Energie, santé, applications sociétales

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Contents

1 Introduction

In medical physics the main areas related to the use of the ionizing radiation are the following.

1. *Medical imaging.*

   (a) *Radiography* uses the X-rays in the range of 20 – 150 keV to image the patient body. An example of the radiography modalities are X-ray planar imaging, computed tomography (CT), mammography, etc.

   (b) *Nuclear medicine imaging*, see item 4b.

2. *Radiation therapy* is one of the main modalities for cancer treatment. Its includes several different types.

   (a) One of the most frequently used is the *X-rays treatment*, where X-rays (or gamma rays) are usually produced with the with linear accelerator in the range 4 – 25 MeV or with radioactive sources with the energies around of 1 MeV.

   (b) *Electrons* from the linear accelerators could be also used for treatment. Usually the same linac could be use for X-ray and electron treatment.

(c) *Hadron therapy* is the actively growing field, which uses mostly protons for cancer treatment, but use of the light ions is also under study.

(d) *Nuclear medicine therapy*, see item 4a.

3. *Radiation dosimetry* is a part of medical physics devoted to the control and prevention of health risks related to the exposure to the natural and artificial sources of ionizing radiation.

4. *Nuclear medicine* uses an internal source of radiation for treatment and diagnosis.

   (a) *Interventional nuclear medicine* used for cancer treatment. It can be divided in *unsealed source radiotherapy* and or *sealed source radiotherapy* (or *brachytherapy*, or *curietherapy*).

   (b) *Nuclear imaging technique* is widely used nowadays in oncology, cardiology and neuropsychiatry. It have three main modalities. *Scintigraphy* uses the "gamma camera" to detect the single photon emission and build a 2d planar image. The *single photon emission computed tomography (SPECT)* are used when the 3d imaging is necessary. The most powerful technique is a *positron emission tomography (PET)*, see 2. The CALIPSO group of DPhP currently develops the new type of detectors to be used in PET and these developments are described in section 2.2.

2 Positron Emission Tomography

The PET technology consists in injecting the patient with a radioactive tracer, often ^{18}F-fluorodeoxyglucose (FDG) with a half-life-time of 109.7 min. The tracer is retained preferentially by tissues with high metabolism, like most type of tumors. The decay of ^{18}F emits a positron which annihilate with an electron in the tissue after travelling a distance of about 0.6 mm[1]. As a result of the annihilation, two 511 keV gamma quanta are emitted back-to-back and registered in the coincidence by the dedicated detectors (Fig. 1). The conventional detectors are using the scintillation crystals with high photon yield. Currently the most popular crystals are the LSO or LYSO, despite their high price, mainly because of the high number of emitted photons (up to 40000/MeV) and fast scintillation (decay time $\sim$ 40 ns) [1]. The line-of-response (LOR) connects two points where photons are detected. Accumulation of the millions of LORs allows one to reconstruct the distribution of tracer and image the organs with high consumption of FDG.

Three types of PET scans are used in clinical practice and research. The *full body scan* is use to image the body of patient. It typically require an activity of about 3 to 5 MBq/kg to obtain an image with a good quality, corresponding to the typical effective dose up to 15 mSv and higher for an oncology scan (see, for example [2, 3]). This dose corresponds to several years of the natural radiation background (for example in France, 2.4 mSv/year) and may increases the risk of cancer appearance. This limits the use of the full body PET to cases with positive benefits-to-risk ratio. The full body scanners have large field of view (FOV) of about 40 cm and limited in spatial resolution mainly by the natural body movement, e.g. respiration, to values about 4 – 5 mm^3.

The *brain scan* plays an important role in research of the neurodegenerative diseases because PET technique allows one to reach a high sensitivity to the biochemical cellular activity with chemical abundances down to 10^{-12} mol [4]. At the same time its has only a moderate spatial resolution. The best dedicated devices, i.e High-Resolution Research Tomograph by Siemens reaches a precision of about 2.5 mm^3 [5] for the FOV of about 20 cm, while conventional MRI device with a 3T field

[1]In the following all precision numbers are given as FWHM

allows to obtain a 1 mm^3 precision, but only a moderate sensitivity to the biochemical cellular activity, about 10^{-4} mol. As described bellow, the CaLIPSO group of DPhP develops a new gamma-detection technique for PET to reach a sub-millimeter precision in brain scan.

