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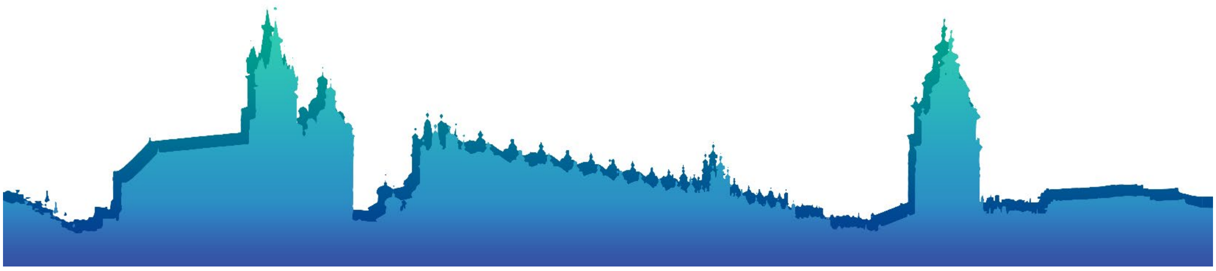
ABSTRACT BOOK



Potential Applications of Total Body PET Imaging with Emphasis on CV, MSK and Malignant Disorders

Prof. Abass Alavi; University of Pennsylvania, USA

The introduction of X-Ray by Roentgen in 1895 started a major revolution in medicine and still continues to have an impact on its current practice on a daily basis. However, no major, physics-based invention was initiated until the 1960s when David Kuhl at the University of Pennsylvania (Penn) introduced the concept of tomography as we know today. He and his colleagues were first to design an instrument that allowed radiation-based imaging of brain tumors by a technique that was called “emission tomography” at the time. The invention of Computed Tomography (CT) by Hounsfield in 1971 added a major dimension to modern imaging armamentarium. While prototype CT imaging was somewhat complicated and limited in scope, over the past 5 decades, this very powerful imaging modality has matured significantly and is nowadays the workhorse of clinical practice of medicine. The introduction of the concept of MRI in 1970s by Lauterbur added a major dimension to medical imaging and its role in complicated diseases and disorders.

Initial applications of emission tomography were primarily focused on assessing blood-brain barrier abnormalities by conventional radiotracers. However, the significant superiority of contrast enhanced CT over emission tomography propelled investigators at Penn to introduce the concept of assessing brain glucose metabolism by radiolabeled deoxyglucose. Efforts at Penn soon led to synthesizing 18F-Fluorodeoxyglucose (FDG) and the first human studies were performed in August 1976. The success of this effort was a major stimulus to mobilizing forces for practical applications of positron emitting radiopharmaceuticals for both research and clinical purposes. Investigators at Washington University, led by Michael Ter-Pegossian, designed and built prototype positron emission tomography (PET) instruments that further enhanced the role of the modality in many settings. Over the years, significant advances have been made in designing CT, MRI, and PET imaging which has improved practical applications of such instruments. In 2000, the first hybrid PET/CT instrument was introduced by investigators at the University of Pittsburgh, and this allowed combining molecular images acquired by PET with those of CT. During the past 10 years, PET/MRI instruments have further enhanced our ability to combine the advantages of these two powerful modalities as a single powerful unit.

During the past several years, investigators at University of California, Davis and United Imaging in Shanghai have designed and built total body PET/CT instruments for simultaneous imaging of the entire body with a single acquisition. Similar approaches have been adopted by investigates at Penn, the University of Kraków, and Siemens which is further enhancing the role of this approach worldwide.

Over the past few decades, molecular imaging with PET has made a major impact in many domains in medicine. While initial interests were focused on brain imaging because of the

limitations of available instruments during the early years of PET technology, the introduction of body imaging has expanded interests into imaging various malignancies, cardiovascular disorders, and many infectious/inflammatory diseases. The application of PET to the day-to-day practice of medicine has substantially improved patient care in many disciplines including neurology, oncology, orthopedics, and other disorders of mankind. These approaches have substantially influenced management of patients and avoiding unnecessary and costly procedures. Because of the success of FDG, many new tracers have been introduced over the years that have shown great promise in assessment of both benign and malignant abnormalities. The ability for successful quantification by PET has also made a major contribution to the success of this modality. During the past few decades, great interest of global disease assessment by the medical imaging for many systemic disorders has become a reality employing conventional PET instruments with a limited field of view. This approach provides a single number that represents disease activity throughout the body and has significant implications for optimal management of the affected population. Therefore, the ability to image the entire body with total body PET instruments combined with such quantitative capabilities will have far reaching impact in the future. In convulsion, the revolution that has evolved over the past 5 decades in medical imaging is unparalleled in any discipline in medicine and this will lead to substantially improved patient care in the future worldwide.

Clinical and Technical Consideration for Fast TOF PET

Prof. Georges El Fakhri, Gordon Center, Massachusetts General Hospital, Harvard Medical School, USA

Co-authors: G. El Fakhri[a], J. Álamo[i], J. Barberá[i], J.M. Benlloch[i], G. Borghib, R. Dolenec[c,d], J. M. Fernández-Tenllado[e], D. Gascón[e], S. Gómez[f,e], A. Gola[b], K. Grogg[a], D. Guberman[e], S. Korpar[g,d], P. Križan[c,d], S. Majewski[h], R. Manera[e], T. Marin[a], A. Mariscal-Castilla[e], J. Mauricio[e], S. Merzi[b], C. Morera[i], M. Orehar[c], G. Pavón[i] M. Penna[b], R. Pestotnik[d], G. Razdevšek[c], H. Sabeth[a], A. Seljak[d], A. Studen[c,d]

[a]Gordon Center for Medical Imaging and Harvard Medical School, Boston, MA 02114, United States
[b]Fondazione Bruno Kessler, 38123 Povo TN, Italy
[c]Faculty of Mathematics and Physics, University of Ljubljana, Ljubljana, Slovenia
[d]Jožef Stefan Institute, Ljubljana, Slovenia
[e]Dept. Física Quàntica i Astrofísica, Institut de Ciències Del Cosmos (ICCUB), University of Barcelona (IEEC-UB), Barcelona, Spain
[f]Serra Húnter Fellow, Polytechnic University of Catalonia (UPC), Barcelona, Spain
[g]Faculty of Chemistry and Chemical Engineering, University of Maribor, Maribor, Slovenia
[h]University of California Davis, Davis, CA 9b616, United States of America
[i]Oncovision, Valencia, Spain

The paradigm shift in medicine from treatment of acute and/or advanced disease to very early diagnosis and even prevention in cancer, neurodegenerative as well as cardiac fields, puts more stringent requirements on PET imaging both in terms of sensitivity as well as specificity. Likewise, recent developments in Targeted Radionuclide Therapy (TRT) where theragnostic pairs are used to tailor a personalized treatment in terms of dose using PET initial imaging and subsequent alpha or beta emitting radionuclides have introduced a clear and urgent need for more widespread and accurate PET imaging. Standard clinical scanners are sub-optimal both in terms of cost that, limit widespread use, as well as performance. Standard clinical PET scanners use sets of tightly arranged rings of detector modules, consisting of scintillation crystals optically coupled to light sensors with readout electronics. They cover only a limited solid angle, and just a small few percent fraction of the positron decays is registered. Novel long axial PET scanners with axial field of view offer a very attractive solution to many of the challenges detailed above, especially in terms of increased sensitivity and enabling fast dosimetry and biodistribution for pharmacokinetic studies, that will pave the way to personalized TRT. However, these scanners pose significant challenges both financially and logistically. In this talk we present a joint effort between JSI-Ljubljana, FBK-Trento, Univ-Barcelona, Oncovision and MGH-Harvard-Boston to address these challenges using fast coincidence timing resolution. On the front electronics, our challenge is to develop a low-noise, high-dynamic-range ASIC with a time resolution of 20 ps or better, and with on-chip time-to-digital converter (TDC). To achieve sub-100 ps CTR we intend to explore 2.5 D integration with the photo-sensor. Recent advances in Time-of-flight (TOF) PET technology afford a rare opportunity to improve signal-to-noise-ratio (SNR) without increasing the cost associated with axial coverage by resorting to very sparse angular coverage of the patient and long axial field coverage (>1m). This would yield affordable long axial PET scanners with increased sensitivity that can enable full body pharmacokinetics and pharmacodynamics.

Idea of theranostics in nuclear medicine. Where we are?

Prof. Leszek Krolicki; Medical University of Warsaw, Poland

Theranostics is a relatively new field of medicine, although its roots go back at least 70 years. This principle implies that treatment should be based on well-defined medical/biological goals defined by imaging methods.

Over the last decade, there has been rapid progress in this area. In recent years, the number of publications on theranostic techniques has reached around 1,000/year. Theranostics covers various areas: radioisotope-based therapy, bioimage guided radiotherapy, optical imaging, laser ablation and surgery or nanotherapy.

Radiotheranostics is perhaps the most advanced clinical application of theranostics, with many advances and emerging opportunities. In these procedures, indications for radioisotope therapy are based directly on the results of scintigraphic images: scintigraphy indicates whether a given radiopharmaceutical accumulates in the appropriate amount in the tumor; a therapeutic radiopharmaceutical is used only when the scintigraphy indicates a sufficiently large accumulation of the diagnostic form of the radiopharmaceutical. Therefore, pairs of radioisotopes are sought - emitting gamma radiation (for diagnostics) and emitting beta or alpha radiation (for therapeutic purposes). Examples include 123I (for diagnosis) and 131I (for treatment) in malignant or benign thyroid diseases. The second direction of the development of radiotheranostics is the use of known theranostic radiopharmaceuticals in the diagnosis and treatment of other diseases. An example is the use of somatostatin analogues labelled with 177Lu in the treatment of pheochromocytoma, breast cancer, small-cell lung cancer or meningioma. 177Lu labelled PSMA is adapted for treatment of thyroid, hepatocellular or renal cancer. The examinations are conducted on the use of various radioisotopes depending on the type and severity of the disease. The search for new therapeutic targets is also underway. The current results indicate that new therapeutic targets may turn out to be CXCR-4, FAPI, gastrin-releasing peptide receptor, integrin αVβ3 or αVβ5 receptors, CD38, CD45.

The next direction in the development of theranostics is the use of tandem therapies. The combination of radioisotope treatment and chemo-/immunotherapy seems to be more effective. An important achievement in recent years is also the possibility of characterizing the tumor microenvironment: activity of immune cells and fibroblasts, extracellular matrix or angiogenesis. This information is helpful (or even critical) in selecting the appropriate treatment for patients.

Today, radiotheranostics constitutes a new view on therapeutic procedures, and nuclear medicine is currently the best tool for its development.

Molecular imaging of human stem/progenitor cells for pro-regenerative purposese

Prof. Maciej Kurpisz; Institute of Human Genetics, Polish Academy of Sciences, Poland

We have used human stem/progenitor cells of myogenic origin (with mostly CD56+, desmin-positive characteristics) either alone or together with mesenchymal stem cells (MSC) to be applied in the mouse post-infarction heart model (immunocmpromise SCID mice) when tracking them in situ in medium and long-term imaging system. In order to differentiate between myoblasts anbd MSC/s we have used two types of bioluminescent markers (firefly liciferase versus nanoluc) with two different molecular promoters incorporated to the stem cells while delivering the cells intramyocardially to post-infarcted heart using four variants of cellular therapies. We have found by bioluminescent imaging that in a group of mice with post-infarcted heart the highest signal was obtained when myoblasts were applied together with MSC/s vs myoblasts alone ($p<0.0001$). This could be a promising strategy for pro-regenerative future clinical trials.For a long cell imaging we additionally used [18F}-FHBG PET/CT model when applying stem cells with molecular double promoter/reporter sequence that could either link flushed 18F isotopes with FDG (fluorodeoxyglucose) for cell viability. In vivo PET/CT and MRI revealed precise measurement of reporter probes signaling incorporated into the cells for as long as 6 weeks of monitoring.

