] They are divided into two general categories, depending on the specific radiation type: *Gamma probes*, detecting photon radiation or *Beta probes* detecting beta radiation, consisting of either electrons or positrons (e^+/e^-).

The most important performance characteristics of any given detection probe system are the overall sensitivity (efficiency), its spatial resolution, energy resolution and the contrast. The characteristics of the system are tuned according to the type of application but also the radiotracer type, which determines the particle energy and the activity (emitted particle per second).

The radiotracer used so far are quite limited for many reasons both technological and medical. Among the most used are the FDG-18, used for PET and Technetium-99^m which is much cheaper and widely used for in-situ administration as in radio guided sentinel lymph node biopsy (RGSLNB). In general, probe systems require high spatial resolution for more precise localization, as in case of small lymph node candidates, and at the same time of a high sensitivity, to the specific sites of disease while rapidly searching over a relatively large surgical field.

front part making it extremely versatile and usable in many radio-guided applications.

The POSICS camera is based on an innovative large-area position sensitive detector [2], developed at FBK, which allows a large number of pixels to be readout with only few channels. This allow to reach a high spatial resolution (we targeted 1 mm, but it be lower) with a small number of channels (4 channels for 10×10 mm^2 active area of the detector) and therefore a low-power and simpler electronics can be used.

The system is also highly scalable as well, being built by tiling together single units, to cover the desired area.

The readout scheme is such that the number of channels does not increase linearly with total area, i.e. number of sensors in the tiles. As an example, for the first demonstrator, here reported, an array of 2×2 tiles require 6 channels and not 16, i.e. the scaling goes as 2*(n+1) instead of 4n2. In this scheme, a 56×56 mm^2 area can be theoretically read with 16 channels.

Probably, the readout scheme can be further evolved to further reduce the channels at the cost of some resolution degradation.

Another important point is the high sensitivity, which is of capitol importance to reach short acquisition time (~10 sec) or conversely work with smaller doses. These characteristics allow to go for a relatively cheap device, which can be a self-contained, wireless and lightweight unit to be used in surgery rooms and widely in outpatient diagnostic.

3. BREAKTHROUGH CHARACTER OF THE PROJECT.

At present, existing probe system, being a tip-like system, have to trade-off between high-sensitivity and high spatial resolution. This can be overcome by the use of a camera, which have a very high spatial resolution on a relatively-large area thus achieving high sensitivity and high spatial resolution, being capable of taking a snapshot and integrate higher statistics in the same time needed for scanning the area of interest with a tip-like probe. The POSICS system, in addition, can work both as beta or gamma camera by simply interchanging the

4. PROJECT RESULTS.

The POSICS project was aiming at producing a small-scale prototype to assess its performance in positron/gamma detection. The COVID crisis instead delayed the production, but we manage to produce anyhow relevant result working on different tasks, like simulations of the system performance, in parallel to the development of the new detector and the development of a demonstrator (based on existing SiPM technology) with miniaturized front-end electronics. In particular, we focussed on the optimization of the system and also on other the possible application, from which came the idea to use it also as gamma camera

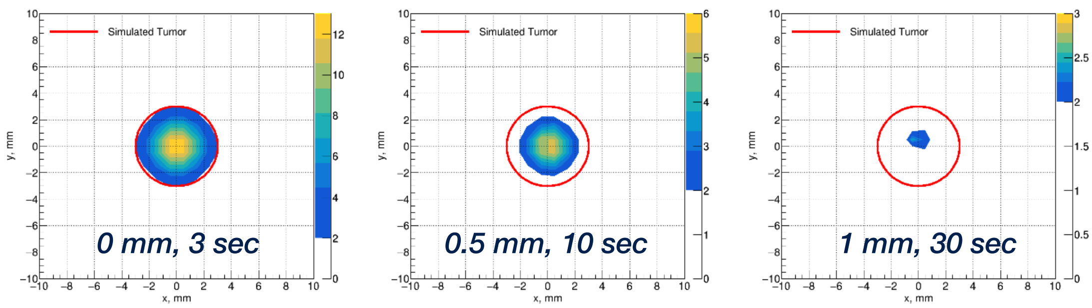

Fig. 1. Simulated performance of Beta camera for a tumour with a radius of 3 mm at different depth and for different acquisition time.