The *small animal scan* is used for the preclinical research and usually require a very good spatial resolution of about 1 mm^3 for the small FOV of 5 – 10 cm.

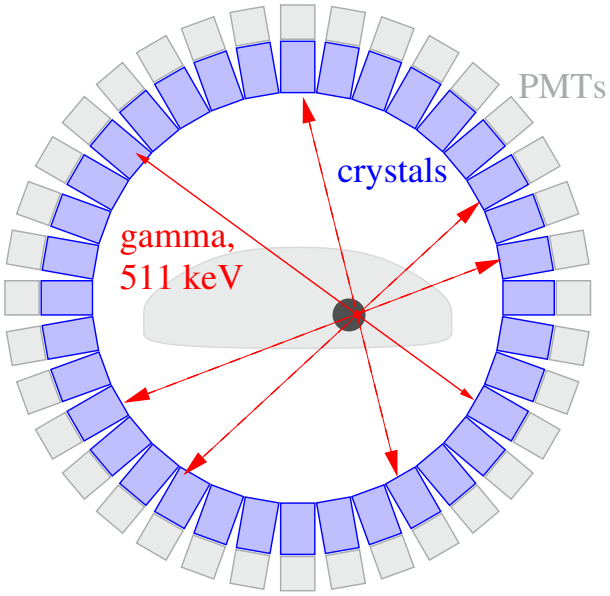

Figure 1: Positron emission tomography scheme.

2.1 Main Research Axes in PET Development

Currently there are several research axes to improve PET devices. In most of the cases the figure-of-merit for the "quality" of the scanner is the quality of produced images. It could be characterized by the contrast recovery factor and spatial resolution, and depends on the scanner sensitivity, the background contribution and scanner "dimensionality". Two sources of background are usually considered:

- *Scatter* coincidences: the events with at least one annihilation photon undergo the Compton scattering in subject.
- *Random* coincidences: events where two photons from the different annihilation vertices are overlap in the same coincidence window. The dark count events due to the natural radioactivity of crystals or photodetectors are usually also accounted as random coincidences.

"Dimensionality" of the scanner is related to the possibility to reconstruct the axial distribution of tracer without changing the bed position. For this, scanner should have more than one ring of detectors and be able to register the *oblique* LOR, e.g. LOR where two detectors have different z-coordinate position. To be able to use the third (axial) dimension, its is necessary to use the 3D image reconstruction algorithms, which usually are slower than 2D algorithms, but allow one to obtain a better image quality for the same accumulated statistics.

Additionally, the *time-of-flight* (TOF) capability is considered as a fourth dimension. The TOF technique consists in measuring the difference in time between two registered photons and use this

information in the image reconstruction algorithm, to limit the region of annihilation along LOR. The current achievable precision in *coincidence resolving time* (CRT) of 350 ps (for commercial scanner) and 150 ps (for laboratory tests at the test bench) are not sufficient to directly reconstruct the vertex, but allow to improve overall signal-to-background ratio during the image reconstruction. The TOF capability gives the largest gain for the subject of a large size, e.g. for the subject with diameter of about 20 cm, the CRT of 100 ps will give a gain of about $\sqrt{D/2c\Delta t} \sim 3$ (c is a speed of light), which corresponds to an improvement of a factor 9 in statistics comparing to the scanner without TOF. For the brain size object, $D \sim 10$ cm, the gain is smaller, but appreciable, especially, when high resolution is needed.

The following main research directions are currently considered for the PET development.

1. Currently an improvement of TOF precision is a major development axis at the research laboratories. Almost all new designed system have the TOF capability. The main efforts are concentrated on the improvement of the timing performances of photo-detectors, development of the scintillators with higher photons yield and faster scintillation. The CaLIPSO group is also working actively in this direction, but it exploits the possibility to use the Cherenkov light for boosting the TOF performance, as explained below.