Quantitative analysis of tumor hypoxia in nuclear medicine imaging and therapy

Prof. Kuangyu Shi; University of Bern, Switzerland

Tumour hypoxia is a critical hallmark of cancer, which is associated with tumour aggressiveness and resistance to multiple therapies. PET imaging methods have been developed for noninvasive visualization of tumour hypoxia and the emerging radioligand therapy is expected to overcome the limitation of conventional external beam radiotherapy in cancer treatment. However, it is not straightforward to interpret the PET imaging signals for tumour hypoxia due to the complex tumour microenvironment. On the other side, the influence of hypoxia on radioligand therapy is more complex than the penetration distance of therapeutic radioisotopes. This talk will give an overview of computational methods including pharmacokinetic modelling and reaction-diffusion modelling in the interpretation of hypoxia in PET imaging and radioligand therapy. The combination of experimental data and computational modelling may accelerate the development of hypoxia-related nuclear medicine imaging and therapy.

Nuclear Imaging in Infective Endocarditis

Prof. Magdalena Kostkiewicz; Nuclear Medicine Department, John Paul II Hospital, Poland

Infective endocarditis is a complex disease with cardiac involvement and multiorgan complications. Its prognosis depends on prompt diagnosis that leads to an aggressive therapeutic management combining antibiotic therapy and early cardiac surgery when indicated. However, IE diagnosis always poses a challenge. In recent years, nuclear imaging (technetium99m hexamethylpropyleneamine oxime-labelled autologous leukocytes (99mTc-HMPAO-SPECT/CT) and 18FDG PET) have experienced significant technical improvements, and their application to the detection of cardiac and extracardiac IE-related lesions seems to be a strategic way forward in the management of patients with suspected IE. The accumulation of time-dependent radiolabelled leucocytes (99mTc-HMPAO-WBC) is registered to evaluate in vivo inflammatory lesions. The main added value of this technique is its high specificity and detection of peripheral embolic events. Sensitivity and specificity of 99mTc-HMPAO-SPECT/CT was 86% and 97%, respectively. Positron emission tomography with fluorodeoxyglucose (18F-FDG PET) technology delivers high-resolution images by the use of biologically active compounds labeled with positron emitters. Uptake of the radiopharmaceutical in PET is based on the high expression of glucose transporters, which actively incorporate the tracer into the cells. A radiolabeled glycogen analog accumulates into cells such as activated inflammatory cells in infection and inflammation processes.Metabolic activity is evaluated both qualitatively and quantitatively. If PET/CT acquisition is combined with cardiac CT (PET/CT), the metabolic findings provided by the [18F]FDG uptake distribution and intensity might be added to the anatomic findings already described for cardiac CT within a single imaging procedure. Notable advantages of PET/CT and WBC SPECT/CT are their ability to perform the extracardiac workup within a single imaging procedure and to reveal the concomitant presence of extracardiac infection sites as the consequence of both septic embolism and primary infective processes. Nuclear examination may provide opportunities for personalized evaluation in order to choose the best therapeutic strategy.

A statistical reconstruction algorithm for positronium lifetime imaging using time-of-flight positron emission tomography

Prof. Hsin-Hsiung Bill Huang; University of Central Florida, USA

As an emerging technology, positronium lifetime imaging (PLI) using time-of-flight (TOF) positron emission tomography (PET) provides supplemental information reflecting the microenvironment surrounding the tissue, in addition to the radiotracer activities from PET scan. However, due to the finite coincidence resolving time (CRT), typically on the order of 200 – 600 ps, reconstruction of the lifetime image from PLI list-mode events has yet to be fully developed.

Previous studies have established the feasibility of positronium lifetime imaging using TOF PET scanners that have superior CRT to allow precise localization of each event in space [Moskal 2019, Shibuya 2020]. Currently, no practical TOF PET scanners have the needed CRT and therefore the studies consider only well-separated sources that can be resolved by systems having a finite CRT. The existing positronium imaging method [Qi 2022] considers the marginal likelihood of the lifetime parameter given the radiotracer activity parameter and applies a surrogate function to estimate the lifetime parameter. In contrast, our proposed method directly models the lifetime and activity parameters and estimates them jointly. Our method overcomes all these challenges and produces quantitatively correct lifetime images beyond the resolution limit of the system CRT.

We address the problem of reconstructing the lifetime image from TOF PET data with finite CRT. We present a statistical reconstruction framework that maximizes the likelihood of observed PLI events, each comprising the following observable attributes: the detector receiving the prompt gamma, the detector pair receiving the annihilation pair, the time difference between the detection of prompt gamma and annihilation pair, and the time difference between the two photons within the annihilation. In our study, our simulation data include the flight time of the photons before detection and our method does not require having sub-100 ps TOF resolution for accurate localization of each detected event. We have verified our method using PLI events generated by the Monte-Carlo simulation.

Positron Annihilation Spectroscopy of oxygen content tissue-equivalent samples

Dr Ali Biganeh; Nuclear Science and Technology Research Institute, Iran

Positron Annihilation Spectroscopy (PAS) has numerous applications in material science such as studies of structural defects, free volumes, porous materials, and their chemical environments. In recent years, the applications of this technique in chemical processes, radiobiology, and medicine have been the subject of research by many researchers [1, 2]. PAS includes Coincidence Doppler Broadening Spectroscopy (CDBS) of annihilation radiation to determine the momentum of the electrons involved in the annihilation process and Positron Annihilation Lifetime Spectroscopy (PALS) for the investigation of the mechanism behind the positronium annihilation in the sample. In this paper, the possible application of the PALS technique for the characterization of healthy and cancer tissues is evaluated. The purpose of the experimental part of this work is to investigate the sensitivity of the PALS technique to the oxygen concentration in tissue-equivalent samples.

The accepted hypothesis for this research is that the concentration of oxygen in cancer tissues is less than in healthy tissues due to the massive cell proliferation [3]. To conduct the experiments, the PALS spectrometer based on digital signal processing has been designed, commissioned, and optimized in the NSTRI positron lab. This spectrometer makes it possible to record the time difference of events with a channel width of 10 ps and the timing resolution of 173 ps using the plastic scintillation detectors. To determine the sensitivity of the technique to the presence of the polar groups including carbon-oxygen bounding, 4 polymer samples were measured using PALS and CDBS techniques, and the correlation between the parameters was clarified. The results of this investigation confirmed that the position and height of the peak in the Orbital Electron Momentum Spectrum (OEMS) obtained in the Doppler experiment and the component of the positronium lifetime in the PALS technique are both sensitive to the presence of oxygen in the content [4]. To determine the PALS parameters related to the amount of oxygen, 6 tissue-equivalent polymers with different concentrations of oxygen were selected. The positron lifetime spectra in these samples were measured using the developed digital PALS spectrometer and the results were analyzed using LT-10 software. The results of this experiment confirmed that in general, as the oxygen concentration in the sample increases, due to the quenching role of oxygen atoms in the formation of the positronium atoms, the I_3 and τ_3 parameters decrease significantly. However, in the samples with a difference of about 4% in the oxygen concentration, the behavior analysis of the positronium lifetime and its intensity requires a systematic study of the effect of density, porosity, crystallinity, and the bond type in the polymer samples. The results of this work apply to the development of a tumor imaging system based on the PALS technique.

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Multiphoton time-of-flight MLEM reconstruction for the positronium imaging in J-PET

Dr Roman Shopa; National Centre for Nuclear Research, Poland

We modify the positronium imaging method for the Jagiellonian PET (J-PET) scanners, using the simulated data for the decays of a metastable ortho-positronium (o-Ps) based on the pick-off and conversion processes resulting in two 511-keV annihilation photons [1, 2]. An analytical model, embedded into the time-of-flight maximum likelihood expectation maximisation (TOF MLEM) reconstruction algorithm, is introduced for the assessment of the multiphoton detector response and the estimation of the o-Ps mean lifetime.

The detection probabilities of the J-PET system matrix are calculated for the coincident events each constituted by two annihilation and one deexcitation photons. TOF information is used for the iterative MLEM run and the estimation of a time difference between the annihilation and the positron emission, the distribution of which is built for each voxel. The latter is updated in event-by-event way using the weights for the ultimate MLEM iteration.

Employing the Geant4 software [3], we simulated the experiments with four point-like sources put into two existing J-PET prototypes, each corresponding to a tissue of a different o-Ps lifetime, with total activity 1.1 MBq for the injected 22Na [2, 4]. The decay model was restricted to include only the decays into back-to-back photons, implying the exponentially modified Gaussian shape for the aforementioned time difference histograms.

Utilising TOF MLEM allowed to reduce the noise and significantly improve the spatial resolution of the positronium imaging, compared to the earlier studies [1, 2]. The o-Ps mean lifetimes, calculated as a result of fitting the histograms exhibited a good consistency with the simulation setup. The reconstruction algorithm uses the advanced resolution model that accounts for both the geometrical factors and the detector blur of the J-PET, and can as well be extended to include attenuation correction or other contributions, as well as for the o-Ps decay into three photons.

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Pionic atoms and chiral symmetry

Prof. Kenta Itahashi; RIKEN, Japan

We have been working on pionic atoms to extract information on the chiral symmetry of the vacuum at the nuclear density. In the recent analysis, we evaluated the chiral condensate at the normal nuclear density (arXiv: 2204.05568). In 2021, we have conducted a new systematic measurement of pionic atoms along the long chain of the Sn nuclei. I will report the recent progress and the future perspectives.

Alpha and cluster decay of thermally excited nuclei

Prof. Neelima Kelkar; University of los Andes, Colombia

The unprecedented observational data from compact object mergers in recent years have confirmed that the nucleosynthesis of heavy and super heavy nuclei can be considered to proceed via the rapid neutron capture or r-process. The r-process nucleosynthesis path is along highly unstable, exotic, and neutron-rich nuclei. Thus, it is not only the photo-dissociation and neutron capture cross sections but also fission (spontaneous and induced) and the decay rates which are important for the abundance evolution.

The explosive conditions in supernovae and neutron star mergers leading to considerably high temperatures could result in nuclei existing in excited states. Though the thermal excitations of nuclei are usually taken into account in the production reactions and their reverse reaction rates

entering the network calculations, the alpha decay rates are taken to be those corresponding to the terrestrial decays of ground state nuclei.

In this talk, we shall discuss the effects of thermal excitations on the half-lives of heavy nuclei which decay by emitting an alpha particle (4He) or light clusters such as 14C, 20O, 28Mg etc.

Nuclear instabilities in white dwarfs

Prof. Marek Nowakowski; University of Los Andes, Colombia

A special class of white dwarfs violating the standard Chandrasekhar limit are right now a timely topic. These Super-Chandrasekhar objects could be understood as the progenitor of supernovae type Ia (SN Ia) and this is the main reason for their astrophysical interest. Some early studies tackled the possibility of white dwarfs surpassing the Chandrasekhar limit by means of magnetic fields. More recently modified gravity has turned out to be a new possibility that the researchers have discovered. In such a setting however, the theory becomes more sensitive to the the nuclear instabilities at the center of the star and a rigorous treatment of the latter becomes obligatory. In this talk we shall discuss the problem with a realistic equation of state to describe the white dwarfs in modified gravity taking into account the nuclear instabilities. A reliable limit of the maximum mass can be reached and put to test.

Decay probabilities in the multichannel case

Prof. Francesco Giacosa; Jan Kochanowski University of Kielce, Poland

In the context of an unstable state with more than a single decay channel, we present a novel and general formula for evaluating the decay probabilities in each open decay mode. We also discuss numerical examples in Quantum Mechanics (QM) and Quantum Field Theory (QFT). Just as for the survival probability p(t), these partial decay probabilities are also not exponential and their ratio turns out to be not a simple constant, as it would be in the exponential limit. Quite remarkably, these deviations may last relatively long, thus making them potentially interesting in applications.

Biomedical Applications of Radioactive ion Beams: First results of the BARB project at GSI

Prof. Marco Durante; GSI Darmstadt, Germany

Heavy ion particle therapy is a rapidly growing and potentially the most effective and precise radiotherapy technique. However, range uncertainties remain one of its limitations: they jeopardize the benefits of the sharp Bragg peak and force to use wide margins extending in the normal tissue.

The use of radioactive ion beams (RIBs) for simultaneous treatment and online range verification using positron emission tomography (PET) could help overcoming this limitation, due to increased signal/noise ratio and alignment of the activity peak with the Brag peak compared to PET imaging of fragments produced by primary, stable ions.

In this context, the BARB (Biomedical Applications of Radioactive ion Beams) project was initiated at GSI aiming to assess the technical feasibility and investigate possible advantages of RIBs in preclinical studies.

During the first year of experiments within this project, radioactive Carbon and Oxygen beams (10,11C and 15O) were produced by isotopic separation with the fragment separator and transported to the medical vault of GSI.

