A proposal for a high performance γ-camera based on liquid Xenon converter and gaseous photomultiplier for PET

Dominique Thers, A. Breskin, T. Carlier, R. Chechik, O. Couturier, Jean-Pierre Cussonneau, L. Ferrer, C. Grignon, L. Luquin, Vincent Métivier, et al.

A proposal for a high performance γ-camera based on liquid xenon converter and gaseous photomultiplier for PET

Thers D.[1], Breskin A. [2], Carlier T.[4], Chechik R. [2], Couturier O.[4], Cussonneau J.P. [1], Ferrer L.[4], Grignon C. [1], Luquin L. [1], Métivier V. [1], Peskov V. [3], Phéron F.[1], Servagent N. [1],Vasseur A.[4]

[1] *Subatech Laboratory, La Chantrerie, 4 rue A. Kastler, BP 20722, 44307 Nantes, Cedex 3, France.*
[2] *Weizmann Institute, Herzl St., 76100 Rehovot, Israel.*
[3] *Pôle universitaire Léonard de Vinci, Paris, France.*
[4] *Service de médecine nucléaire, Hôpital de Nantes, France.*

ABSTRACT:. The lXe-PET project aims at initiating an international scientific cooperation to study a new generation of γ-cameras for Positron Emission Tomography (PET). Our approach consists of coupling a liquid Xe converter with an advanced large-area, fast gas-avalanche imaging photomultiplier (GPM). The foreseen method is based on detecting both the ionization and Xe scintillation signals, to provide the three coordinates and the energy of the converted γ. For that purpose, we will develop ionization detectors based on Micromegas or PIM (Parallel Ionization Multiplier) operating in liquid Xenon and cryogenic GPMs with CsI photocathodes for the detection of the scintillation signal; these will include: multi-GEMs (Gas Electron Multipliers), Thick GEM-like multipliers (THGEM), PIM, glass capillary plates and wire-type.
Expected characteristics of such γ-camera will be presented.

1. INTRODUCTION

Since their conception, PET cameras have considerably progressed and are today widely used for research on small-animal models and clinical diagnostics. The imaging agents used for PET contain a positron emitter coupled to a molecule that drives the radio-nuclide towards organs or tissues. The detection in coincidence of the two 511 keV photons originating from e^+e^- annihilation, that finally results from the β+ decay, identifies a disintegration in the radiotracer. Table.1 shows the main characteristics of several existing PET gamma-cameras; these combine different γ-converters like solid scintillators and photon detectors (generally PMT and avalanche photodiodes) or heavy metal and gaseous MWPC multipliers.

PET scanner	Sensitivity (cps/kBq)	Spatial Resolution (mm)	Technology	Ref
SHR-7700	23	22	BGO/PMT	A
MADPET	0.35	17	LSO/PMT	B
APD-PET	5.4	13.7	BGO/APD	C
YAP-PET	17.3	5.8	YAP:Ce/APD	D
MicroPET R4	24.5	5.1	LSO/APD	E
ClearPET	17	3.4	LuAP:Ce/APD	F
HIDAC	18	1.1	Lead/MWPC	G

Table 1. Different PET cameras and their performance. References : (A [Ref [i]], B [Ref [ii]], C [Ref[iii]], D [Ref[iv]], E [Ref[v]], F [Ref[vi]], G [Ref[vii]])

PET imaging has become an essential tool in the management of a growing number of cancer patients [Ref [viii]] due to the insufficient sensitivity and specificity of other diagnostic methods. Computed tomography (CT) is the most commonly used non-invasive tumour staging method but is far less accurate than invasive surgical staging (ISS) [Ref [ix]]. For example, the data of the Radiological Diagnostic Oncology Group (RDOG) [Ref [x]] indicates upon sensitivity and specificity values for thoracic CT of only 52% and 69%; the best results were obtained when nodes with a diameter equal to or larger than 1.5 cm were considered to be metastatic [Ref [xi]]. Magnetic