2. Improvement in scanner sensitivity by increasing the scanner solid angle. This is a rather straightforward development, which nevertheless rise several challenges. In particular, the high price of such scanner; large number of channels and high data acquisitions rate; large number of the possible LOR and, consequently, necessity to adapt the image reconstruction algorithm to deal with large number of LORs in a reasonable time scale. Recently the *Explorer* US consortium received a funding to build the first total body scanner [6].

3. The typical radial thickness of crystals required for the efficient one-layer detection of 511 keV photons is about 20 mm. Such thickness leads to a significant bias in the LOR reconstruction, known as *depth of interaction* (DOI) parallax error. Indeed, the position of the photon conversion along the crystal radial axis is not known and usually assigned to the most probable position during reconstruction. This assumption leads to the bias in the LOR position, which depends on the scanner radial size and could be as large as several millimeters for LOR far from the center. One can reduces this bias either by reducing the crystal thickness for the price of sensitivity or adding the possibilities to reconstruct the DOI coordinate. There are many different approaches for DOI determination. For example, two-layer detection system, where two different crystals are glued together [5]; crystals with a special surface treatment which provide an indication about DOI; crystals divided by a specially designed separators and/or having the dual readout, etc. Most of these systems reach only a modest precision on the DOI coordinate and only the simplest one (i.e. the two layer detection) is implemented in commercial systems [7, 8, 9, 10].

4. The recent development in silicon photo-multipliers (SiPM) production, boosted a lot of development in PET. Indeed, a rather low price, compact size, low sensitivity to the magnetic field and excellent amplitude and time resolution are the attractive points of such device. The temperature dependence and the huge dark count rate are the factor which limits the use of SiPM. Most of the current development in the research labs are designed to use the SiPM. Additionally, such device could be easily integrated with a read-out circuit at the surface of one channel (typically several square millimeter) and provide a digital-only read-out [11].

5. There are several development which are using the monolithic crystals, i.e. crystals with a large surface (typically 10 x 10 or 20 x 20 mm^2), not divided to small dyes. In such crystals the information about the conversion point is extracted by the center-of-gravity or more complicated estimators using the distribution of scintillation photons at the photo-detection surface(s). This method, potentially could improve the spatial precision of the conversion point localization and provide a DOI information [12, 13, 14].

6. A lot of works are currently are done by combining a different imaging modalities. In particular, the use of CT scanner with PET is a well establish technique. It allows to improve the quality of the PET images a lot by using the anatomical information from CT to estimate attenuation correction in PET imaging.

   The use of PET and *magnetic-resonance imaging* (MRI) together is also investigated, but progress is rather modest. The main obstacle, that MRI are mainly sensitive to the soft-tissue and not so-sensitive to the bones, so the estimation of the scattering correction is not trivial. Another problems, that PET system is need to be equipped with the photo-multipliers insensitive to the magnetic field in order to work inside or close-by the MRI. The obvious advantage of the PET-MR system is an absence of the additional radiation exposure due-to the CT scan.

7. Another research axe is an improvement of the spatial resolution for the full body scan, by using the motion sensor and either correcting the image according to the sensor information or gating a data acquisition to a part of the respiratory cycle [7].

2.2 Current activities in DPhP

The CaLIPSO group of DPhP is working on several PET projects. The aim of the CaLIPSO project (french acronym for Liquid Ionization Calorimeter, Scintillation Position Organometallic) is to develop the proof of concept of a fast and efficient gamma detector using the new liquid: the TriMethyl Bismuth (TMBi). This innovative liquid allows a very efficient detection of positron annihilation (idea is protected by a CEA patent [15]). The CaLIPSO detector has been designed to meet the demanding specifications of a high precision brain-scanning PET device. The 511-keV photons from the positron annihilation in tissue are efficiently converted in electrons through the photoelectric effect in TMBi. Relativistic electrons produce photons through the Cherenkov effect and release electron-ion pairs in the liquid TMBi. The CaLIPSO detector works as a time-projection chamber and detects both ionization and light signals, Fig. 2. The simultaneous detection of light and ionization signals leads to very promising performances. It is anticipated to reach a precision on gamma conversion localisation in detector volume down to 1 mm^3 (due to the time projection ionization signal), 10% photon energy resolution, single interaction (photoelectric) conversion probability above 47% and a CRT better than 150 ps. Once fully developed and integrated with an acquisition system, the CaLIPSO technology will allow one to produce a brain PET-scan with a spatial resolution of 1 cubic millimeter, typical of clinical MRI imager, uniform over an entire head, and to map the biochemical (cellular) activity of the brain down to 10^{12} mol.

