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Case for setting up a 10 ps challenge: A step toward reconstruction-less TOF-PET

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Summary. — The future generation of radiation detectors is more and more demanding on timing performance for a wide range of applications, such as particle identification in nuclear physics and high-energy physics detectors, high-resolution hadronic calorimetry in finely segmented detectors, precise event time tagging in high-luminosity accelerators, time-of-flight (TOF) techniques for PET cameras and a number of photonic applications based on single photon detection. There is in particular a consensus for gathering Europe's multidisciplinary academic and industrial excellence around the ambitious challenge to develop a 10 ps TOF PET scanner (TOFPET). The goal is to reduce the radiation dose (currently 5–25 mSv for whole-body PET/CT), scan time (currently >10 minutes), and costs per patient (currently >1000 € per scan), all by an order of magnitude. To achieve this very ambitious goal it is essential to significantly improve the performance of each component of the detection chain: light production, light transport, photodetection, readout electronics. Speeding up progress in this direction is the goal of the challenge and will have an important impact on the development of a new generation of ionization radiation detectors. It will be shown that the possibility to reach 10 ps time-of-flight resolution at small energies, as required in finely granulated calorimeters and PET scanners, although extremely challenging, is not limited by physical barriers and that a number of disruptive technologies, such as multifunctional heterostructures, combining the high stopping power of well-known scintillators with the ultrafast photon emission resulting from the 1D, 2D or 3D quantum confinement of the excitons in nanocrystals, photonic crystals, photonic fibers, as well as new concepts of 3D digital SiPM structures, pave the way to new radiation detector concepts with unprecedented performance.

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1. – Introduction

Since the seventies, positron emission tomography (PET) has become an invaluable medical molecular imaging modality, especially for cancer diagnosis and the monitoring of its response to therapy and more recently in direct combination with X-ray computed tomography (CT) or magnetic resonance (MR).

PET is an incredibly sensitive imaging technique based on electron-positron annihilations and the nearly coincident detection of the corresponding pairs of photons simultaneously emitted in opposite directions and electronically collimated along a common line, also known as a line of response (LOR). Accumulated detections of different annihilation events along various LORs produce projections of the radioactive concentration volume distribution of a radiopharmaceutical labelled with a positron emitter radioisotope, such as ^{18}F or ^{11}C. Tomographic image reconstruction from all the measured projections then leads to the 3D volume representation of the estimated radionuclide distribution, whose accuracy depends mainly on the ability to associate coincident detections with actual annihilation photons.

The localization of the emission point of an annihilation pair along a LOR depends on the detection of the time difference between the two annihilation photons, also known as the time-of-flight (TOF) difference of the photons, whose accuracy is given by the coincidence time resolution (CTR), fig. 1. This additional information makes the tomographic inversion problem much less ill-posed, hence resulting in a better signal-to-noise ratio of the activity measurement, fig. 2. Taking into account the speed of light, which is approximately 30 cm/ns, a CTR better than 10 picoseconds FWHM will ultimately allow to obtain a direct 3D volume representation of the estimated activity distribution of a positron emitting radiopharmaceutical, at the mm level and without the need for tomographic inversion, thus introducing a quantum leap in PET imaging and quantification.

Moreover, a 10 ps capability will increase effective PET sensitivity, as compared to the state of the art, at least by a factor of 16, with the following expected consequences:

- reduction of the radiation doses of molecular imaging procedures to negligibly low levels;
- reduction of the synthesized quantity of radiopharmaceutical needed for each examination, and thus of the relatively high cost currently associated with *in vivo* molecular imaging procedures;
- further extension of the benefit of molecular imaging procedures beyond oncology and towards cardiovascular, neurological, metabolic, inflammatory, infectious or metabolic disease (such as diabetes), including in the paediatric, neonatal, and prenatal contexts;
- maximizing the spatial and temporal resolution of PET-based molecular imaging;
- precise dynamic studies of molecular processes of high interest in pharmacology for screening and selecting candidate molecules for the next generation of drugs or new applications thereof;
- potentially further extension of molecular *in vivo* imaging to study "systems biology" of the whole human body through whole-body imaging systems;
- no need for full angular coverage of the patient, opening many new opportunities for PET system design.