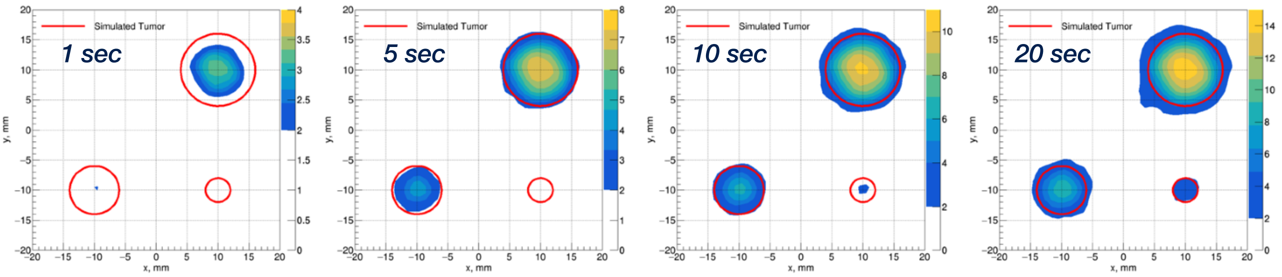

Fig. 2. Reconstructed image of tumours for three different radius (2 mm, 4 mm and 6mm) and for different acquisition time, when the camera is in direct contact. For tumour of 6 mm in radius, 1 second is enough to detect it and after 5 seconds the full size is detected with significance greater than 3 σ. For tumours of 4 mm in radius, slightly more than 5s seconds are needed to define its margin with significance greater than 3 σ. For tumours of 1 mm in radius, 10s seconds are needed to detect it and 20 to define its margin with significance greater than 3 σ.

We decide to focus then on two specifics cases, being complementary and also being based on the two most used radiotracer, the FDG-18 and the Technetium-99^{m}.

The original focus of the project was on the RGS in superficial brain tumours where spatial precision is of capitol importance and the beta are not absorbed being the tumour exposed. The idea was of using a double layer, one for beta and a second for the detection of the gamma coming from beta annihilation but proven to be redundant in the sense that a single layer is highly efficient in detecting beta, when working in close contact, while the second layer for gammas do not add much information. In **Fig. 1** is shown the performance of the beta camera using the FDG-18 as radiotracer, assuming an activity standard for PET, of 240 kBq/ml for the tumours 30 kBq/ml of the surrounding tissue, usually called uptake.

The beta camera can perfectly reconstruct a tumour with a radius of 3 mm with a 1 mm precision after 3 s of data taking, given the high sensitivity of the probe when in contact. To reach a similar level of precision for a tumour located 0.5 mm inside the tissue, 30 seconds are needed, and the margins resolution is not more than 2 mm. Going more in depth, the tumour cannot be correctly reconstructed.

The gamma camera instead can reach much higher depth as shown in **Fig. 2** and **Fig. 3**. Here, to give a comparison of the performances, the activity used for gamma is the same used for beta, even if the radiotracer for gamma camera is the Technetium-99^{m}. In specific applications, as in local administration, Technetium-99^{m} administered dose can be much higher than the one used here, and therefore performance can significantly improve. It is important to remark that the precision in reconstructing the tumour margins and its maximum depth, are strongly dependent from the activity of the radiotracer and the acquisition time. This is evident from **Fig. 2**, where three tumours of different radius (2 mm, 4 mm and 6 mm) are reconstructed for different acquisition time in case of superficial tumours (0 mm depth). In **Fig. 3** instead, the same tumours are reconstructed at different depth for the same acquisition time. The results shown are quite promising and can be further improved. We are exploring also the possibility to use the uptake of the surrounding tissue to estimate the average tissue uptake and, from this, evaluate the expected tumour activity.

This 'nominal' activity will then be attenuated depending of the tumour depth, which can be extrapolated comparing the measured and expected activity from simulation.

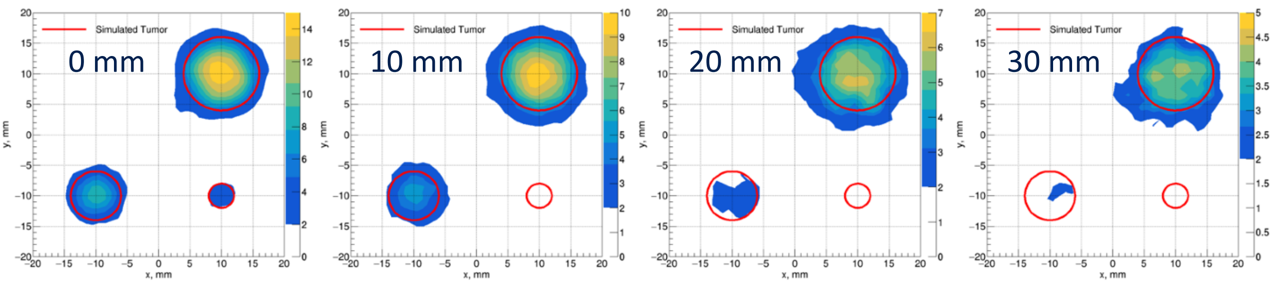

Fig. 3. Reconstructed image of the same tumours in Fig. 2 for an acquisition time of 20 seconds but situated at different depth into the body. When the probe is in contact all three tumours are well reconstructed. The 2 mm tumour can't be reconstructed at depth greater 10 mm. The 4 mm tumour is detected even 30 mm in depth but above 10 mm the margins are not well resolved. The 6 mm tumour is well reconstructed even at 30 mm.