Recently CaLIPSO demonstrated the efficient detection of the Cherenkov light in TMBi liquid [16]. Currently the study with a new optical prototype constructed in July 2017 is on-going. This prototype used with the fast *micro-channel-plate photomultiplier* (MCP-PM), will allow to measure the resolution in time for this prototype. In parallel the study of the ionization signal is continued. As a first step, the ionization yield is measured both, in TMBi and in the reference liquid

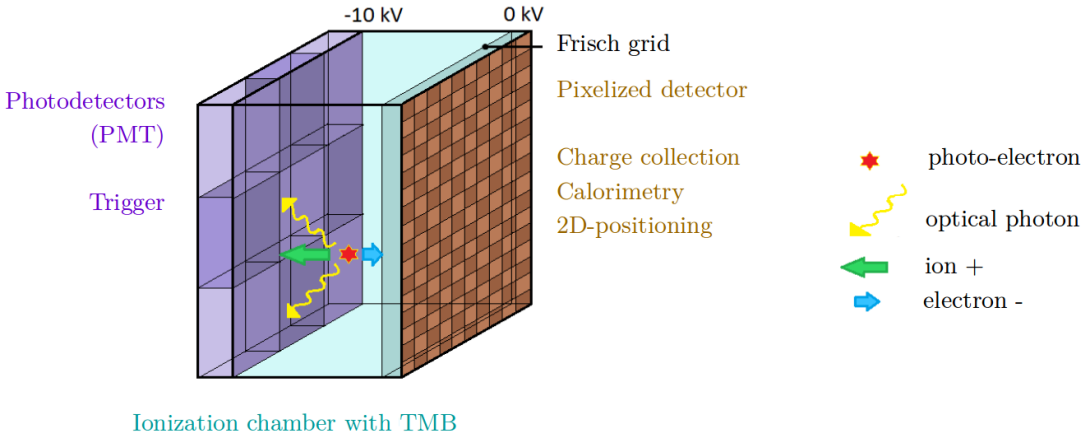

Figure 2: Main components of a foreseen CaLIPSO detector.

TMSi. As a next step, the demonstration of the individual signal and measurement of the electron life-time in TMBi liquid is foreseen. CaLIPSO group is also working actively on the simulation of the full body scanner using the GATE software in collaboration with SHFJ, I^{2}BM, CEA. Such simulation allows to estimate the performance of the proposed technology.

Another project PECHE studies the potential of the Cherenkov light for the full body PET scanner with enhanced TOF performance using the crystalline lead fluoride of chemical formula PbF_2. This crystal produces no scintillation light, but only Cherenkov radiation. It is very dense (7.8 g/cm^3) and has one of the highest photoelectric fraction, 46%. Due to these facts, it is possible to create an efficient gamma detectors with a very small thickness of the order of 10 mm and hence minimize the dispersion of the photon trajectories, Fig. 3. The low efficiency is a major limiting factor for making when using Cherenkov light. To overtake this limitation we are improving the optical interface between crystal and MCP-PMT with the sapphire window. The goal of the project is to reach a 100 ps resolution in time or better. Currently the first results are obtained with a 150 ps per detector. The work is continuing on improvement of the read-out electronics and detector optimization.

The third project, ClearMind, launched by CaLIPSO group this autumn is a further development of the idea of Cherenkov detectors, but using together with the scintillation in a monolithic crystal. This idea may allow to have a good timing performance together with a good 3D spatial resolution. The patent describing this idea has been deposited in September 2017.