Thanks to the upgrade of the SIS-18 in the FAIR in Darmstadt, it was possible to achieve RIB intensities sufficient to treat a small animal tumor.

Beam implantation in plastic phantoms was visualized by two independent imaging setups: a dual-panel PET scanner from the University Medical Center Groningen and a subset of a high resolution small animal -PET detector in development at the Ludwig-Maximilians-Universität in Munich. Range and depth dose distributions measurements have been performed with a water column setup. These first experimental results will be presented.

Work supported by ERC Advanced Grant BARB (2020, Marco Durante)

Dose-3D - towards measuring radiation dose with spatial granulation

Prof. Tomasz Szumlak; AGH University of Science and Technology, Poland

In this talk, I introduce a breakthrough idea of a detector with a 3D active measuring matrix capable of sampling the spatial distribution of the radiation dose. Such a device can perform a measurement in quasi-real-time and may bring the quality control of delivered therapeutic dose and the personalisation of the treatment plans to a new level.

A new perspective for NCT: besides cancer, can it be effectively used for Alzheimer’s disease?

Dr Nicoletta Protti; Pavia University, Italy

Neutron Capture Therapy (NCT), since its first theoretical hypothesis of 1936 [1], was understood and applied mainly as a cancer treatment with few and occasional studies regarding other diseases [2,3]. Indeed, the high LET secondaries of 10B neutron capture reactions with their short ranges in tissues (less than 10 µm) makes the treatment selective at the single cell level, opening the route for an effective “locally activated” hadrontherapy useful for challenging scenarios such as wide spread tumours [4] and micro-infiltrating malignancies [5]. As cancer treatment, it is actually more correct to speak of BNCT being B10 almost the sole nuclide in clinical use and under investigation for future NCT agents.

Gadolinium, in particular the isotope 157 (Gd157), aroused the interest of the scientific community since a while [6]. The extremely short ranges of the charged secondaries (internal conversion and Auger electrons) set a very strong constraint on the NCT agent localisation inside the targeted cell which must bind DNA molecule directly. Nonetheless, the spread clinical use of Gd-enriched systems as MRI-probes prevents the definitive decline of the interest in GdNCT [7].

Alzheimer’s disease (AD) is the most common form of dementia (50-60% of all cases) [8]. Currently over 55 million people worldwide live with dementia and the number is expected to rise up to 139 million by 2050. Statistics say a new case of dementia arise somewhere in the world every 3 seconds. AD destroys nerve cells thus limiting or abolishing higher brain functions (memory, mobility, behaviour…). In the most advanced stages, patients are unable to care for themselves and need constant help with their daily life. This means huge costs, economically and psychologically, and indeed if we consider dementia as a country it would be the 14th largest economy worldwide, with a US$ 1.3 trillion current cost.

Despite the ongoing debate on AD pathogenesis and development, still the central role of the misfolded beta amyloid protein (Aβ) is widely accepted. In particular, recent studies [9] identified the oligomers, one of the first stages of aggregation of Aβ, as the most neurotoxic species thus supporting researchers of innovative treatments for AD.

In the late 1990's, the effectiveness of conventional radiotherapy in the treatment of TracheoBronchial Amyloidosis (TBA) suggested the idea of a possible beneficial effect of photon irradiation in AD as well [10,11]. Presently, evidences are under collection to demonstrate preclinically and in very small patient's cohorts the feasibility of such treatment [12,13].

In this scenario, Pavia University (Italy) proposed a further extension of the positive effects of ionising radiations in AD through the EU FET project "NECTAR": NEutron Capture enhanced Treatment of neurotoxic Amyloid aggRegates.

Thanks to the match between the Aβ aggregates dimensions and the ranges of B10 and Gd157 neutron capture reactions, a depolymerisation of the aggregates is suggested by the ionisation events. In parallel, the glia cell compartment of brain is supposed to be stimulated by the highly penetrating photons emitted by the very same capture reactions and so promoting the clearance of the Aβ debris. NECTAR will be the proof of concept at the preclinical stage of a bimodal treatment for AD capable of being sensitive to all the phases of aggregations of Aβ thanks to the development of specific new molecules designed to selectively bind Aβ protein.

Due to the progressive and chronic features of AD, we further expect to demonstrate the effectiveness of the treatment using highly fractionated irradiation protocols based on low doses and low dose rates per fraction, thanks to the evidences of a positive effect of LDIR (low dose ionising radiation) in the brain [14].

The presentation will deal with a general overview of NECTAR project and a brief description of the first results.

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Design and Application for a new intense positron beam at the Antimatter Laboratory in Trento

Luca Povolo; University of Trento, Italy

Co-authors: Sebastiano Mariazzi, Luca Penasa, Ruggero Caravita, Sushil Sharma, Roberto Sennen Brusa

At the Anti-Matter Laboratory (AML) of the Department of Physics of the University of Trento a new positron beam is currently under development. It is being constructed for the production into vacuum of Positronium (Ps, the bound state of an electron and the positron, e+), which will be used for fundamental studies, like inertial sensing [1]. However, Ps is emitted into vacuum in the ground state which has a lifetime of only 142 ns, while studies with positronium require lifetime in the microsecond range. This becomes possible by exciting Ps into a metastable state via a two-photon transition, as we demonstrated [2].

The production of positronium atoms start by injecting positron into a target, called e+/Ps converter [3-6]. The new positron beam of our laboratory is based on a 22Na radioactive source coupled with a solid noble gas moderator held at cryogenic temperature [7]. Up to now we obtained a continuous beam with up to 50000 positrons per second per milli-Curie. The next step will be the bunching of the continuous beam with a Buffer-Gas Penning trap [8] which will be followed by the positron bunch injection into the converter.

In this work, we will present the preliminary design of the apparatus with simulations. The extraction of the positron continuous beam from the source-moderator via magnetic field will be discussed in detail. The plan for the trapping and injection of the positron will be presented. Moreover, we will discuss the tests for a possible detector for Positronium inertial sensing, which needs to have the capability of 3D reconstruction of the Ps annihilation point.

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Calibration of Silicon Drift Detectors for the SIDDHARTA-2 Experiment

Dr Aleksander Khreptak; National Laboratory of Frascati (LNF), Italy

The main aim of the SIDDHARTA-2 experiment at the DAΦNE collider in the LNF-INFN (Italy) is to perform the high precision measurement of the kaonic deuterium exotic atom, which is formed when a negatively charged kaon (K−) is captured in a highly atomic excited state, replacing an electron [1,2].

To achieve this goal, a large area Silicon Drift Detectors (SDDs) system has been developed by the SIDDHARTA-2 Collaboration [3]. The energy response of each detector should be calibrated and monitored to reduce the systematic error (to the level of 2-3 eV).

The poster will present a calibration method for the SIDDHARTA-2 setup [4], which should guarantee high precision spectroscopic performances of the system during the data taking.

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Monte Carlo simulation platform and software stack in Dose-3D project

Jakub Hajduga; AGH University of Science and Technology WFIIS, Poland

As part of the Dose-3D project titled "Reconfigurable detector for measuring spatial distribution of radiation dose for applications in preparing individual patient treatment plans", in addition to the construction of the new type of phantom itself, it is necessary to develop high-end software for dose simulation, configuration and control of the entire device and finally the data analysis. Within the project comprehensiveness the software stack comprises a number of packages for data processing and analysis (Monte Carlo generators, Raw data preprocessing, Machine Learning tools, Python/C++ modules, Medical Physics specific software for DICOM standard).

The Monte Carlo simulation itself is an essential element for the success of the Dose-3D project. This is related to the fact that MC physics simulations are the gold standard cross-check for planning and cross validation of experimental data. Using a framework based on the Geant4 engine we will produce data that mimics real apparatus. The data will be used to optimize the parameters of the Dose-3D cell and ensure proper calibration of the prototype phantom.

One of the most important features of the final simulation platform is the possibility to read-in and setup within simulation environment irradiation plans stored in DICOM-RT format.

One of the most important parts of the Dose-3D software stact is the middleware that bridges gaps between the low and high level data processing. Based on the Python-like packages (with specific c++ modules binded to Python) we provide unified services to users. The presented work embraces a modern approach of software engineering for the interdisciplinary scientific project which is the Dose-3D.

The aforementioned middleware in-house software is being developed as Python package called pydose3d. Its modules are responsible for such functionalities as handling data from different sources (internal MC simulation based on Geant4, PRIMO simulation and phantom measurements), where these data are then unified in a high-level data exchange format (Pandas Data Frame), modules responsible for basic visualization and analysis of acquired data, or a set of tools responsible for loading information about the planned course of radiotherapy from DICOM-RT files, which can then be loaded into the simulation itself.

Application of the PALS technique in the investigation of the nanostructure of enzymatic biosensor matrices for biomarkers detection in medical diagnostics

Magdalena Goździuk; Maria Curie-Skłodowska University, Poland

Co-authors: Bożena Zgardzińska, Taras Kavetskyy

Biosensors are devices widely used in many fields of medicine. Using biosensors we can detect biomarkers of pathological states. One of very popular biosensor types are enzymatic biosensors. The biggest advantage of enzymatic biosensor is detection of specific molecules depending on the enzyme used which is associated with the absence of false positives. Sensors of this type are characterized by high sensitivity and selectivity. Enzymatic biosensors have a matrix which improves biosensor detecting abilities and immobilize an enzyme. Matrices can be produced from many types of materials e.g. gel, carbon nanotubes, chitosan, nanowires, polymers etc.

We use Positron Annihilation Lifetime Spectroscopy to investigate nanostructure of biosensors biopolymer matrices based on soybean oil. The matrices are the part of amperometric enzymatic biosensors. The advantage of using polymer matrices is their low resistance so they do not interfere with the detection mechanism. The second important issue is good liquid sorption to a matrix to get better sensitivity. Soybean- oil based matrices were investigated in wide range of temperatures (120 K÷320 K) to determine the phase transitions in samples and analyze nanostructure changes due to temperature. The next stage of research was sorption/ desorption using deionized water, NaCl solution and polluted water. Using PALS we can forecast matrix properties used in biosensor construction basing on ortho-Positronium lifetimes ($\tau3$) and intensities (I3) changes under given humidity conditions and correlate results received using other investigation methods.

Double photon coincidence detection method for gamma-ray imaging in medicine

Dr Mizuki Uenomachi; Kyoto University, Japan

Co-authors: Kenji Shimazoe, Hiroyuki Takahashi

Positron emission tomography (PET) utilizes the coincidence detection of annihilation gamma-rays with energy of 511 keV produced after a positron-electron collision. The positron position can only be constrained on a line connecting the detection points because two annihilation gamma-rays emit at the opposite direction. On the other hands, some nuclides emit successive gamma-rays via an intermediate state with a short duration such as 111In, 177Lu, 60Co, and so on. These successive gamma-rays are emitted at almost isotropic direction; thus, the radionuclide location can be identified by using direction-resolving radiation detection system. We have exemplified the position identification capability of double photon coincidence method by applying to Compton imaging and mechanical collimation-based gamma-ray imaging. Moreover, we have demonstrated its crosstalk reduction capability in multi-nuclide Compton imaging. In the presentation, we will show the experimental results of the double photon coincidence method application.

Intelligent data analysis for the next generation medical phantom Dose-3D

Kamila Kalecińska; AGH University of Science and Technology, Poland

Co-authors: Dose-3D Collaboration

Medical data intelligent analysis is the part of TEAM NET

Dose3D Project "A Reconfigurable Detector for Measuring the Spatial Distribution of Radiation Dose for Applications in the Preparation of Individual Patient Treatment Plans". The goal of the Dose3D consortium is to build a three-dimensional measurement system containing a detector capable of directly measuring the spatial distribution of the deposited therapeutic dose in real-time. The keyword "reconfigurable" means that such a tissue-like phantom can be configured to mimic a specific part of the patient 's body. Delivery of a proper geometry which is in the form of 3D Computed Tomography (CT) scans of the patient body with highly precise delineation of the area of affection to the detector is the important step of the whole process. The idea is to build a reliable, fully automatic tool that would be able to extract the desired volume from 3D CT images. Technically this process (named segmentation) refers to assigning each voxel of the 3D image to a specific class.