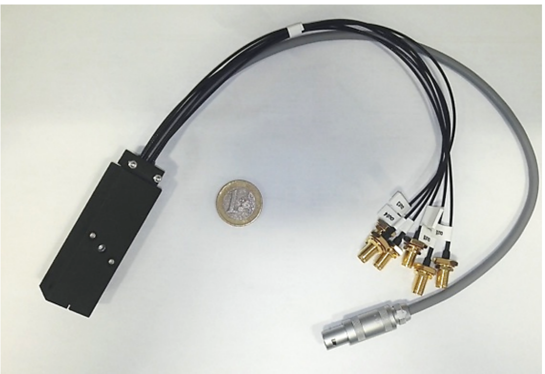

Fig. 5. Picture of the prototype camera with a 2×2 array of SiPMs. The active area is 1.6x1.6 mm^2. The final POSICS camera will be built with a 3x3 array to cover 2.4×2.4 mm^2.

In parallel we also worked on the development of a new compact and handy detector, to be used as demonstrator of the beta/gamma camera. It is based on a 2×2 tile of position sensitive LG-SiPMs [3]. They are based on FBK RGB-HD. Each SiPM have a total dimension of 8×8mm^2, with 20µm cell pitch. The SiPMs are connected in way to have only 6-output channels (starting from 4 output per each device), in particular 3 channels for the X coordinate and 3 for the Y coordinate. The photon position is determined based on the amplitude or charge of these 6 channels. The probe is very compact (~2.2×2.2×7 cm^3) and contains the SiPM tile, 6 amplifiers and biasing electronics (see **Fig. 5**).

We tested the performance of the LG-SiPM probe, scanning the active area with a pulsed LED with a collimator of 200µm in front of the SiPM tile to reduce spot size. We scanned the active area of with a step of 0.7 mm, between -7 mm to +7 mm, with average of 800 ph/pulse. Reconstructed map is reported in **Fig.4**. It can be seen that, despite the small pincushion distortion, and some minor detector non-idealises, the accuracy is much better than required 0.5 mm.

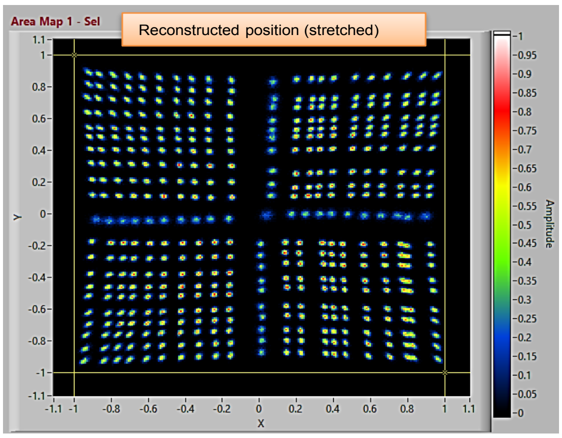

Fig.4. The measured reconstructed-position map of the 2x2 probe. Scan has been done with a step of 0.7mm, using a pulse LED, with 200µm pinhole. The reconstructed positions show a clear pincushion distortion, due to the reduce-channel readout method. However, a 0,5 mm precision is achieved.

5. FUTURE PROJECT VISION.

5.1. Technology Scaling.

The sensor technology is well established but at system level some more developments are needed to reach TRL 4.

The current sensor is only two side buttable, while to produce large areas it would be better to have a 4 side buttable device. This can be achieved with a limited work on the sensor (about 6 man-months and about of 100’000 €). The technology used for the position sensitive device can be considered CMOS compatible. FBK has already experience in technology transfer to external foundry for mass production, which facilitate the scaling of the detector technology.

The ideal camera would have a dedicated low-power and wireless electronics which allow to run on battery and provide a complete wireless, light weight handled devices. This would be preferably an ASIC, to make it cheap and easy manufactured (18-24 man-months and about 200’000 € for the production). It is as well possible that solution also from other ATTRACT projects can provide what needed (see next section 5.2).