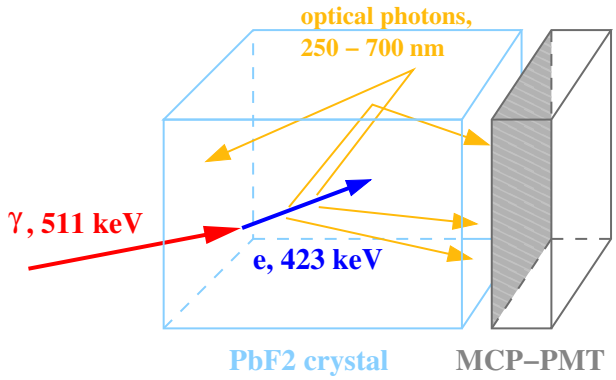

Figure 3: Schematic view of the 511 keV gamma detector with PbF_2 crystal using Cherenkov radiation.

3 Possible Axes of Development at DPhP

The specificity of medical imaging research at DPhP, is that we are investigating the new detection methods, rather than simple optimization of the existing ones. In this approach we are working on the breakthrough technologies, which potentially has a large impact on the field; are important for other domain, e.g for the particle physics; allow to have a technological expertise with modern photon detection technique; are complementary to the fast electronic development at IRFU (SAMPIC technology). The future developments should includes the development of the current activities, but could be also extended to other field. In particular:

1. Further development of the TOF technologies for PET using Cherenkov radiation. This activities is important, since the Cherenkov radiation is very fast, compared to the scintillation technologies and with further improvement in photo-detection time resolution, it will became even more important. In particular, one can notice that the *transition time spread* (TTS) of the single SiPM micro-cell currently is about 20 ps, allowing a further improvement in timing of the SiPM. The development of the tynode photomultiplier expect to have a TTS of the order of 10 ps or better [17]. The development of the radio-frequency PMT investigate the possibility to reach a 10 ps TTS or better [18]. Large area MCP PMT are developed in order to have a reasonable price per surface unit and to have the same or even better characteristic than the currently existing PMT [19, 20].

2. The development gaseous photo-multiplier for the UV and visible light based on the micromegas technology could be a good synergy between the different IRFU departments and give a possibility to build a large surface TOF PET.

3. The currently developed PET detectors could be investigated in the context of the radiation treatment of cancer. Indeed, there is a growing interest in development of the on-line monitoring for the hadron therapy during last years. It is related to the fact that hadron therapy allows to deliver a dose in well-defined volumes due to the Bragg-peak effect, that is why it is usually used for the treatment of cancer near a critical organ. However, because of the steep dose profile of hadrons, this technique is much more sensitive to spatial uncertainties than conventional photon treatments. Uncertainties in particle range and anatomical changes during treatment may cause over-dosage or under-dosage in the target. Since hadron are absorbed in the patient, on-line monitoring is required to detect secondary radiation. One of the option currently under investigation is the PET scanner to detect the short lived isotope (^{11}C, ^{15}O) generated by the hadron beam in a tissue [21, 22, 23, 24].

4. The gamma detectors developed at DPhP could be used in other configuration. In particular, it is interesting to use the as Compton camera. This device uses the Compton scattering kinematic to reconstruct the direction of arrived photon. For this one needs to reconstruct a 3D position of the Compton scattering vertex and absorb the scattered photon, measure its energy and position. The possibility to measure an electron energy at the Compton scattering vertex allows to improve the precision of the angle reconstruction. The CaLIPSO technology is very well suited for such type of measurement, since it could measure both vertex position, electron and photon energies in one volume. The ClearMind technology could be also adapted for such use by means of the multilayer detector.

   The interesting direction for using the Compton camera in medical physics are the in-vivo monitoring of the hadron therapy treatment, with the same motivation as described below [25].

The advantage of the Compton camera compare to PET that it could use the prompt-photon generated during the treatment in a large quantity. Generally the energy of such photons are above 1 MeV, and more specifically, the 4 MeV photons are seems to be an optimal choice for such devices.

5. The Compton camera mentioned before has also a potential for societal use and in particular for the radiation monitoring in the context of nuclear decommissioning, see section 4.3.