resonance imaging (MRI) did not improve the results in the RDOG data [Ref [ix]]. During the past decade, PET is able to provide "biological" images of tumour tissues based on the altered glucose metabolism of tumour cells, visualised by the radio labelled glucose analogue fluorine-18 fluoro-2-deoxy-D-glucose (FDG). Furthermore, visual correlation with CT images yields combined anatometabolic images, which often improves the diagnostics results. However, present clinical PET or PET/CT cameras are not accurate in distinguishing benign from malignant lesions, when their diameter is smaller than 1 cm, due in part to partial volume effects or to body or organ motions during emission steps - of several minutes each. This sometimes leads to errors in stage designation and therapeutic choice; e.g.: in lung cancer, when surgery is refused for stage N4 (controlateral node) [Ref [xii]]; for assessment of residual disease in patients with lymphoma [Ref [xiii], Ref [xiv]]; or for evaluation of suspected recurrence and restaging of colorectal cancer at an early stage when conventional methods did not reveal the site of tumour recurrence [Ref [xv]]. Therefore, there is need for cameras with better resolution for routine clinical PET; higher sensitivity will help reducing the injected volume and the radiation dose to patients; it will increase the lesion detection, which depends both on system resolution and on tumour tracer uptake, and will reduce the duration of a PET whole-body scan (from head to feet) to less than 20 minutes (at present, PET cameras with LSO or GSO crystals are able to perform a partial "whole-body" scan in 20 minutes, only from the neck to below the bladder, namely about half the body). More effective PET analysis would also have strong impact on the medical diagnostics cost. More recently, radio synthesis from prosthetic group precursors, which allows easier radio labelling of bio molecules, has led to the development of numerous new PET tracers and of novel research cyclotron equipment. Such tracers may be well develop into important routine clinical PET tracers or for research studies, in particular in small-animal research for the assessment of new therapy or functional studies, in view of new concepts of biological imaging. Therefore, in the next decade, the need for micro-PET, micro-CT and micro-SPECT (single photon emission computed tomography) is expected to grow extensively, as well as the demand for hybrid γ-cameras (SPECT and PET) for performing dual-isotope studies. In view of the growing medical needs, there has been an extensive R&D on new PET concepts, aiming to improve its analysis power. Research in this field mostly concentrates on instruments made of crystal converter rings; it involves both, novel crystals and advanced photon detectors (e.g. APDs [ref [xvi]] coupled to fast γ converters (e.g. multi-layer fast/slow scintillators [ref [xvii]]), new faster/heavier scintillator materials [ref [xviii]]). There are also many attempts to develop small-animal PET with BaF2 crystals viewed by gaseous wire-chambers filled with a photosensitive gas [Ref [xix]] Investigations of fast PET cameras system, e.g. TOF-PET (TOF: time-of-flight) are also actively pursued [Ref [xx]]. The latter could localize in three dimensions the position of the emitter, and thus reduce the number of events needed for the image reconstruction [ref [xxi]].

2. **Discussion of the scientific and technological background of each element of the project.**

Our proposed approach consists of a LXe-based detector coupled to large-area fast gas-avalanche imaging photomultipliers (GPM). The properties of LXe, relevant to PET, are compared in table 2 with those of common crystals. The relative light outputs are expressed as a fraction of the NaI(Tl) yield (for LXe, the relative light output and the ionization yield are given in presence of an electrical field of 2 kV/cm).

Lavoie [ref [xxii]] was the first to point out the potential applicability of liquid xenon for PET; he showed that by measuring both, scintillation photons and ionization, it is possible to accurately determine the three coordinates of the incident photons. A team at Coimbra [ref [xxiii]] designed a first prototype of LXe detector for PET, combining ionization and scintillation recording. They used the scintillation signal, measured with a vacuum photomultiplier tube, to trigger the data acquisition system and the ionisation signal to measure the position and the energy of the γ. As compared to

scintillation-crystal systems (BGO and LSO blocks), their LXe detector yielded better time (1.3 ns), spatial (0.8 mm) and energy (80 keV) resolutions [ref [xxiv]]. Developments taking benefit of the very fast response of the LXe scintillation are under consideration for TOF-PET [ref [xxv]]; time resolutions of 650 ps are reported with PMTs.