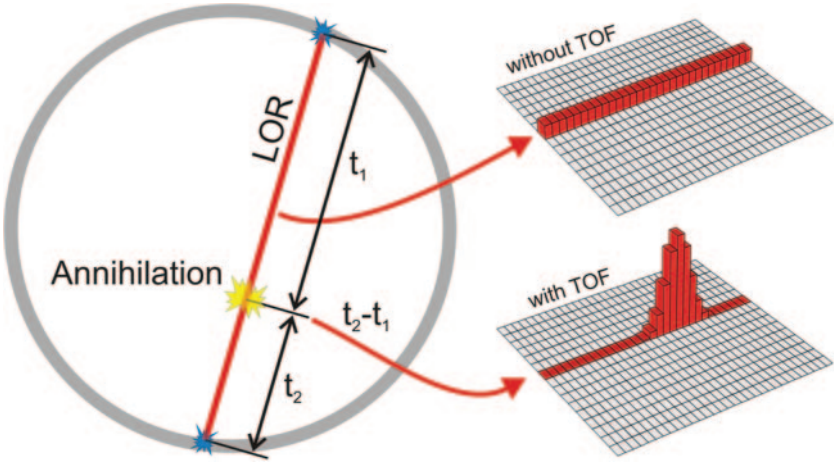
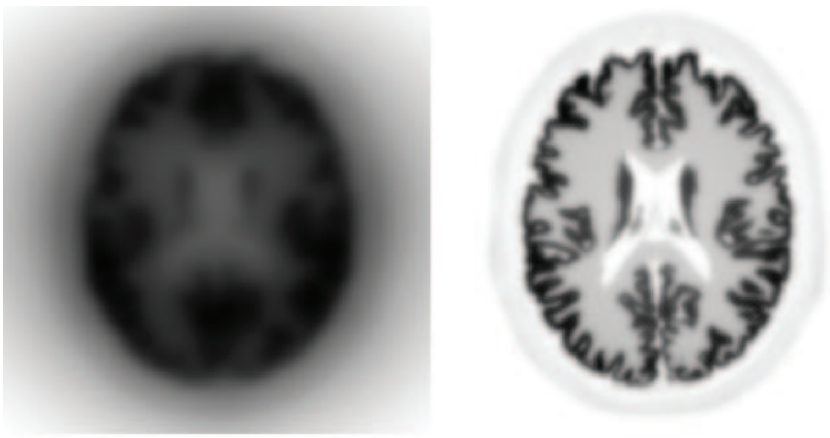


Fig. 1. – Distribution of the probability of the position of the radiotracer emission point on the LOR in a PET scanner without or with time-of-flight information.

While crossing the *10 ps frontier* will increase the performance of TOF-PET and lead to the advent of reconstruction-less PET, it will also permit efficient proton range monitoring in hadrontherapy (including with protons), improve the performance of Compton camera developed for conventional scintigraphy and nuclear waste management, impact both the development of positron annihilation lifetime spectroscopy (PALS) used in material science and the development of laser imaging detection and ranging (LIDAR) systems for automotive solutions, *e.g.*, for self-driving cars, and more generally instrumentation for nuclear and particle physics. Such a feat will not only require to make progresses on the development of new scintillators (*e.g.*, to produce enough photons with a minimum time jitter in the first 10 ps after their excitation), but also



(a) (b)

Fig. 2. – Hoffman brain phantom simulated analytically without noise (courtesy: Johan Nuyts, University of Leuven): (a) Non-TOF back-projection; (b) TOF back-projection with 10 ps FWHM CTR.

on markedly improving light collection, photo-detection and photo-detector electronic readout.

A number of emerging technologies in the domain of scintillating materials, nanotechnologies, solid state photodetectors and electronics support the idea that crossing the 10 ps frontier is not just a wild dream and that, as hinted at in preliminary studies [1], an ambitious and coordinated effort could lead to a new generation of TOF-PET scanners with unprecedented performance.