Training data for segmentation tasks consists of raw CT scans in DICOM format as well as already manually segmented data in DICOM-RT Structures format. Medical data format complexity and data limitations mostly caused by privacy issues that require the preparation of a special preprocessing pipeline. One of the important steps in this procedure is to perform an effective data augmentation, which refers to artificially increasing the amount of training data. Both data augmentation and 3D image automatic segmentation tools will be built on the basis of the most advanced deep learning models.

High computational power and GPU's support are required in the process of training 3D deep learning models. Fortunately, the modern platform delivered by NVIDIA (NVIDIA Clara) with Python framework MONAI is dedicated to healthcare data analysis. This framework provides state-of-the-art pre-trained ML models, a set of tools for medical preprocessing and domain-specific GPU optimization.

The presentation will be about prospects, challenges and the current stage of developing medical data analysis tools with the potential to improve the individual treatment plans.

Silicon as a candidate for a proton beam-activated tracer for range verification in proton therapy

Barbara Kołodziej; Jagiellonian University, Poland

Co-authors: Aleksandra Wrońska, Aleksandra Kaszlikowska, Mareike Profe, Ronja Hetzel , Barbara Beus, Magdalena Garbacz, Renata Kopeć

Proton therapy is a radiotherapy method which is superior to conventional radiotherapy performed with photons because of the achievable dose conformality. However, to fully benefit from the favorable dose-depth profile of the ion beams, new methods are required to monitor the treatment process online. A class of methods is under development based on the analysis of prompt gamma radiation, which can provide information on the dose distribution in real time [1]. The idea of a proton beam-activated tracer, discussed in this poster, is based on detecting a prompt gamma signal from an element delivered to the tumor selectively and excited by the proton beam [2]. In the poster, silicon will be presented as a suitable candidate for such a tracer.

Investigation on silicon was performed using Geant4 simulations. The aim of the simulations was to obtain a prompt gamma spectrum and the response of a detector. In the simulations, a cuboid PMMA phantom was used as the target, housing in its center a silicone-doped insert (mass concentration of 2%). The phantom was irradiated using a treatment plan layer by layer, and the results were adjusted to include the anticipated acceptance of a detector. The use of an HPGe detector of RWTH Aachen [3], equipped with an active Compton shield, was considered. Its response and effect on the registered spectrum were also investigated.

For proximal monoenergetic layers, the signal from the tracer was statistically significant when the Bragg peak was completely located in the insert. For distal layers, when Bragg peak was outside the insert, the signal dropped noticeably, but it was still visible because the cross section for producing gamma particles is non-zero for higher-energy protons. Inclusion of the detector response did not change this observation. However, reduction of statistics resulting from detection efficiency lead to the necessity of including the active Compton shield in the detection setup, otherwise the signal was buried by background.

The results showed a dependence between the signal from silicon and the Bragg peak position, and this observation can be used to develop monitoring methods based on tracers activated by the proton beam. The next planned step is to confirm this result by experiment, whose pilot run took place in February 2022 at the Cyclotron Centre Bronowice. This research was funded by the Priority Research Area Digiworld under the program Excellence Initiative – Research University at the Jagiellonian University in Kraków and by the Polish National Agency for Academic Exchange.

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Design of spread-out Bragg peaks in spatially fractionation proton therapy

Agata Tobola-Galus; Institute Of Nuclear Physics Polish Academy of Sciences, Poland

Co-authors: Jan Swakoń, Paweł Olko

Purpose

In spatially fractionated proton therapy SFTP (proton grid therapy) the arrays of parallel and pencil proton beams generated by grid collimator are applied to reduce the impact of irradiation on healthy tissue. At the beam entrance the locally irradiated skin benefits from the ununiform profile of beam causing faster repair of irradiated tissues. In the same time, due to the multiple Coulomb scattering of the proton beam, the target volume can be uniformly irradiated. In this paper, use of proton grid therapy is considered designe Spread-Out Bragg Peak (SOBP) at the target depth. The aim of these studies was dosimetry verification produced grid collimator and range modulator to form uniform SOBP for spatially fractionated proton beams.

Material and Methods

The experimental verification of the depth dose distribution was performed at the eye proton therapy unit with 60 MeV proton beam from AIC-144 cyclotron at IFJ PAN Krakow. Mesh-like brass collimators with the lateral centre-to-centre (c-t-c) spots distances of 2 mm (spot diameter 1 mm were prepared were prepared. A spread out Bragg peaks (SOBP) of half modulation (from 1.5 cm to 3 cm-depth in water) and full modulation were formed by specially designed for this collimator range modulators. ProBImS scintillator system with a CCD camera were placed at several depths in a solid-water slab phantom to evaluate the relative 2-D dose distribution. As a figure of merit, the ratio between the central dose of one minibeam (peak dose) and the dose in the middle of two consecutive beams (valley dose) was evaluated. This magnitude, named peak-to-valley dose ratio (PVDR), is a very relevant parameter in such spatially fractionated techniques. The dosimetry was complemented by measurements of the depth dose distribution performed in water phantom using the Markus ionization chamber and 2D-TLD in the solid phantom.

Results

Our results show that for parallel beams 1 mm in diameter with c-t-c 2 mm, the optimal distance of the collimator from the eyelid surface is 35 mm, obtaining an almost uniform dose in the target and satifiable values of PVDR (3-5) in the region of the beam entrance. A decrease in the PVDR value is observed with increasing distance of the phantom from the collimator. Changing the distance of the measurement system from the grid collimator (snout) affects the shape of the dose depth distribution. The differences are not large, mainly an increase of the dose at the entrance, and negative slope of the plateau are observed.

Conclusions

Spatially fractionated proton therapy SFPT (proton grid therapy) is being considered for the treatment of eye tumors. A favorable dose distribution at the beam entry would allow the eye to be irradiated through closed eyelid sparingly due to spatial fractionated dose.

Designing range modulator wheels to SOBP for parallel proton min-beams with energy of 60 MeV, and diameter of 1 mm were found to be sufficient achieve homogeneous irradiation of the target and to obtain a flat plateau SOBP with full and half modulation.

The results of this work can be used to guide future radiobiological experiments using artificial skin.

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Angular DOI Calibration Methods towards PET In-System Calibration of (Semi-) Monolithic Scintillators

Yannick Kuhl; RWTH Aachen University, Germany

Co-authors: Florian Mueller, Stephan Naunheim, David Schug, Volkmar Schulz

Introduction

Available clinical positron emission tomography (PET) systems commonly consist of one-layer segmented detector arrays with planar 2D gamma positioning. However, without 3D positioning in the additional depth-of-interaction (DOI) direction the system's spatial resolution is reduced at off-centered positions due to parallax errors. This effect is particularly relevant for small ring diameters, or for total body PET devices with a large axial field of view. Monolithic and semi-monolithic detectors represent an attractive alternative with overall good performance characteristics and intrinsic DOI capability. Currently, the best positioning performance of (semi-)monolithic detectors is achieved with individual calibration and subsequent processing, e.g., with machine learning-based gamma position estimation routines. Detector calibration describes the process of acquiring a dataset of gamma interactions in the detector at known positions to generate, e.g., a training dataset for machine learning-based preprocessing approaches. In this work, the machine learning technique gradient tree boosting (GTB) is used that establishes a relationship between the known gamma interaction position and its light distribution and is thus able to assign an interaction position to unknown light distributions. However, the individual calibration is time-consuming, especially for large PET systems, with calibration times of several days per detector using a conventional parallel hole beam collimator. By introducing a fan beam collimator, also used in this work, the process can be accelerated to hours per detector and even to minutes with the adaption to a multi fan beam collimator utilizing several fan beams at the same time.

Currently, however, these methods are only prepared for calibration in test setups, making it tedious to recalibrate the detectors once they have been installed in the PET system. A re-calibration may be necessary due to changes in measurement parameters, such as changes in temperature or bias voltage, as well as aging of the detector components. Therefore, an in-system calibration technique may be necessary to establish (semi-)monolithic detectors in a system. For planar calibration with gamma irradiation along the detector normal only an adjustment of the setup is necessary. For DOI calibration with currently proven lateral detector irradiation, however, a new calibration method must be developed since the detector sides are inaccessible in a ring.

The challenge for in-system calibration is now to generate an appropriate DOI training dataset with known irradiation position, exclusively by measurements in the installed PET system. As a proposed solution, this work introduces two DOI calibration routines based on angular detector irradiation.

Materials

The coincidence setup consists of a fan beam collimator and two PET detectors based on 8 semi-monolithic LYSO slabs with a height of 19 mm and a width of 3.9 mm coupled to a DPC3200-22 dSiPM (PDPC). One of the detectors is the one to be evaluated and can be rotated in steps of 11.25° between lateral irradiation (0°) and the detector normal (90°) in relation to the fan beam plane by a special bracket. In the set position, the detector can be driven through the fan beam using a linear translation stage to irradiate the entire crystal volume for complete calibration datasets.

Angular Irradiation Methods

In the first “monoAngle” method, the DOI position of the gamma interactions is obtained from a previously performed planar position estimation, based on GTB as well, and the known geometric course of the gamma beam inside the detector.

In the second “duoAngle” routine, the DOI position is calculated geometrically from the intersection of two successively irradiated beams and then assigned to the gamma interactions within that intersection. The main task here is to find the gamma interactions in the area around the intersection. The initial assumption is that the light distributions of both beams are similar at the intersection. An iterative, mutual search algorithm narrowing down the light distributions via similarity to this intersection showed the best results. In this iterative search, each light distribution of one beam is compared with all gamma interactions of the other beam for similarity using a Nearest Neighbor routine with a Euclidean distance metric, applied to the inverse optical photon counts. 20% of the most dissimilar gamma interactions per beam are discarded per iteration until a termination criterion is reached, which is based on the Lambert-Beer law and the penetration depth of the beams. Further calculated features based on the light distribution as a supplement showed no improvement. Using a planar position estimation, based on GTB and performed in advance, the gamma interactions in question can be restricted to a planar Y-position range around the intersection prior to the iterative search.

Results and Conclusion

Both methods showed a positioning performance within 5 % to the lateral irradiation (0°) up to an irradiation angle of 45°. Thus, both methods are suitable candidates for in-system calibration. Comparing monoAngle and duoAngle, the monoAngle method is simpler in application and implementation and could provide even better positioning performance for higher resolution detectors than those used here.

Developing a phantom for the positronium imaging evaluation.

Gabriela Łapkiewicz; Jagiellonian University, Poland

Co-authors: Pawel Moskal, Szymon Niedźwiecki, on behalf of J-PET collaboration

Phantoms used in PET technique, such as NEMA IEC allow for measurement of activity concentration accumulated in different volumes. New imaging method developed by the Jagiellonian PET collaboration in addition to the annihilation density distribution enables measurement of positronium lifetime [1-4]. To qualitatively determine the precision of this method it is essential to construct a phantom, which will allow for measuring ortho-positronium lifetime alongside activity concentration.

The proposed phantom (much like NEMA IEC) will consist of 6 volumes of high activity accumulation immersed in the lower activity background. Each volume will feature different mean lifetime of ortho-positronium. Isotopes used for measurements must not only exhibit β+ activity, but also need to emit prompt gamma quanta (i.e. 44Sc or68G a) [5], [6]. In this contribution a method for controlling ortho-positronium lifetime is discussed along with preliminary results.

In order to evaluate a method for the prepration of media with different ortho-positronium lifetime we have studied the ortho-positronium lifetime in water suspension of XAD4 porous material. XAD4 is characterized with the average pore size of 50 Å and can absorb water up to 60% of its mass [7].

Five samples of XAD4 with controlled amount of water were measured using PALS technique. Additionally one dry sample of XAD4 and one sample of pure water were measured. Obtained spectra were fitted with PALS Avalanche [8] and components corresponding to the ortho- positronium annihilation in XAD4 pores were established [9]. The results showed the correlation between the lifetime and production intensity of ortho-positronium and the concentration of XAD4 in water.

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Estimation of 511 keV gamma scatter fraction in WLS layer in Total Body J-PET, A simulation study

Keyvan Tayefi Ardebili; Jagiellonian University, Poland

Co-authors: Szymon Niedźwiecki , Paweł Moskal, on behalf of the J-PET collaboration

A positron emission tomography (PET) scan plays an essential role in medical diagnostics and monitoring therapy. A new generation of Total-Body PET scanners based on plastic scintillators is being developed by the J-PET collaboration at Jagiellonian University [1].