Scitillation materials	NaI	BGO	LSO	GSO	LXe
Effective atomic number	50	73	65	58	54
Density (kg/l)	3.7	7.1	7.4	6.7	3.0
Relative light output (%)	100	15	45-7	20-40	25
Decay time (ns)	230	300	40	60	2.2, 30
Ionisation Yield (per MeV)	/	/	/	/	~ 60000

Table 2. Comparison between the properties of common crystals and liquid xenon

The possibility of detecting ionization and scintillation light in liquid noble gases with gas-avalanche photomultipliers has been investigated by Peskov et al. [Ref [xxvi]] for nTOF and ICARUS experiments and Bondar et al. [Ref [xxvii]] for dark matter and solar neutrino detectors. For that purpose they studied different solutions of gaseous photon detectors like wire chambers, capillary plates and GEMs. Bondar et al. proved that GEM photon detectors could operate at cryogenic temperatures, as required by LXe cameras.

3. The proposed detector:

The concept of the proposed LXe γ camera prototype, combining a LXe converter with a gas-avalanche photomultiplier (GPM) is shown in Fig. 1. Following a γ conversion, both ionization and scintillation signals are collected. The ionization signal of drifting electrons is recorded by the anode, after micromesh "Frish-Grid", while the UV photons resulting from LXe scintillation are detected in the GPM. The camera will be assembled in a stainless-steel vessel, filled with 100 cl of high purity xenon; it will be pumped to high vacuum prior to filling; all parts will be made of ultra clean materials. The prototype design will fully benefit from the established knowledge and know-how in LXe purification and handling. There has been long ongoing activity in this field, mostly directed towards the search for Dark matter or neutrinos physics like in: EXO [ref[xxviii]], XMASS [ref [xxix]], MEG [ref [xxx]], ZEPPLIN [ref[xxxi]], XENON [ref[xxxii]], LXe-Grit [ref[xxxiii]].

When a γ-photon interacts with a liquefied rare gas, it gives rise to an electron-ion pair and excited species. At 511 keV, photoelectric absorption and Compton scattering are the predominant processes occurring (22% photoelectric, 78% Compton with xenon). Photoelectric interaction leads to the creation of one photoelectron that ionizes the liquid along a short distance (half a mm for 511 keV photoelectron). During its stopping process, secondary electron/ion pairs created along the photoelectron trajectory are dissociated, allowing the localization of the photoelectric vertex and the measurement of the energy loss. For each Compton scattering, an electron is created and is accompanied by a lower energy γ, leading to a sequence of Compton vertices, up to the last photoelectric interaction of the γ with the liquid. The localization of the photoelectric and Compton vertices in the liquid volume are provided by a "time projection chamber" (TPC) read-out: the conversion depth is determined by the electron drift time and the two other dimensions by the anode sampling.

Under an electrical field, a fraction of the ionization signal escapes recombination and the electrons drift in LXe with velocities of ~2.3 mm/μs at 2 kV/cm; the ions remain almost stationary. As the electron diffusion in liquid is low, the charge induced by their motion can provide excellent position resolution. Moreover, as liquid rare gases have high free electron yield and low Fano factor, good energy resolutions are reported with the induced-charge measurement [ref [xxxiv]]. In addition, LXe is a very good scintillator, emitting strongly at 179 nm, with a short 2.2ns decay-time. Hence, the scintillating light can provide the missing information in the induced charge, the

absolute time of the γ interaction. It will provide a very fast signal for coincidences and trigger for the data acquisition system.