Therefore, we intend to launch a *10 ps Challenge*([1]) to foster the next quantum leap in PET imaging and make reconstruction-less, high-sensitivity PET scanners a reality, thus paving the way towards reducing by an order of magnitude the radiation dose (currently 5–7 mSv for a total-body PET), the scan duration (currently >10 min), and the scanning cost per patient (currently >1000 € per scan). Combining 10 ps TOF-PET with other modalities (X-ray CT, MRI, ultrasound, optical) will further enable multi-parametric data acquisition and lead to a paradigm shift for *in vivo* molecular imaging. This will in turn durably impact societal healthcare challenges not only in oncological disease, but also in neurodegenerative, inflammatory, infectious or metabolic diseases, from prenatal to old age.

In order for the 10 ps TOF-PET Challenge to become a reality, we are looking for single or multiple sponsors willing to support several prizes corresponding to the various

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([1]) The 10 ps challenge is presently endorsed by EANM, European Association of Nuclear Medicine; EIBIR, European Institute for Biomedical Imaging Research; WMIS, World Molecular Imaging Society; IEEE NPSS, Nuclear and Plasma Sciences Society; IEEE NPSS Nuclear Medical and Imaging Sciences Committee (NMISC); ESHI^{MT}, European Society for Hybrid, Molecular and Translational Imaging; Crystal Clear Collaboration (31 Institutes worldwide); PETsys Electronics, SA; Crystal Photonics, Inc.; Multiwave Imaging SA; and Pedro Almeida, University of Lisbon; Etiennette Auffray, CERN, Geneva, Switzerland; Luc Bidaut, University of Lincoln, UK; David Brasse, IPHC, CNRS/IN2P3, Strasbourg, France; Simon Cherry, UC Davis, USA; Fabrizio Davi, Polytechnic University of the Marches, Ancona, Italy; Christophe Dujardin, University Claude Bernard, Lyon; Réjean Fontaine, University of Sherbrooke, Canada; Sanjiv Sam Gambhir, Stanford University School of Medicine, USA; Antonio J. Gonzalez, Polytechnic University of Valencia, Spain; Stefan Gundacker, CERN, Geneva, Switzerland; Hossein Jadvar, University of Southern California, Los Angeles, USA; Jae Sung Lee, Seoul National University, South Korea; Terry Jones, UK; Nikolaos Karakatsanis, Cornell University, New York, USA; Mark Ladd, DKFZ, Heidelberg, Germany; Roger Lecomte, University of Sherbrooke, Canada; Paul Lecoq, CERN, Geneva, Switzerland; Homer A. Macapinlac, UT MD Anderson Cancer Center, Houston, USA; Steven Meikle, University of Sydney, Australia; Laurent Ménard, IMNC, University Paris Descartes, France; Christian Morel, CPPM, Aix-Marseille University, Marseille, France; Johan Nuyts, University of Leuven, Belgium; Sergey Omelkov, University of Tartu, Estonia; Jörg Peter, DKFZ, Heidelberg, Germany; Jean-François Pratte, University of Sherbrooke, Canada; John Prior, CHUV, University of Lausanne, Switzerland; Magdalena Rafecas, University of Lübeck, Germany; Dennis Schaart, Delft University of Technology, Netherlands; Volkmar Schulz, RWTH-Aachen University, Germany; Markus Schwaiger, Technical University of Munich, Germany; Viatcheslav Sharyy, CEA-IRFU, Saclay, France; Kuangyu Shi, University of Bern, Switzerland; Gintautas Tamulaitis, Vilnius University, Lithuania; Marc-André Tétrault, Mass General Hospital, Boston, USA; Kris Thielemans, UCL, London, UK; Harry Tsoumpas, University of Leeds, UK; Stefaan Vandenberghe, University of Gent, Belgium; Joao Varela, University of Lisbon, Portugal; Dimitris Visvikis, LaTIM, University of Western Brittany, Brest, France; Dominique Yvon, CEA-IRFU, Saclay, France; Karl Ziemons, FH-Aachen University of Applied Sciences, Juelich, Germany.