We will go in parallel for a wired solution which would allow to use standard electronics and can be ready in short time for laboratory test. Some development is needed both for the receiving station of the data (6 man-months and 50’000 €) as well as all the software for the image reconstruction and GUI for data presentation and camera parameter settings (18 man-months).

The design of mechanics it is also a mandatory step before going to TRL 5. It is necessary to produce an ergonomics design for easy and comfortable handling in clinical application (6-10 man-months and 20’000 €).

Scaling to TRL 6 can be relatively fast, as the prototype for TRL 4 can be used without major modification for the intensive test needed (12-15 man-months and 30’000 € for test set-up and phantoms). Here we are clearly targeting the gamma imaging camera for outpatient treatment for which the clinical trial needed for TRL 7 can be easy to agree with hospitals.

A mandatory step for the clinical trial is the CE certification of the systems, but the path for it is not particularly difficult for this device. A certification company, for this type of application, can deal with the whole process for a reasonable cost (~20’000 €).

5.2. Project Synergies and Outreach.

To reach TRL 7, new competences are needed in the consortium in particular ASIC design, software design for readout system and image reconstruction, design for ergonomics, wireless communication.
Particular important would be the involvement of clinical research group for the clinical trial and validation.

Some synergies with existing ATTRACT Phase 1 project is being explored with the respective project leaders. The project SP-LADOS is led by FBK, a partner of POSICS, aims at developing a sensor with a large area, which can also be segmented to provide spatial information. It can be possible to think about multi-modality imaging and investigations techniques, combining NIR and gamma-ray imaging capabilities.

The technology can be exploited in both systems, creating a compact probe and reducing the development time and costs. The FastICpix project, aiming at a reconfigurable low light-level (LLL) hybrid sensor that can be scaled to arbitrarily large areas, whose granularity is configurable with dedicated electronics, which can be uses for POSICS. There could be, as well, a synergy between CERN and FBK on the sensor development.

5.3. Technology application and demonstration cases.

POSIC projects is clearly targeting the societal challenge on Health in the field of improving the way to detect, treat and manage disease. It can impact on patient quality life after treatment in RGS, but it would also introduce a new non-invasive detection tool for sentinel lymph node detection, or mammal cancer. POSICS is the proof-of-concepts of the paradigm from basic science to societal impact via innovation. New technology can go to market and open new possibility. What is needed is to increased is the awareness of the research community about the private investor as resource to move to market their technologies. Initiative like ATTRACT have this big added value, to put in contact research (public and private) and economy (private investors, incubators, etc). For this it would be very useful to start a forum Industry-Research in which researcher can propose their project and private investor can go and look for innovation and new solutions; conversely private investors or technology experts can present open challenges and call for new ideas seeding in researcher new line of research.

5.4. Technology commercialization.

POSICS can have a quite short path to the market for the gamma application. The application has judged interesting from a start-up on gamma probes. POSICs is clearly targeting the TRL-7. In three years and with a budget of about 1.5 M€, TRL-6 can be reached. The time and the budget match ATTRACT Phase II Scheme.

Otherwise, it will be possible to move to TRL-7 with private investors or business angels or creating a start-up.

Nothing in this direction has yet been started as results on performance, demonstrate on prototype, are not yet available.

5.5. Envisioned risks.

Even though we are targeting further innovation, POSICS has no major technological risk as it has already a sensor technology that can make it to work. On the contrary, there are risk related to its clinical application.

How its use can fit the clinical protocol and standards, and also the type of information and the way to provide it to the surgeon, needs to be better refined. To this goal we are establishing contact with medical research institutes both in Switzerland (HUG, CHUV) and in Italy to study their protocols and discuss their needs and expectation for such type of devices.

5.6. Liaison with Student Teams and Socio-Economic Study.

This project involves a research institute and a University, both with a solid a strong background in communication and outreach. As matter of fact, a MSc student is working on the POSICS projects for her MSc thesis. The project coordinator as well, is teaching since year detector technology at university and it has done several public conferences on detection technique.

In ATTRACT Phase 2 a dedicate effort as part of the project can be envisaged, starting collaborations with MSc student but also from other discipline (art, design, communication), to prepare dedicated material (cartoon, video, brochures, etc) to target a wide public audience.

The goal is to increase in the general public awareness of the nuclear medicine, advantages and risks, and show how basic science can tackle societal challenges through innovation.

This can be also beneficial for the ATTRACT initiative, showing its impact in promoting innovation in the EU community, via the building of a solid network between industry, research and private investors.

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