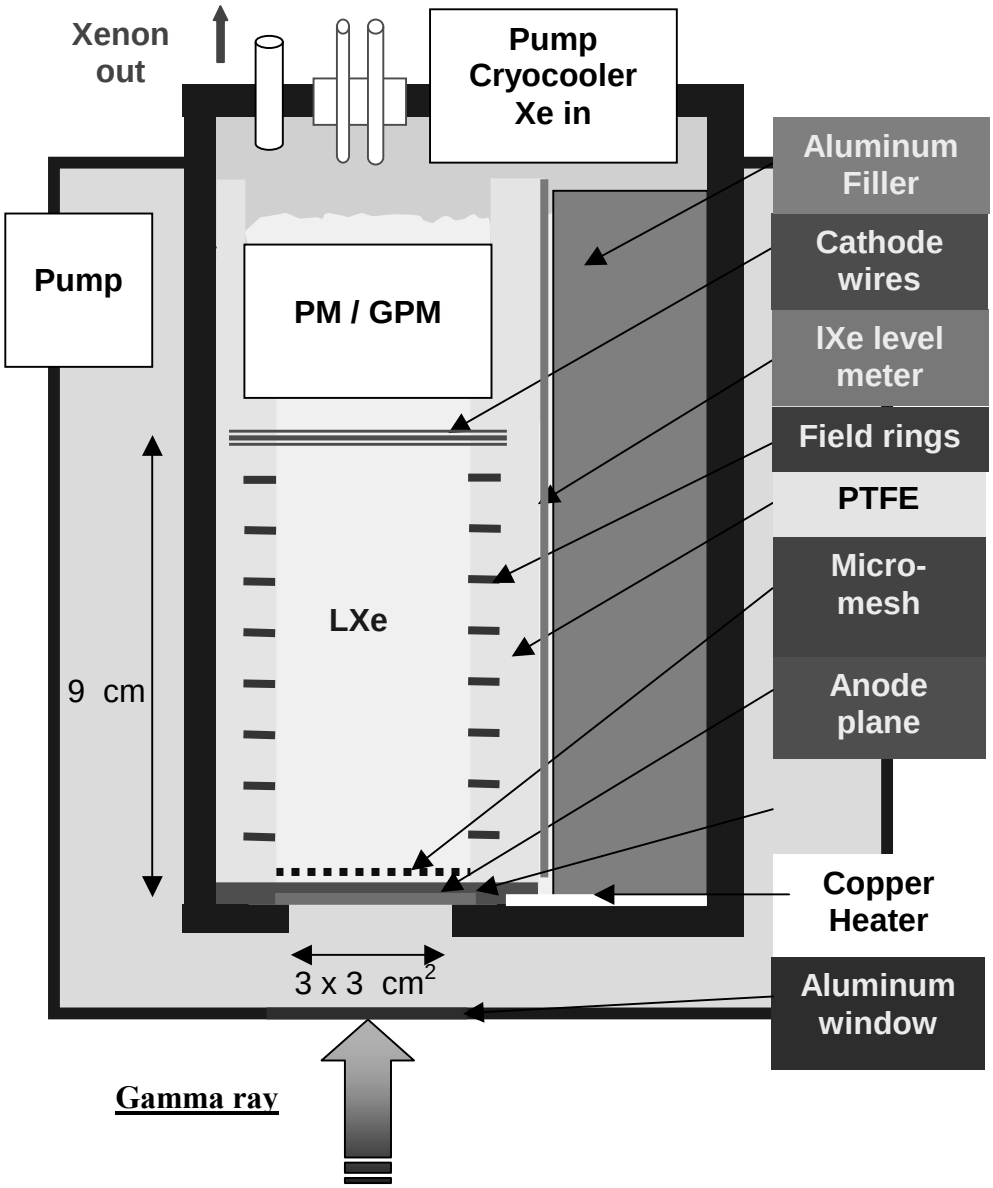

Figure 1. Scheme of the LXe γ-camera prototype

Moreover, in a classical PET system, simultaneous detection of back-to-back γ rays sign the presence of the β^+ disintegration somewhere on the LOR (Line Of Response) between the two fired detectors (scatter and random events unconsidered). Time-of-Flight (TOF) PET systems measure also the difference between the two then arrival times in order to determine the position of the disintegration along the LOR. The time resolution of the detector is then the crucial point, which allows to reduce the length of the LOR, reducing the PET exposure time. Nevertheless, such considerations have to be moderated by the very good time resolution required, 100 ps for 1.5 cm spatial resolution along the LOR. Facing this problem, TOF-PET systems achieve today time resolution of 350 ps with BaF_2 [ref [xxxv]], 500 ps with LSO [ref [xxxvi]] and 650 ps with LXe [ref[16]]; but these pure scintillation systems suffer from an additional difficulty coming from the multiple Compton interactions within the same volume element, and then to a non- negligible bias on the absolute time measurement. We propose in our prototype to show the feasibility of a LXe device