The total body J-PET scanner comprises of 7 rings, each ring consisting of 24 modules. A single module is built of 2 layers each one 16 axially arranged plastic scintillator strips of 33 cm in length, read out by silicon photomultiplier (SiPM) arrays from both ends, and an additional layer of 50 wavelength shifter (WLS) fibers. In this study, an estimation of the scatter fraction of the Total-Body J-PET manufactured from plastic scintillator strips according to the NEMA NU 2-2018 standards by using GATE software. The scatter phantom was simulated as a solid cylinder with a length of 700 mm and an outside diameter equal to 203 mm while at a radial distance of 45 mm we have a hole with a diameter of 6.4 mm that linear source with total activity 1 MBq is placed [2,3]. For data processing, sinograms were generated and the Single Slice Rebinning (SSRB) algorithm was used for the calculated scatter fraction amount.

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Breast Cancer diagnosis study along with the introduction of new detection technology

Shivani; Jagiellonian University, Poland (Jagiellonian University)

Co-authors: on the behalf of J-PET collaboration

In both developing and developed countries, breast cancer is the top cause of mortality among women. Medical imaging plays an important role for breast cancer screening, for classifying and examining indistinct breast abnormalities, as well as for defining the extent of breast tumors [1]. Positron Emission Mammography is one of the most widely used imaging modalities today (PEM). The goal of the J-PET group is to develop, build, and test the J-PEM (Jagiellonian Positron Emission Tomography), which is based on a novel concept using plastic scintillators[2,3,4,5] and a wavelength shifter (WLS) [6,7]. readout.

The results of the examination of data acquired from the hospital, which included 131 lesions, will be presented in this poster. The cases involved 114 individuals, with 98 having one lesion, 14 having two lesions, and one patient having three lesions. The findings of the BI RADS-based diagnostic test will be presented. A comparison of ROC curves will also be shown.

The performance of a newly designed J-PEM scanner prototype is also characterised in this work. The goal of the J-PET group is to develop, build, and test the J-PEM (Jagiellonian Positron Emission Tomography), which is based on a novel idea using plastic scintillators[2,3,4,5] and wavelength shifter (WLS) [6,7] readout. The prototype system is made up of two layers of plastic scintillators (6x24x500 mm) and one layer of wavelength shifters [3] (3x10x100 mm) arranged orthogonally between them. For signal reading, each scintillator bar is connected to Silicon Photomultipliers on both ends. This three-dimensional device is based on the innovative notion of using plastic scintillators to detect annihilation photons and wavelength shifters to improve spatial resolution (WLS). Gate simulation was used to calculate the point spread function, sensitivity, and scatter fraction. To understand the difference, simulations were run with WLS strips (Z = 1.28 mm) and without WLS strips (Z = 10 mm). It is apparent that utilising WLS strips lowered the value of PSF along the Z-axis by about half (4.7 mm).

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Determination of 10B concentration in melanocytes and melanoma cells

Monika Szczepanek; Jagiellonian University, Poland

Co-authors: Anna Telk, Ewa Stępień

Melanoma is the most aggressive skin cancer, difficult to treat when metastatic. It is also cancer that may become a candidate for Boron Neutron Capture Therapy (BNCT). BNCT is type of radiation therapy that employ the altered metabolism of cancer cells and additionally minimizes side effects. During treatment, the patient is administered a compound containing the non-radioactive isotope of boron (10B), which accumulates in the melanoma cells due to its increased metabolism compared to normal cells [1]. Then, the diseased area of the patient's body is irradiated with a thermal neutron beam. As a result of irradiation, cells with accumulated 10B are destroyed, while neighboring cells, not loaded with 10B stayed undamaged. Selectivity in this therapy is based on the increased metabolism of neoplastic cells, which ensures a higher boron concentration compared to normal cells [2,3]. The principle of efficient BNCT depends on the amount of boron delivered to cancer cells , which must be 3 times higher in compare to normal cells. Therefore, the aim of proposed research is to assess the uptake of the 10B isotope by normal and cancer cells in an 2D in vitro model.

In our research, we used normal skin cells – melanocytes and two melanoma cell lines, delivered from primary tumor (WM115) and metastasis (WM266-4). Cells were incubated with boron carrier (boronophenylalanine, BPA) in concentration 50 µg B/ mL, for 2, 4, 6 and 12 hours. The effective boron carrier ensures a high concentration of 10B atoms in the cells at the level of 20-35 µg10B / g of tumor tissue (1.2-2.1x109 10B atoms per cell) [4]. After incubation cells were harvested and 10B isotope concentration was measured using inductively coupled plasma mass spectrometry (ICP-MS).

Both melanoma cell lines reached maximum concentration of 10B after 4h of incubation with BPA, 9,2 µg10B/g and 27, 9 µg10B/g for WM115 and WM266-4, respectively and these concentrations seemed to fluctuate within 12 hours of incubation. In case of melanocytes 10B concentration in cells increased during the incubation time up to reach the highest boron concentration at 33,7 µg10B/g in 12 hour of incubation.

Our results showed different kinetics of boron uptake in different cell types which is in confirms previous studies [5]. These data suggest the need to investigate the mechanism of BPA uptake and metabolism in other melanoma cell lines to eligible BPA for BNCT cancer treatment.

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Detection of concentration and survival of HL-60 human acute promyelocytic leukemia cells by the PALS technique

Katsiaryna Yankova; Maria Curie-Skłodowska University, Poland

Co-authors: Bożena Zgardzińska, Bożena Jasińska, Marek Gorgol, Marcin Czop, Janusz Kocki

The HL-60 human acute promyelocytic leukemia cells obtained from the Clinical Genetics Department of Medical University in Lublin were investigated with the use of positron and positronium probes. The HL-60 cell line is a popular and convenient test object due to easy reproduction. The cell line comes from the patient, 36-year-old Caucasian female with acute promyelocytic leukemia. The 16 samples were used for the study: 15 with HL-60 cell-line with different concentration of cells and 1 sample with a pure medium, as a reference. The studies were performed with positron annihilation lifetime spectroscopy (PALS) and the results were correlated with cell survival. Examined samples were subjected to various external factors during measurements: ionizing radiation, time and light.

In contrast to our expectations, we found that the o-Ps component in PALS spectra does not differentiate the samples sufficiently and can't be used as the only analyzed parameter. The components of para-positronium and free annihilation should also be considered. Our studies indicate the possibility of assessing the concentration of cell lines using the PALS technique, but a much more important factor differentiating the obtained results turned out to be the concentration of live cells in the sample. The positron annihilation shows a very close correlation with viability of the cells in the samples. Relaying on gathered information we can conclude that the PALS technique can be used as a highly sensitive method for estimating the quantity of living cells in sample.

Study of differences in the composition of glycosphingolipids between the extracellular vesicles from β-cell and endothelium cell lines using ToF-SIMS

Dr Magdalena Marzec; Jagiellonian University, Poland

Co-authors: Carina Rząca, Ewa Stepien

Time of Flight Secondary Ion Mass Spectrometry (ToF-SIMS) is used to analyze biomolecules in tissues, cells and membranous structures. This type of mass spectrometry enables qualitative semi-native testing without the need for isolation, fixation or labelling of target elements with simultaneous 2D imaging. The analyzed mass range is less than 1000 Da, which makes it possible to study of amino acids and lipids [1]. Extracellular vesicles (EVs) are spherical cellular structures surrounded by a lipid bilayer in size from 30 to 1000 nm. The basic classification of EVs distinguishes three subpopulations: exosomes derived from endosomes (50–150 nm), cell ectosomes (100–1000 nm) and apoptotic bodies (1000–5000 nm). Due to the constantly growing importance of EVs in the diagnosis and treatment of diseases, more and more attempts are made to effectively isolate, detect and analyze them [2]. So far, it has not been demonstrated whether the increased sugar concentration in the external environment modifies the composition of glycosphingolipids (GSL) in the composition of cell membranes and EVs.

The aim of the study is to compare the GSL composition in EV subpopulations: ectosomes and exosomes. In this study, EVs were purified by a low-pressure filtration and concentrated by an ultracentrifugation. EVs come from two cell lines: pancreatic β-cells and microvascular endothelium cells (TIME). Both cell lines were grown under normoglycemic (NG) and hyperglycemic (HG) conditions. The experiment also investigated the change in the content of the analyzed biomolecules in EVs due to high glucose concentration influence.

As a result of the conducted research, we have shown that we can perform glycosphingolipid analysis in extracellular vesicles using ToF-SIMS. The analysis showed significant changes in GSL composition depending on the cell line (β-cells and microvascular endothelium cells) for both ectosome and exosome populations. Cell culture conditions (hyperglycemia) affect the glycosphingolipids profile both in the group of ectosomes and exosomes.

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Gold nanoparticles as contrast agents for micro-CT imaging

Dominik Panek; Jagiellonian University, Poland

Co-authors: Bartosz Leszczyński, Paweł Moskal, Ewa Stępień

Micro-computed tomography (micro-CT) is nowadays often used to examine biological samples. This technique, based on the attenuation of X-rays, is capable of achieving micrometric resolution. However, the challenge is to stain the samples in such a way that they will be opaque to the X-ray radiation with a given energy. That is why different types of contrast agents are being currently developed in order to obtain the highest contrast. But the contrast itself is often not enough for the biological studies. It is also important for the contrasting agent not to be toxic in any way – it has to be biocompatible. Example of such contrasting agents are gold nanoparticles (AuNPs), which are by far the most studied nanomaterials and, amongst other metallic nanoparticles, are believed to be the most appropriate for biological research [1, 2]. In our studies, the □CT scanner (SkyScan 1127) was used in order to visualize the uptake and accumulation of AuNPs. The nanoparticles were incubated with melanoma cell line (WM266-4) spheroids – a 3D cell model of cell culture intended to imitate tumor tissue, especially the environment inside it [3]. In this case, micro-CT was used to check if it is possible to visualize AuNPs inside spheroids created from a the same number of cells (2000) and on different days of growth (3rd and 7th), incubated for 24h. The concentration of gold NPs used in this study was identical for all the samples and equal to 2.5 µg/ml. Additioanlly, the same concentration of AuNPs was added to the cells from the beginig of spheroid creation to comapre it with standard method. The results of experiments indicate that AuNPs are promising contrast agents, due to their high atomic numer, which does not require the use of high concentraions. The spheroid was not created in case of the method where AuNPs were added to the cells from the beginning.

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Relevance of Monte Carlo simulation validation analysis in the scope of the Dose-3D project

Wioleta Górska; AGH University of Science and Technology, Poland

Co-authors: DOSE-3D Collaboration

Radiotherapy aims to deliver a specific dose of radiation to the treated area, destroying the tumour. Thanks to the use of newer technologies and their continuous development, it is possible to very precisely deliver the planned doses of radiation to the treated areas, while reducing the exposure of healthy tissues to radiation. Undoubtedly, physical simulations and the use of algorithms supporting the work of medical physicists contributed to the improvement of the quality of treatment. Due to their advantages, MC simulations are used both in the area of treatment planning and scientific research. However, to obtain reliable calculation results, it is necessary to previously validate the MC simulations, concerning experimental and reference data. This milestone has been already achieved in the scope of the Dose-3D project and this presentation is aimed to present its summary.

The Dose-3D project is a novel reconfigurable detector intended for a full spatial therapeutic dose reconstruction to improve radiotherapy treatment planning. The main challenge of the project is the construction of a 3D measurement matrix. One of the crucial challenges is the development of high-quality software for dose simulation, configuration and control of the entire device, and data analysis. A key issue in the research will be to obtain a high agreement between the simulated dose distributions and those measured during the detector tests. For this purpose, The GEANT4-RT simulator platform was assembled. The implementation of a reliably functioning platform using the GEANT4 engine to simulate the interaction of radiation with matter is crucial for the success of the entire project.

To verify the reliability of the modelled Varian Clinac 2300 C/D medical linear accelerator head and used physics model in the GEANT4-RT the spatial dose distributions were calculated and then correlated with the respective measurements provided by The Maria Sklodowska-Curie National Research Institute of Oncology in Krakow. The comparisons were conducted using a variety of methods including the common and standard verification approaches used in clinical practice like dose difference analysis and gamma test. The validation was extended by comparison with the results generated by Penelope engine based MC simulator - PRIMO, whose reliability was verified in addition to Geant4-RT scope of studies. Once the geometry specification of linac's is not publicly available we rely on the linac model defined in the PRIMO simulator. Extracting phaspace for the given beam model from PRIMO we continued simulation in GEANT4-RT application including field modelling here.