Fig. 3. – The Flash Gordon logo, mimicking the back-to-back emission of 2 gamma rays from the positron annihilation in a PET scanner.

anticipated achievements. Herein also are a tentative set of rules and assessment strategy for leading this 10 ps Challenge and ensure it will represent:

- a spur on the development of fast timing across disciplines and technologies;
- an opportunity to collaborate as a community on a complex "final frontier" problem;
- an incentive and opportunity to raise further funding;
- a way to shed light on advanced nuclear instrumentation for medical imaging and beyond.

2. – Organization of the 10 ps TOF-PET challenge

We intend to set up one overarching challenge, which will be launched for a total duration of 5 to 10 years and will be operated by an international organization, following rules issued by the community and based on the measurement of CTR combined to

sensitivity. Our chosen logo and communication design could be based on Flash Gordon's, whose lightning iconography is strikingly similar (at least for the PET initiate) to the emission of an annihilation pair (fig. 3).

Several prizes will be considered in relation to each anticipated significant milestone:

- 1M € are sought for the Flash Gordon Prize delivered to the 3 best certified achievements, 3 years after the launch of the Challenge.
- 1M € are sought for the Leonard McCoy Prize, for the first team meeting successfully the specifications of the Challenge within its total duration.

Challenge objective: To image a 1.5 mm thick slice of a micro-Derenzo phantom through direct back-projection (without filtering) of TOF data that have been acquired over a predefined amount of time via a pair of detector modules with a CTR ≤10 ps FWHM.

Flash Gordon Prize: A contest would be organized somewhere, *e.g.*, at CERN, 3 years after the launch of the 10 ps Challenge. During this contest, teams that would have registered to attend would demonstrate the CTR performance of their prototype consisting in two detector modules operating in coincidence. The three best certified achievements would share the prize. Assessments would be performed using a ^{68}Ge or ^{22}Na point source (the isotope choice to be discussed) positioned at different positions (the number of positions to be discussed) inside a light-tight box. The distance between the detector modules would have to be >10 cm. Positions would be defined randomly within a range of 10 cm between the two detector modules. Statistics larger than 1000 coincidences would be acquired for each source position. Time calibration of the TOF curves would be determined from a linear regression through the TOF curve peaks, knowing the source position *a posteriori*. CTR would then be estimated by the mean of the CTR measured for each source position.

Leonard McCoy Prize: This Prize would remain open until a team succeeds in separating —on an event-to-event basis— 1.6 mm rods of a micro-Derenzo phantom, or until the 10 ps Challenge expires. Image of a slice of a micro-Derenzo phantom type would need to be produced exclusively by back-projection (without filtering) of TOF data acquired over a predefined time duration via a pair of detector modules and associated instrumentation (*e.g.*, including both hardware and software) with a CTR ≤10 ps FWHM and an efficiency of at least 10%.

Once a team claims to have achieved a CTR ≤10 ps FWHM, a *preliminary characterization* would then be performed at the 10 ps Challenge certification platform, using the team's two detection modules and following the same protocol as defined for the Flash Gordon Prize. In case of success, 10000 € would be granted to each successful team at this preliminary stage.

The 10 ps Challenge certification platform would be equipped with a mechanical test bench to allow two detector modules to orbit either together or separately around the phantom. The same detector modules that would have passed the preliminary characterization test would be used in this second phase of the Prize. A micro-Derenzo phantom (type and design to be specified more precisely, but rods are usually 1.2, 1.6, 2.4, 3.2, 4.0 and 4.8 mm) would be filled with a fixed amount of ^{18}F or ^{64}Cu activity (actual positron emitting isotope to be selected depending on total expected acquisition time). The total duration of the data acquisition would also be fixed (overall duration to be defined, *e.g.*, as long as there would remain some activity in the phantom), whatever type of orbit would be selected to image the phantom. The imaged slice thickness would be 1.5 mm

(possibly the thickness of the rods placed in a longer phantom; to be discussed). A contender team could only once challenge the Leonard McCoy Prize. If a contender team failed to separate the 1.6 mm rods of the micro-Derenzo phantom on the first attempt, they would not be able to run for the Leonard McCoy Prize again. On the other hand, if a contender team could not succeed at the preliminary 10 ps FWHM characterization test, they would still remain eligible to compete for the Leonard McCoy Prize.

REFERENCES

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