using ionization signal to localize and identify Compton vertices and then to improve the time measurement from the bias met with pure scintillation detectors. This goal seems to be realistic regarding both the fast and large scintillation of LXe and the fast response reached with the GPM technology. In the proposed prototype, the distance between the cathode and the micromesh is 9 cm, defining the depth of the converter. The distance between the micromesh and the anode is 50 µm, providing an electromagnetic shielding efficiency better than 2% (evaluated from Bunemann's formula [ref [xxxvii]]) in regards of the slow drift of ions; the grid is copper micromesh of 3 µm thickness and 50µm pitch.
Negative high voltage is applied to the cathode and the micromesh to set a uniform electric field across the drift region. Scintillation photons will be reflected from the walls of a PTFE-metal assembled drift column (with a resistive voltage divider), with about 95% diffuse reflectivity at 179 nm [ref [xxxviii]].
The sensitive area of the GPM electrodes is 3x3 cm^2. In our design, the primary UV photons are detected by the GPM placed above the liquid-gas interface. The GPM combines a CsI photocathode, sensitive to the LXe scintillation (QE = 30% @ 170 nm [Ref [xxxix]]), and a gas-avalanche electron multiplier. The gas filling will be chosen for high-gain and low-temperature operation conditions. We will investigate a few GPM concepts: a multi-GEM (Gas Electron Multiplier [Ref [xl]]) [Ref [xli]], the newly conceived Thick GEM-like multiplier (T-GEM [Ref [xlii]]), both developed at the Weizmann Institute, and the PIM (Parallel Ionization Multiplier) [ref [xliii]], developed at SUBATECH. We abandoned the solution of a windowless GPM operating in the Xe gas phase for a few reasons: it can operate only in a horizontal position above the LXe; The multiplication factor in pure LXe (not yet measured) should be limited to about 10^4 -10^5 even with a multi-GEM GPM [Ref [xliv]]; the effective QE of the CsI photocathode will be very low due to photoelectron backscattering in noble gases [Ref [xlv]].

4. Gas photomultipliers

The PIM electron multipliers has been developed at SUBATECH for high resolution β autoradiography [ref [xlvi]] . It is made of a thin sandwich of two metallic micromeshes separated by 100 microns with an appropriate insulating spacer (see fig.2). The accurate and robust thin gap and the very high electric fields permit reaching gas multiplication factors closed to 5.10^5 at atmospheric pressure with Ne/CO_2 gas mixture and 5.9 keV X-rays [ref [xlvii]].

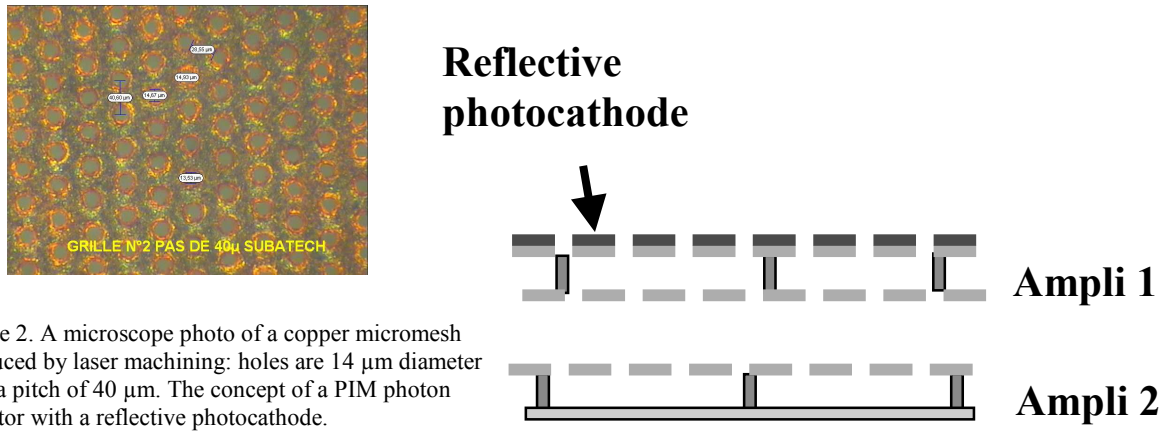

Figure 2. A microscope photo of a copper micromesh produced by laser machining: holes are 14 µm diameter with a pitch of 40 µm. The concept of a PIM photon detector with a reflective photocathode.