Furthermore, MC simulation allows for physics model specifications and tuning values correlated with it like production cut. For this reason, it is necessary to verify the reliability of selected configurations. To execute such validation, an analysis of the photon interactions in the water phantom was performed.

In conclusion, MC simulation platform within the Dose-3D project has been initialised and verified as the in-house application for further development for reconfigurable scintillator phantom purposes.

Assessment of the influence of the Beta parameter in the reconstruction of Q.Clear

Konrad Skórkiewicz; Jagiellonian University, Poland

Co-authors: Anna Sowa-Staszczak, Kazimierz Łątka

Aim/Introduction: The aim of the study is to determine the appropriate value of the β parameter using the Q.Clear reconstruction algorithm in the imaging of patients with neuroendocrine tumors. Materials and Methods: The analysis concerned the measurements of the NEMA IEC Body Phantom, filled with Ga-68 gallium chloride. Within the phantom we placed the 4 smalles hot spheres filled with a higher isotope concentration in comparison with the body part. Imaging was performed in the PET/CT scanner in few time intervals. The raw data were reconstructed with the use of the Q.Clear reconstruction algorithm with 18 values of the β parameter (150-1000, every 50). Results: The obtained results show that together with an increase of the values of the β parameter, the image quality in the Q.Clear reconstruction algorithm increases. Referring to the scientific reports, one can see that the signal to noise ratio in the image increases. The effect of the change of the β parameter on the SUV mean value is the largest for the smallest sphere. The percentage decrease is much higher also with the lower values of the activity, reaching a value of 3.7% and 8.5% for large and small sphere with β=450, in comparison with β=200. With β=1000 a very significant decrease is observed, especially for the smallest sphere and for the lowest activity measured, which is 18.5 % when β=200. Conclusion: An increase of the values of the β parameter has an adverse effect on the quantitative assessment of SUV. In the visual assessment, a satisfactory image quality is present with β=450. This value results in a relatively low decrease of the SUV mean and SUV max.

Measurement of correlation between polarization of annihilation photons emitted in e+e- system to detect entanglement at sub-MeV range

Deepak Kumar; Jagiellonian University, Poland

Co-author: Sushil Sharma, on behalf of the J-PET collaboration

Quantum electrodynamics predicts that photons originating from the decays of e+e- annihilations are entangled and have mutually orthogonal linear polarization [1]. Since the polarization of the photons is orthogonal to each other, correlation can occur in subsequent interactions. Compton scattering of photons can be used as a polarization analyser to measure such correlations [2]. To measure the correlation between the scattered photon due to entanglement, the two photons must be detected before and after the scattering [3]. Thanks to its unique geometry, J- PET can be used as a potential detector to perform such studies in full phase space [4,5,6]. It consists of 192 plastic scintillators with dimensions 50 x1.9 x 0.7cm3 (length x width x height) arranged in 3 cylindrical layers with increasing radial distance 42.50 cm, 46.75 cm and 57.5 cm, respectively [4]. Photons interact mainly via the Compton effect inside plastic scintillators. Since an incident photon interacting with the plastic scintillator is mostly scattered perpendicular to the polarization direction of the incident photon, the polarization of a single photon is defined as the cross product of the momentum vectors of the photon before and after scattering ($\epsilon=k \times k'$) [7].

Our goal is to study the correlation between the polarization vectors of annihilation photons produced either by direct annihilation of electron and positron or by the formation of a positronium atom in the presence of a medium. In this presentation, the methodology to perform such studies in the framework of J-PET detector and the preliminary results will be presented.

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Characterization of spheroid growth based on a new dynamical model

Dr Kamil Dulski; Jagiellonian University, Poland

Co-author: Monika Szczepanek

Cell cultures are a recognized model that helps understand interaction of cells with certain external factors, such as radiation or drugs [1,2]. In particular, characterizing the growth of a given cell line for a different intensity of a therapeutic agent allows for non-invasive assessment of its effectiveness [1], and in some cases also for optimization of therapeutic conditions for cells of a given type [3,4]. Currently, there are two types of cell culture - 2D, where cells grow in a planar monolayer and 3D, an example of which are spheroids. 3D cultures are characterized by greater similarities to tumours in the conditions occurring in the body. The common features between spheroids and tumours allow for a more complete understanding evaluation of the effectiveness of therapy [3-6].

Currently, the growth of biological systems is mainly described by logistic models, most often with the Gompertz model [7,8]. However, this model does not always describe the experimental data perfectly, and it also fails to characterize the cell line based on parameters such as cell size, nutrient consumption, and separation zones of strongly dividing cells from zones with dead and non-dividing cells. A new, dynamic model of spheroid growth will be presented, allowing to characterize the above-mentioned parameters and additionally better reflecting the spheroid growth curve. Additionally, the simulations performed using dedicated software allowed for a detailed characterization of the WM266-4 skin cancer cell line, as well as for the theoretical visualization of the distribution of various zones inside the spheroid at different growth times.

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Characterization of the 192-strip J-PET detector for multi-photon positronium imaging

Dr Kamil Dulski; Jagiellonian University, Poland

Co-author: on behalf of the J-PET collaboration

Positronium imaging is a promising new technique that can enhance the diagnostic capabilities of Positron Emission Tomography (PET), based on a new structural index derived from ortho-positronium interaction with the environment in which it annihilates [1,2]. A positronium (Ps) can be formed during a standard PET scan when a positron emitted from a radiopharmaceutical administered to a patient forms a bound state with the electron. Depending on the total spin number S, the positronium can be formed in one of two states - para-Ps (p-Ps, S = 0) and ortho-Ps (o-Ps, S = 1). These two states differ mainly in the average lifetime (in vacuum: 0.125 ns for p-Ps and 142 ns for o-Ps) and the number of photons that are emitted during the annihilation (p-Ps even, o-Ps odd number of photons). In particular, the lifetime of o-Ps may be shortened when interacting with the environment in which it is formed. Therefore, by simultaneously reconstruction of the position of o-Ps annihilation and its average lifetime, it becomes possible to characterize the structure of a given part of the sample in space, which is the basis for positronium imaging [1]. Currently, the J-PET detector [1-3] is the only detector that is able to obtain positronium images. The positronium images of the two phantoms measured by the 192-strip J-PET detector will be shown [1,4]. Additionally, data on the sensitivity and purity of two- and three-photon positronium imaging will be presented on the basis of simulation data [4].

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Development of a high-resolution PET detector for small animal in-beam PET system

Dr Munetaka Nitta; Ludwig Maximilians University, Germany

Co-authors: Munetaka Nitta, Giulio Lovatti, Kang Han Gyu, Rohgieh Haghani, Chiara Gianoli, Georgious Dedes, Andrea Zogular, Yamaya Taiga, Christoph Scheidenberger, Marco Durante, Peter Thirolf, Katia Paodi

We have been developing a high resolution small in-beam PET system in the framework of the project "Small animal Irradiation for Research in Molecular Image-guided radiation Oncology (SIRMIO)", which is an EU-funded endeavor aiming to realize a prototype platform for accurate image-guided small animal proton irradiation at clinical facilities. In this project we plan to deliver a proton beam to the mouse tumor and monitor the positron emitters generated by the beam using a dedicated in-beam PET scanner. The PET scanner exhibits a unique spherical shape for high detection sensitivity along with sufficient open space for accommodating the beam and integrating additional beam monitoring detectors as well as a mouse holder. In addition to that, uniform sub-millimeter spatial resolution is required for accurate range verification. In order to achieve these requirements, in a collaborative effort between LMU and QST, we have developed a 3-layers depth-of-interaction (DOI) PET detector [1]. The PET detector is composed of LYSO scintillator pixels with 0.9 mm×0.9 mm×6.67 mm size read out by an 8×8 SiPM array. A charge division circuit is used to reduce the 64 signals of the SiPM array to 4 signals for an Anger calculation. 56 PET detectors are embedded in a spherical housing frame.

In this study, a point source experiment was carried out to evaluate the spatial resolution of the PET scanner especially in the central region of the field of view and along beam axis. There, we could achieve the targeted 1 mm spatial resolution, confirming satisfactory performance for our project. In addition to that, we will show the capability of our PET detector for high resolution radioactive ion beam imaging of C-11, as explored in the context of the EU-funded project "Biomedical Applications of Radioactive Beams" (BARB).

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CP Discrete Symmetry study in the decay of ortho-Positronium atom using the J-PET detector.

Kavya Valsan Eliyan; Jagiellonian University, Poland

Co-authors: Juhi Raj, On Behalf of the J-PET Collaboration

Interaction between electron-positron pair leads to direct annihilation into photons or creation of a bound state called Positronium. Positronium is the lightest purely leptonic object decaying into photons [1-3]. Positronium atom can be formed in two states based on the spin alignment of its constituting particles, Singlet state (1S0 -para-Positronium (p-Ps) and Triplet state (3S1- ortho-Positronium (o-Ps). Constrained by conservation laws, the o-Ps annihilate into odd number of photons (o-Ps → 3γ, where γ = 1, 2, ...), while the p-Ps decay into an even number of photons (p-Ps → 2γ, where γ – 1,2, 3, ...) [4,5]. As an atom bound by a central potential, it is a parity eigenstate, and as an atom built out of an electron and an anti-electron, it is an eigenstate of the charge conjugation operator [1]. Therefore, the positronium is a unique laboratory to study CP discrete symmetry involving correlations of photons momenta originating form o-Ps annihilation [6]. The Standard Model predicts that the photon–photon interaction and weak interactions will mimic the symmetry violation in the order of 10−9 and 10−13 respectively [6]. Violation of CP invariance in purely leptonic systems has never been seen so far [7]. The experimental limits on CP and CPT symmetry violation in the decays of o-Ps are set at the level of 10−3 [2,8].

In the year 2021, the limitations of the previous experiments were overcome by the J-PET detector due to its much higher granularity and improve the world result by a factor of three and reaches the statistical precision of 10−4. The reported result is the present best upper limit on the CP violation in the decay of ortho-Positronium, leaving us 5 orders of more statistical sensitivity to be explored in this aspect. J-PET detector is constructed of 192 polymer scintillators, where each scintillator is attached with photomultipliers at each end. 192 scintillators are arranged co-axially in three layers at 3 different radii 42.5 cm, 46.75 cm, 57.5 cm respectively. Positronium atom can be formed in the center of J-PET detector using the beta-emitter 22Na source placed inside a small chamber. The source is sandwiched between an aerogel material. Plastic scintillators offer high time and angular resolution. Time Over Threshold is adopted as a measure of energy deposition. The signals are measured by using the trigger-less data acquisition [9-12]. All of the previous investigations with Positronium, which tested the discrete symmetries, were based on symmetry odd operators constructed as the products of photons momenta ($\vec{k}_i$) and Positronium spin ($\vec{S}$) vectors [2-4,6]. This project describes an extended study using another proposed operator [4], taking advantages of properties of the 3 layered J-PET detector, which enables to determine the linear polarization direction of annihilation photons. Measurement of polarization direction of annihilation photons (511 keV) is a unique feature of the J-PET detector which allows the study of CP symmetry violation by determining the expectation values of the CP symmetry odd operator ($\vec{\varepsilon}_i \cdot \vec{k}_j$) where $i \neq j$). As a future prospect, the J-PET collaboration has developed a modular version of the J-PET detector to improve the detection efficiency of this measurement and provide larger statistics in a shorter duration of measurement time to improve the precision significantly.

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Towards improving the sensitivity of testing CPT symmetry in positronium decays with the Modular J-PET detector

Neha Chug; Jagiellonian University, Poland

Co-authors: on behalf of the J-PET Collaboration

The Jagiellonian Positron Emission Tomograph is the first plastic scintillator based tomographic device used to test discrete symmetries in the charged leptonic sector [1]. One of such tests is for CPT symmetry, under the combined transformation of charge, parity and time reversal, in the decays of positronium atoms [2]. J-PET performed its first measurement for CPT symmetry test by searching for non vanishing CPT-violating angular correlations between the spin and orientation of decay plane of ortho-positronium (o-Ps) atoms, which is the triplet state of positronium [3, 4]. Sensitivity of testing CPT symmetry with the J-PET detector reaches the precision level of 10-4 [4]. Here we will discuss the prospects of improving the sensitivity of this test beyond the level of 10-4 by enhancing the photon registration efficiency using a new layer of densely packed plastic scintillators and a spherical annihilation chamber as a positronium production medium [5].