6. Use of the developed detectors for the *Positron Annihilation Lifetime Spectroscopy* (PALS) [26] measurement in material science:

   - at pulsed accelerators
   - using the *single-shot positron annihilation lifetime spectroscopy* (SSPALS) [27, 28].

7. Three-gamma detection in PET. The detection of three gamma is particularly well suited for the CaLIPSO technology, which could be used to build a detector with a large coverage of solid angle and good detection efficiency for the mutli-vertices events. The detection of three-gamma events is considered in the context of the development of new bio-markers, in particular Scandium-44(β^+,γ), lifetime of $\sim$ 4 h, for the liquid xenon PET scanner at Nantes [29].

   Another possibility is to study the feasibility of the three-gamma detection for the positron-only tracer. In fact, the positron formation in vacuum leads to formation of the orto-positronium with spin 1 in 3/4 of cases which decays to three photons. In matter, interactions with the surrounding electrons leads to a direct annihilation of the positron with one of the electrons (pick-off process), of to the conversion of o-Ps into the p-Ps decaying rapidly to two photons. In nonmetallic materials, like water, the three photon yield is usually of about the order of 0.5%, but in some cases it could be higher. There are some speculation that registering the three gamma events in parallel with two gamma events may bring an additional biological and clinical information [30, 31] and even detect directly if the cancer cells [32, 33].

4 Societal Application, Security

The DPhP activity could potentially leads to spin-off technologies important for different societal application and security. In the following the three directions are discussed: renewable (solar) energy, control systems for the nuclear non-proliferation, detectors systems for the nuclear decommissioning.

4.1 QUYOS

The QYOS project aims at developing an innovative device made of fluorescent plastic optical fibres with very specific microstructure, capable of concentrating the solar light onto photovoltaic cells. The device transforms a polychromatic, multidirectional radiation (as the solar light) into an intense flux of monochromatic, unidirectional light, with high conversion efficiency. The specific behaviour of these fibres comes from the convergence of an ensemble of quantum phenomena. The basic idea is to match the fluorescence band of a colorant with the forbidden bands of a photonic crystal thanks to a specific index profile of the fibre that reduces the phase space to desexcitation along its axis.

Currently the project is in the "proof-of-pricipal" stage. The dedicated laboratory has been constructed at CEA-Saclay, allowing to produce optical fibers with a necessary micro-structure. The first fibers are produced, but for the moment the quality is not sufficient for measuring the efficiency.

If succeeded, this project open the way to the different applications. First of all, it is a possibility to reduce the cost of the solar energy significantly. The same technologies could be used for the different applications, e.g. the nuclear plants tomography with the goal of non-proliferation; for concentrating and use of the solar energy for laser induced hydrogen production, etc.

4.2 Nuclear non-proliferation

Neutrino detectors have the ability to monitor from outside a nuclear reactors operational status, thermal power, and fissile content in real time. They could confirm the absence of unrecorded production of fissile materials in declared reactors and estimate the total burnup of a reactor core. The Nucifer experiment [34] has demonstrated the possibility of such control, but further development in this field are necessary.

4.3 Nuclear decommissioning (Démantélement)

The detectors of gamma rays developed in the context of PET could also be used as Compton camera (CaLIPSO and ClearMind technologies). In particular, its allow to control and visualize the radioactive background in environment and especially in the context of nuclear decommissioning. For example, project TEMPORAL [35] develops a detector for nuclear decommissioning in nSv environment. In reality, during the decommissioning outside the core of reactor, the radiation dose are in the range of $\mu Sv - mSv$. so there is no instruments capable to work in this condition with good angular resolution. Another example is a ORIGAMIX project, a Compton camera developed at IRFU and based on the CdTe pixelized detector [36]. While this camera has very good performance, it is sensitive mainly to photons with energy less than 1 MeV. The precise camera with a good efficiency to photons with the energy more than 1 MeV (e.g. ^{60}Co) would be really helpful. In addition, a highly automatized instrument capable to build a radiation 3D model of the environment will be really a beneficial for such types of work.

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