Multi-GEM GPMs were proposed and extensively investigated by the WIS team and yielded very good performance both with CsI UV photocathodes and with visible-range bialkali photocathodes. The GEM (see fig.3) is a densely perforated metalized dielectric (KAPTON), about 50 microns thick, with typically 50 micron diameter holes, 200 micron spaced [Ref[xli]]. Gains of the order of 10^3

to 10^7 are obtained in single GEM electrodes and in 3-4 cascaded GEMs, respectively [Ref [xlviii]][Ref [xlix]]. Multi-GEM GPMs with a CsI photocathode deposited on the top GEM surface (~80% coverage) operate in a stable way and are sensitive to single photons. Time resolutions in the 300ps range were recorded with a ~ 200 photons and single photons were localized with 150 microns resolution [Ref[xlix]].

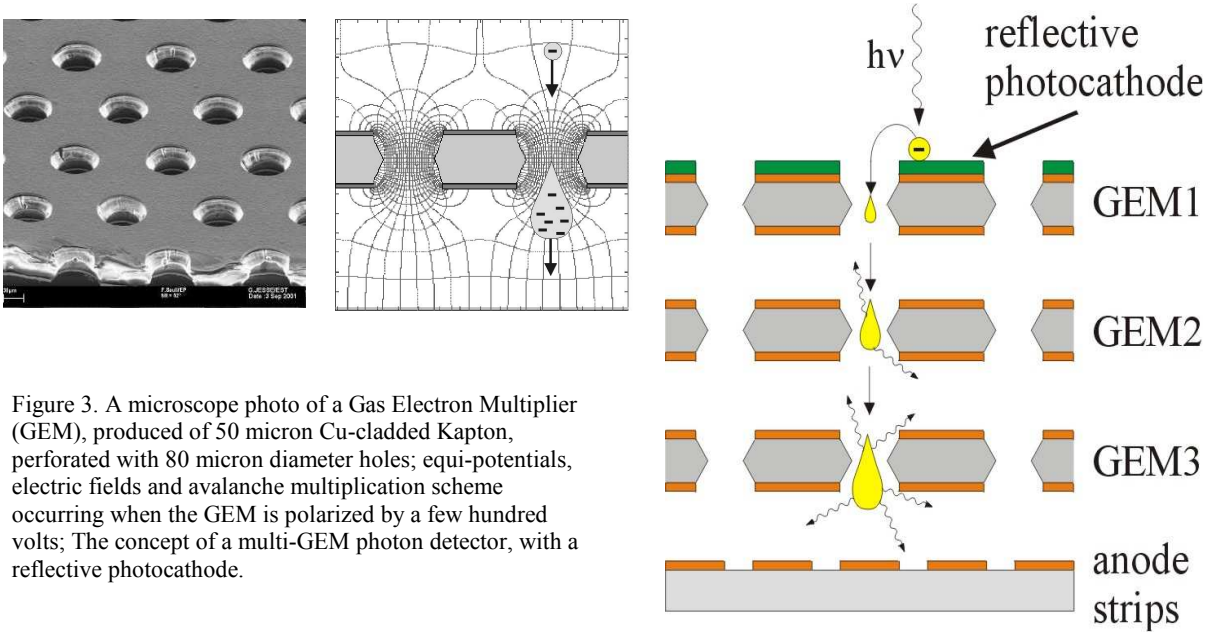

Figure 3. A microscope photo of a Gas Electron Multiplier (GEM), produced of 50 micron Cu-cladded Kapton, perforated with 80 micron diameter holes; equi-potentials, electric fields and avalanche multiplication scheme occurring when the GEM is polarized by a few hundred volts; The concept of a multi-GEM photon detector, with a reflective photocathode.