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Testing Quantum Foundations in the Cosmic Silence

Dr Kristian Piscicchia; Centro Ricerche Enrico Fermi - Museo Storico della Fisica e Centro Studi e Ricerche "Enrico Fermi", Italy

The VIP experiment, operated at the Laboratori Nazionali del Gran Sasso (LNGS) of INFN, aims to perform high sensitivity tests of the Pauli Exclusion Principle (PEP) for electrons. In the context of Local Quantum Field Theories, deviations from PEP are strongly constrained by the Messiah Greenberg Superselection (MGS) rule, which forbids superpositions of states with different symmetry. Such models can then be only tested with open systems. Such a condition is fulfilled in VIP-2 by introducing new electrons in a pre-existing system of electrons, and testing the resulting symmetry state. An overview of the latest VIP-2 Open Systems result will be presented.

PEP violations, transgressing MGS, were recently shown to be induced by space-time non-commutativity, a class of universality for several models of Quantum Gravity. High sensitivity tests of PEP violation in closed systems represent the better candidates to test the non-commutativity emergence in Quantum Gravity, at unexpectedly high energy scales. The results of exploratory studies will be shown.

The extremely low background environment of LNGS is also suitable for investigating the measurement conundrum, one of the main mysteries of Quantum Mechanics Foundations. Dynamical models of wave function collapse explain the quantum-to-classical transition by a progressive reduction of the superposition, proportional to the increase of the mass of the system. The results of our analyses, setting the strongest bounds on the collapse models, will be presented.

A bound diproton: is it “illusive” particle or exotic nucleus?

Prof. Ihor Kadenko; International Nuclear Safety Center of Taras Shevchenko National University of Kyiv, Ukraine

We report on a search for a bound diproton, or 2He nucleus, by analyzing the results of irradiation of Tb and Ta samples with protons of 5.8 and 6.9 MeV energy, correspondingly. These proton energies are about threshold energies for corresponding (p,2p) nuclear reaction channel. The irradiated Tb and Ta samples were then counted with application of HPGe gamma-spectrometer. The peaks of 511 keV energy and of high intensities were detected in the instrumental gamma-ray spectra. We measured its intensity vs time and derived the corresponding values for half-lives. These values are the following:

- for Tb sample: 5,603 ± 385 s after extended cooling of irradiated sample;

- for Ta sample: 1,224 ± 56 s and 6,307 ± 340 s.

In order to assign these half-lives to any reaction products on (p,x) nuclear reactions on Ta and Tb as well as impurities in these samples, we could not identify any significant contributors to the 511 keV peak intensity of certain half-lives.

Then we make an assumption about the formation of the diproton, or 2He bound and proton-excess nucleus, to be a source of positrons with subsequent annihilation of them in a sample volume. The idea for the diproton to exist is based on the prediction of A. Migdal in 1973 for two identical particles to become bound in the potential well of a heavy nucleus but outside of its volume. This prediction was experimentally proved by us for two neutrons, bound together in one nucleus – the dineutron and does not exclude the existence of a similar bound system, but comprised of two protons.

In the same time, theoretical estimates for a positron decay mode of the diproton were obtained as follows:

- for a diproton decay into a triplet deuteron state: 1140 ± 216 s;

- for a diproton decay into a singlet deuteron state: 5516 ± 1031 s.

Possible algorithms to calculate diproton binding energy and radius as well as mutual space arrangements between a heavy nucleus and the diproton are also considered.

Based on our preliminary results and estimates one can assume that such an approach to generate and study diprotons in detail may result in discovery of the very unusual system “the heavy nucleus-diproton” to confirm for the diproton the status of being the unique nucleus rather than an “illusive” particle.

In addition, the existence of such out-and-outer 2He nucleus may have far-reaching consequences on our understanding of nucleon-nucleon and nucleon-nucleus interactions as well as practical app.

Search for η′-mesic nuclei in (p,dp) reaction at GSI/FAIR

Dr Yoshiki Tanaka; RIKEN, Japan

Possible existence of η′ meson nucleus bound states (η′-mesic nuclei) has been attracting both theoretical and experimental interests due to their relation to axial U(1) anomaly and chiral symmetry breaking in QCD. Experiments to search for η′-mesic nuclei were recently performed by using the (p,d) reaction at GSI and by the (γ, p) reaction at SPring-8. However, no significant peak structure of the bound mesic states was so far observed, which lead to upper limits of the formation cross sections as well as constraints on the η'-nucleus potential. In order to further investigate η'-mesic nuclei, new experiments with an increased experimental sensitivity are necessary.

At GSI/FAIR, we have performed a new experiment in 2022 by combining the large-acceptance detector system WASA with the forward high-resolution spectrometer FRS to search for η'-mesic nuclei with an improved sensitivity. We employed a 2.5 GeV proton beam from the SIS-18 synchrotron and used the FRS for high-resolution missing-mass spectroscopy of the 12C(p,d) reaction near the η'-meson production threshold. Simultaneously, possible decay particles from the produced η'-mesic nuclei, particularly high-energy protons, were detected and identified by the WASA detector system surrounding the reaction target to enhance the signal-to-background ratio of the missing-mass spectrum.

In this contribution, we will report on this recent experiment including the status of the data analysis.

Kaonic atoms at DAΦNE: where we are and where we go?

Prof. Catalina Curceanu on behalf of Dr Alessandro Scordo; National Laboratory of Frascati (LNF), Italy

The DAΦNE machine at the INFN Laboratories of Frascati is still the most suitable facility in the world, in terms of purity of the kaon beam, luminosity, and kinematic conditions, to perform measurements of kaonic atoms.

Recent progress in the field of X-ray detectors and their readout electronics contributed, in these last years, to a renewed interest in new and more precise measurements.

Beyond the SIDDHARTA-2 experiment, presently installed on the DAΦNE Interaction Point exploiting 450 mm thick Silicon Drift Detectors (SDD) to measure for the first time X-rays from kaonic transitions in deuterium, several other important measurements are still planned or proposed.

These new measurements, among which transitions in kaonic helium, carbon, sulfur, lead, wolfram, nitrogen, and molybdenum, are now feasible thanks to new technologies: 1 mm thick SDDs, CdZnTe, and HPGe detectors as well as crystal spectrometers and TES microcalorimeters.

In this talk, an overview of the already planned and foreseen measurements, together with others proposed for future campaigns, will be presented together with their physics case, possible impacts, and details of the experimental setups.

Sensitivity of the deeply bound pionic atoms to the pion-nucleon sigma term

Dr Natsumi Ikeno; Tottori University, Japan

The deeply bound pionic atom is known to be a very useful system to investigate the pion properties and the aspects of chiral symmetry at finite density. The pion-nucleon sigma term σπN is one of the essential quantities to investigate the value of the chiral condensate in the nuclear medium. However, the σπN value has not been determined accurately enough. Therefore, it seems to be very interesting to determine the σπN value by the deeply bound pionic atoms.

We have theoretically studied the sensitivity of the observables of the deeply bound pionic atoms to the pion-nucleon sigma term σπN to investigate the possibility of the precise determination of the value of σπN by the accurate data of the deeply bound pionic atoms expected to be obtained at RIBF/RIKEN. I will give a presentation based on the paper of Ref. [1].

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Study of the eta-prime meson in nuclei in the LEPS2/BGOegg experiment

Dr Natsuki Tomida; Kyoto University, Japan

A large mass reduction of the η′(958) in nuclei is expected in several theoretical models. If there is large mass reduction, an η′ meson and a nucleus can form a bound state. We investigated the η′-nucleus system in the LEPS2/BGOegg experiment. To search for the η′-nucleus bound state, we carried out the missing mass spectroscopy of the 12C(γ,p) reaction. To suppress background events from mult-meson productions, the one nucleon absorption decay products were simultaneously measured for the first time. In addition, we also carried out the simultaneous measurement of escaping η′ mesons from nuclei. We will report the η′-nucleus optical potential evaluated by using both data. We will also show the preliminary results of the direct measurement of η′ mass spectra from the η′→γγ decay in nuclei.

Mass modifications of vector mesons in a finite density matter

Prof. Kyoichiro Ozawa; Institute of Particle and Nuclear Studies, KEK, Japan

Origin of hadron masses have wide interests in the field of nuclear physics. Light quarks, such as up and down quarks, only have “bare” mass of a few MeV/c^2. A proton and a neutron, which contains only three quarks, have mass of ~1 GeV/c^2. This difference between quark mass and hadron mass can be theoretically explained as dynamical generations of hadron mass by a spontaneous breaking of a symmetry in a “QCD vacuum”. In this point of view, hadron masses are not a stable and it can be changed in a finite temperature and/or density medium. Several experimental efforts are performed to measure mass modifications of hadrons in a finite temperature and/or density medium. In high temperature region, high energy heavy ion experiments, such as SPS, RHIC, LHC, are performed. Experiments at KEK-PS, CLAS, CBELSA/TAPS are also performed to study hadron masses in a nucleus, as a finite density matter.

We are carrying out a new experiment to measure mass spectra of vector mesons in nuclei at J-PARC in Japan. The experiment is a successor to the experiment at KEK-PS. In the experiment, we measure electron-positron decays of vector mesons, since mass spectra of the vector mesons have strong relations with an order parameter of the symmetry breaking in the medium. We focus on electron-positron decays to avoid final state interactions between medium and daughter particles. We constructed new spectrometer which consists of four layers of tracking detectors and two kinds of electron identification counters. Tracking detectors are one layer of Silicon Strip Detector and three layers of Gas Electron Multiplier (GEM) Trackers. For electron identifications, GEM-based gas Cherenkov counters, so called Hadron Blind Detector, and Lead Glass EM calorimeters are used.

We started constructions of a beam line and detectors in 2012. We had the first beam in 2020 and started beam study and detector shake down. We collected pilot data in 2020 and 2021 to evaluate detector performances. We are planning to have the first physics data-taking period in early 2023. We will introduce recent activities of related studies and show status of our experiment.

Also, future plans to measure mass modification in a high-density matter which can be created using heavy ion collisions will be discussed.

Studying the process γd→π0ηd

Prof. Alberto Martinez Torres; University of Sao Paulo, Brasil

In this talk I will present a theoretical study of the γd→π0ηd reaction and show that the observed shift of the peaks of the π0d, ηd invariant mass distributions with respect to the phase space distributions are related to the dynamics of the γp→π0ηp.

Exotic properties of N*(1895) and its impact on photophroduction of light hyperons

Prof. Kanchan Khemchandani; Federal University of Sao Paulo, Brasil

In a recent work, we have studied the decay properties of N(1895), which was found to arise from meson-baryon interactions in an earlier work. We investigate the decays to different meson-baryon systems and to final states involving \Lambda(1405) and a proposed \Sigma(1400). In this talk, I will show that the width of N^(1895) can get an important contributions from the decay to light hyperon resonances and such findings can be relevant for processes like the photoproduction of \Lambda(1405).

Polarisation observables Sigma, T, P and H in pi0 and eta photoproduction off quasifree nucleons

Nicolas Jermann; University of Basel, Switzerland

The excitation spectrum of the nucleon is an important testing ground for quantum chromodynamics in the regime where it cannot be treated perturbatively. During the last two decades much progress has been made on the theory side, e.g. lattice gauge methods and in experiments, particularly using energy tagged photon beams at electron accelerators, which has now reached a state where not only differential cross sections but also asymmetries measured with polarised photons

and polarised targets allow for detailed partial wave analyses. This provides much more stringent information about the involved reaction multipoles and thus the contributing nucleon resonances. The present experiment was done at the ELSA accelerator in Bonn with the Crystal Ball/TAPS detector setup. The incident electron beam of 3.2 GeV impinged on a diamond radiator where it produced coherent bremsstrahlung photons with linear polarisation, which again impinged

on a transversely polarised, deuterated butanol target. This allows the simultaneous measurement of the polarisation observables Σ, T, P and H. Analysed were the final states Nπ0 and Nη with the almost 4π covering electromagnetic calorimeter Crystal Ball/TAPS.

One of the main motivations of this experiment was a more detailed investigation of the not yet understood narrow structure in the excitation function of the γn→nη reaction at approximately 1 GeV.