The TGEM (Thick-GEM) [Ref[xlii]] is a ten-fold dimensionally expanded version of the standard GEM (fig. 4). It is produced by standard printed-board technologies, where a dense array of small, mm-size holes is mechanically perforated in a millimetre-scale thick copper claded G-10 plate. Avalanche multiplication occurs upon the application of a few hundred volts across these millimetric gas volumes. The multiplication within the holes prevents secondary effects, which yields gains for singe electrons of the order of 10^5-10^7 [Ref[1]] in single and double-TGEM elements, respectively. The TGEM electron multiplier has a fast response, yielding current pulses of a few ns rise-time [Ref[xlii]]. The efficient extraction of photoelectrons from a CsI photocathode deposited directly on top of the front TGEM face was recently demonstrated.

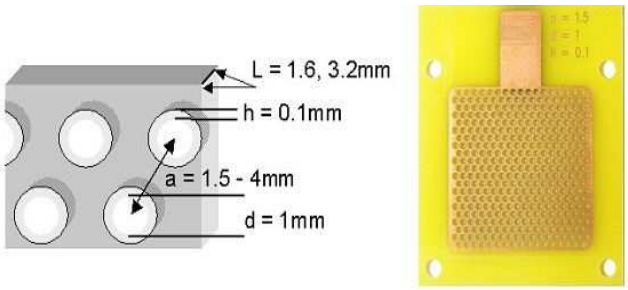

Figure 4. A scheme and a photograph of a TGEM

5. Conclusion

The LXe-PET (Liquid Xenon-Positron Emission Tomography) project aims at initiating a strong scientific cooperation having as a goal the development of a new generation of γ cameras based on liquid xenon (LXe) technologies. The proposed γ camera will present intrinsic characteristics paving the way to new type of diagnostics in oncology and dynamical functional

imaging. The main issue will be to evaluate concepts and technologies developed by the respective cooperating teams (SUBATECH and WIS) within a small γ camera prototype; in parallel, to proceed in a full simulation of the potential performance of a PET camera based on the proposed concept (CHU). The results of the proposed evaluation study will constitute an important step towards the potential development of a full LXe-PET camera.

The work was partially supported by the Israel Science Foundation project 151/01. A. Breskin is the W. P. Reuther Professor of Research in the Peaceful use of Atomic Energy.

[i] M. Watanabe et al., IEEE Trans. Nucl. Sci. (1997)
[ii] www.nuk.med.tu-muenchen.de/forshung/information/instrumentierung.shtml
[iii] R. Lecomte et al., IEEE Trans. Nucl. Sci. (1994)
[iv] A. Del Guerra et al., Nulc. Instr. Meth. A409(1998) 537-541
[v] C. Tai et al., Phys. Med. Biol. 46(2001) 1845-1862
[vi] http://crystalclear.web.cern.ch/crystalclear
[vii] www.oxpos.co.uk
[viii] R. Hustinx et al., Semin. Nucl. Med. 32 (2002) 35-46.
[ix] T.C. McLoud et al., Bronchogenic carcinoma : analysis of staging in the mediastinum with CT by correlative lymph node mapping and sampling. Radiology 182 (1992) 319-323.
[x] W.R. Webb et al., CT and MR imaging in staging non-small cell bronchogenic carcinoma: report of the Radiology Diagnostic Oncolgy Group. Radiology 178 (1991) 705-713.
[xi] B. Dillemans et al., Eur. J. Cardiothorag Surg. 8 (1994) 37-42.
[xii] C.A.B Saunders et al., Ann. Thora. Surg. 67 (1999), 790-797.
[xiii] A. Dimitrikopoulo-Strauss et al., Eur. J. Med. 22 (1995), 434-442.
[xiv] M. de Wit et al., Ann. Oncol. 8 (suppl 1) (1997) 57-60.
[xv] H.H. Stirmesiter et al., J. Nucl. Med. 41 (2000), 297.
[xvi] E. Lorenz et al., Nucl. Instr. Meth. A442 (2000) 113-116
[xvii] K. Ziemons et al., The ClearPET project: development of a 2nd generation high performance small animal PET scanner, to be published in Nucl. Instr. Meth. A.
[xviii] A. Annenkov et al., Nucl. Inst. Meth. A 527(2004) 50-53.
[xix] P.Bruyndonckx et al., Design and physical characteristics of a small-animal PET using BaF2 crystals and a photosensitive wire chamber, NIM A382(1996)589-600
[xx] A. Blanco et al., Nucl. Inst. Meth. A 508 (2003) 88-93.
[xxi] T.F. Budinger, J. Nucl. Med. 24 (1983) 73.
[xxii] L. Lavoie, Med. Phys. 3 (1976) 283-293.
[xxiii] V. Chepel et al., Development of liquid xenon detectors for medical imaging, submitted to World Scientific (28-11-02).
[xxiv] V. Solovov et al., Nucl. Inst. Meth. A477 (2002) 184-190
[xxv] F. Nishikido et al., Jap. Jour. of Appl. Phys. 43 (2004) 779-784.
[xxvi] L. Periale et al., Nucl. Inst. Meth. A478 (2002) 377-383.
[xxvii] A. Buzulutskov et al., IEEE Trans. On Nucl. Sci. 50(2003) 2491-2493
[xxviii] M. Danilov et al. Phys. Lett. B 480, 12 (2000)
[xxix] Y. Takeuchi, ICHEP04 in Beijing
[xxx] S. Mihara, Nucl. Inst. Meth. A518(2004) 45-48
[xxxi] H.M Araujo et al., Nucl. Inst. Meth. A521 (2004) 407-415
[xxxii] E. Aprile et al., IEEE Trans. Nucl. Sci.50 (2003) 1303-1308
[xxxiii] E. Aprile et al., arXiv:astro-ph/0212005 v2 4Dec 2002.
[xxxiv] E. Aprile et al., Nucl. Inst. Meth. A480 (2002) 636-650
[xxxv] T. Bäck et al., Nucl. Inst. Meth. A477 (2002) 82.
[xxxvi] W.W. Moses and S.E. Derenzo, IEEE Trans. Nucl. Sci. 46(1999) 474.
[xxxvii] O. Bunemann, T.E Cranshaw et al., Can. J. Res. 27 (1947) 191.
[xxxviii] M. Yamashita et al., Astropart. Phys. 20 (2003) 79-84.
[xxxix] A. Breskin, CsI UV photocathodes: history and mystery. Nucl. Instrum. and Meth. **A371** (1996) 116.
[xl] F.Sauli, GEM: a new concept for electron amplification in gas detectors, Nucl. Instr. and Meth. A **386** (1997) 531.
[xli] A. Breskin et Al., Recent advances in gaseous imaging photomultipliers. Nucl. Instr. Meth. **A513** (2003) 250 and references therein.
[xlii] R. Chechik et al., Thick GEM-like hole multipliers: properties and possible applications. Nucl. Instr. Meth. A, in press.

[xliii] D.Thers et al., Nucl. Inst. Meth. A 504 (2003) 161-165.
[xliv] A. Buzulutskov et al., The GEM photomultiplier operated with noble gas mixtures. Nucl. Instrum. and Meth. **A443** (2000)164.
[xlv] T.H.V.T Dias et al., J. Phys. D: Appl.Phys. 37(2004) 540-549.
[xlvi] J. Samarati et al., To be published in NIMA, 11thVienna Conference on Instrumentation.
[xlvii] D. Thers et al., New prospects on particle detection with a Parallel Ionization Multiplier (PIM), accepted for publication in Nucl. Instr. Meth. A.
[xlviii] D. Mörmann et al.,GEM-based gaseous photomultipliers for UV and visible photon imaging. Nucl. Instr. Meth. **A504** (2003) 93
[xlix] D. Mörmann et al., Operation principles and properties of the multi-GEM gaseous photomultiplier with reflective photocathode. Nucl. Instr. and Meth. A **530** (2004) 258
[l] R.Chechik et al., Progress in the TGEM. to be published.