Preliminary results will be discussed.

Helicity dependent cross sections for the photoproduction of π0π± pairs from quasi-free nucleons

Dr Debdeep Ghosal; University of Basel, Switzerland

Photon induced π0π±-pairs production from quasi-free nucleons bound in the deuteron has been investigated in view of the helicity dependence of those two reactions. Measurements with a liquid deuterium target were used to extract the unpolarized cross sections for protons and neutrons. A deuterated, longitudinally polarized butanol target together with a circularly polarized photon beam was also used to measure the double polarization observable E. Antiparallel and parallel spin configurations of the beam photon and target nucleon correspond to the spin-dependent cross sections σ1/2 and σ3/2 respectively, which have been derived from E. The measurements were done at the Mainz MAMI accelerator with tagged photon beams produced via bremsstrahlung from longitudinally polarized electron beams. The reaction products from the two target types were detected with an almost 4π solid-angle covering calorimeter composed of the Crystal Ball, TAPS detectors and particle identification detectors. The results are sensitive to sequential decays of nucleon resonances via intermediate states and also by emission of charged ρ mesons. Furthermore, the results have been compared to the recent available model calculation.

High throughput cost-efficient Flat panel monolithic Walk Through PET

Prof. Stefaan Vandenberghe; Ghent University, Belgium

The first Total Body PET scanner have been installed in several (>10) institutions in Europe despite its high acquisition price of 8-10 MEuro. The first experiences of these groups have been closely followed and important conclusions are:

•Scan times of 15 sec to 1 min deliver excellent quality for standard doses (used on nowadays standard short axial FOV)

•Data handling and size are challenges due to the very high sensitivity

•Patient throughput is potentially high (one patient every 3 min) not limited anymore by the scan time but mostly by patient handling and a shortage of personnel

Also in the clinical world there are gradual changes ongoing and expected. PET is not only used for detection but more and more for (expensive) therapy prediction and follow-up. There will be more and more selected screening based on genetic information, blood test and/or patient history. Even with selected screening there will be a high number of patients and repeat scans. Patients will also quite often healthy (or in an early stage of cancer).

This change in the patient population and clinical needs can be dealt with PET scanners with the following properties

•Lower dose imaging (healthy patients)

•Faster imaging + higher throughput

•Lower cost imaging (systems + procedure)

•Less personnel per scan (shortage of personnel)

Therefore we redesigned TB-PET towards a fast technique with high throughput. Using the latest monolithic detector technology we propose a new design, departing from the classical patient positioning on a bed. We propose an upright scanner (similar to airports mm-wave scanners or planar X-ray) using TOF technology. This optimises detector area and avoids time consuming patient positioning.

The following key elements enable such a design:

•The presence of TOF gives us direct tomographic information and obviates the need for complete coverage of the patient.

•Scatter and attenuation correction can be done with Deep learning

•CT can be avoided and leads to lower dose to the patient

•The size of the detectors is based on measurement from a PET patient population

The main benefits of this design regarding cost and performance are:

•We need 1.9 x less detector surface for the same axial FOV (due to close detectors)

•The effective sensitivity is higher as there are more oblique incidences with flat panels

•Monolithic detector technology (High resolution + Depth of interaction) enables system resolution below 2mm (over the whole FOV).

Finally the potential clinical throughput, patient experiencse and patient motion was evaluated using a first mockup flat panel scanner in a NM department.

Promising detector concepts to advance coincidence time resolution for time-of-flight positron emission tomography

Prof. Craig Levin; Stanford University and University of Leeds, USA

We are studying novel detection concepts to enhance coincidence time resolution (CTR) for time-of-flight (TOF) positron emission tomography (PET). In this short talk we will briefly discuss fundamental limitations on PET CTR using scintillation detectors and describe new configurations and electronic readout designs that attempt to address those constraints. We also concisely describe an innovative, non-scintillation-based, fast detection concept, which borrows concepts from the field of optics, that could in theory achieve ~1 ps CTR. If successful, these technologies will lead to next generation systems that enhance TOF-PET's ability to visualize and quantify disease.

A new Brain Dedicated PET scanner with 4D detector information

Prof. Jose Maria Benlloch Baviera, Institute for Instrumentation in Molecular Imaging CSIC, Spain

4D-PET is a new scanner dedicated to the brain examination. The scanner is based on an innovative detector design, that obtains full 3D impact position of the gamma ray inside the detector crystal, while providing also a precise (in the order of 250ps) determination of its impact time. The detector design is based on crystal slabs that allow also for good Depth of Interaction measurement, critical for dedicated scanners. We will show in this presentation the results obtained with real data at module level and the overall scanner expected performance with simulated data.

Development of Polarization-Sensitive Positron Emission Tomography Demonstrator based on Single-layer gamma-ray polarimeters

Dr Siddharth Parashari; University of Zagreb, Croatia

The utilization of polarization correlations of gamma-rays originating from para-positronium annihilation is emerging as an important additional handle to identify true coincidences in Positron Emission Tomography (PET) showing the potential to improve the signal to noise ratio in this imaging modality [1-3]. It was demonstrated experimentally that the polarization correlations of annihilation quanta could be successfully measured using segmented single-layer scintillator matrices [4]. In that proof-of-concept study we used 4x4 Lutetium Fine Silicate (LFS) scintillator matrices read out by silicon photomultipliers (SiPMs) to reconstruct the Compton scattering of the gammas in a single segmented scintillator layer acting both as the scatterer and as the absorber. In events where both quanta undergo Compton scattering, the difference between their azimuthal scattering angles could be used to deduce the initial relative polarizations, since the two are highly correlated. In a subsequent exploratory study we tested five detector configurations of 64 pixels each of either GaGG:Ce or LYSO:Ce crystals with cross section varying from 1.9×1.9 mm2 to 3.0×3.0 mm2 with the effective pitch of 2.2 mm and 3.2 mm, respectively, aiming to achieve optimal sensitivity to measure polarization correlations of annihilation quanta [5]. At the same time, Geant4 simulations of the investigated configurations were performed in support of the experimental evidence [6]. Polarimetric performance of different module configurations were assessed by reconstructing the Compton azimuthal angle difference of the annihilation gamma pair in measurements with a 22Na point source (≈1 kBq) positioned between modules. The results showed that higher polarimetric modulation factors are achieved by modules with finer segmentation, the highest being, $\mu=0.34\pm0.1$, for the GaGG crystals of 1.9×1.9×20 mm3 size with 2.2 mm pitch.

The current research focuses on the development and testing of a PET demonstrator (scanner) based on the single-layer polarimeters. The advantage of the single-layer Compton detectors, as opposed to multi-layer configurations, is that their scaling up to large systems does not add complexity or cost, compared to standard PET devices. The demonstrator comprises four large modules with matrices of 16×16 scintillator pixels read out by SiPMs, a pair with 3.2 mm pitch and another with 2.2 mm segmentation pitch. They are placed on radially sliding detector arms enabling choice of the ring diameter from 420 to 700 mm. The mechanical construction also enables precise rotation around the scanner axis to cover the full angular range. The SiPM control and the data acquisition are done by the TOFPET2 system [7]. We will report on the overall performance of the detector modules and the key parameters driving the sensitivity to detect polarized gamma-rays. We will also report on the development of the demonstrator and discuss its potential use with point as well as extended sources keeping gamma-ray polarization as key interest.

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Reconstruction of photon’s interaction position within plastic scintillator based on the WLS strips readout for the Total-Body J-PET

Szymon Parzych; Jagiellonian University, Poland

Registration of gamma quanta is a fundament for many experiments from the field of physics, as well as in nuclear medicine. One of the approaches for its enabling is provided by the means of plastic scintillator detectors. Developed by the J-PET Collaboration multi-purpose device - J-PET tomograph [1,2], consists of axially arranged plastic scintillator strips, read out at both ends by a pair of silicon photomultipliers [3]. Independent on application of this system, either as a PET tomograph or proton beam range detector during proton therapy, the axial coordinate of the photon interaction within the scintillator is derived from the time difference of scintillation signals arrival on the opposite sides of the scintillator. Therefore, the axial spatial resolution for the interaction point reconstruction is limited by the timing resolution. A way to improve the axial resolution was presented in [4], where it has been examined that utilization of multiple orthogonally oriented wavelength shifter (WLS) strips can enhance the axial coordinate determination. Nonetheless, due to the lack of the depth-of-interaction detection, the rest of interaction position coordinates is set to the respective scintillators center.

In this work, a semi-depth-of-interaction method for radial coordinate reconstruction will be introduced based on the simulations of the aforementioned setup. If interaction occurred near to the WLS strips, the photons emitted within the cone dictated by the total internal reflection angle will largely interact in the nearest region, while in case of further place of interaction this region correspondingly expands. Moreover, a different approaches to the axial coordinate reconstruction will be presented.

The abovementioned work is presented on behalf of the J-PET Collaboration. This work was supported by the TEAM POIR.04.04.00-00-4204/17 program, the NCN grant no. 2021/42/A/ST2/00423 and the SciMat and qLife Priority Research Areas budget under the program Excellence Initiative - Research University at the Jagiellonian University. The study was funded by “Laboratories of the Youth” as part of the “Excellence Initiative - Research University” program at the Jagiellonian University in Kraków.

Artificial intelligence in cardiovascular Imaging

Prof. Piotr Slomka; Cedars-Sinai Medical Center, USA

Cardiovascular imaging has been experiencing rapid development recently thanks to refinements in imaging technologies and software for image analysis. Recent breakthroughs in data science, machine learning, and artificial intelligence (AI) have been applied broadly to pre- and post-processing of imaging data.

Novel computing approaches hold the promise of improved image quality, automated detection and segmentation of abnormal regions, image registration, and modality-to-modality transformation. There is a wealth of imaging information that offers new opportunities – while this can be automatically extracted from medical images, new methods are required for integrating the diverse data such as multimodal images and electronic health records.

AI may allow meaningful improvements in diagnostic accuracy and quantitative outcome prediction. Interpretable AI systems can explain the primary factors driving the diagnosis or prognosis to both the physician and patient, dispelling the "black-box" perception of AI. I will overview the latest AI developments in cardiovascular imaging, both classical machine learning and deep learning focusing on nuclear medicine and CT, including application in PET imaging. I will also discuss issues related to the validation and deployment of AI systems for medical imaging applications.

PET imaging innovations

Prof. Taiga Yamaya; National Institutes for Quantum and Radiological Science and Technology (QST), Japan

In current PET, only a few percent of gamma rays emitted from a patient are used for imaging. Therefore, improvement of the sensitivity is a hot topic worldwide. Axial extension, which is referred as total-body PET, is essential in terms of the sensitivity improvement. In organ dedicated imaging, on the other hand, it is possible to improve the sensitivity without increasing the number of detectors. Improvement of spatial resolution is also expected by eliminating the photon non-collinearity effect.

In the former part of this presentation, development of brain-dedicated PET systems will be reviewed. Among them, we have recently developed VRAIN, a PET system with a hemispherical detector arrangement [1]. The hemispherical geometry fits the head best, and minimizes the photon non-collinearity effect by reducing the detector-to-detector distance.

In the latter part of the presentation, alternative approaches to improve the sensitivity rather than increasing the solid angle of the measurement system will be reviewed. Among them, whole gamma imaging (WGI) is a novel concept of combined PET with Compton imaging. An additional detector ring, which is used as the scatterer, is inserted in a conventional PET ring so that single gamma rays can be detected by the Compton imaging method. In addition to conventional PET and Compton imaging, further large impact can be expected for triple gamma emitters such as Sc-44 (~4 h half-life), that emits a positron and a 1157 keV gamma ray almost at the same time. In principle, only a few decays would be enough to localize the source position by calculating intersection points of a 511 keV line-of-response with a 1157 keV Compton cone. We developed a prototype of the WGI system [2][3], and a Na-22 point source, which emits a 1275 keV gamma ray soon after a positron decay, was measured as an alternative to Sc-44. In the triple gamma imaging, where only simple backprojection was applied and no image reconstruction algorithm was applied, spatial resolution for the Na-22 point source was 4.8 mm FWHM (8 cm off-center) - 5.7 mm FWHM (center). WGI can be also used to measure positronium lifetime [4], which may enable a new field of "quantum PET (Q-PET)". One possible application of Q-PET is hypoxia imaging of tumor patients [5].

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Multi-isotope imaging and quantum chemical sensing with PET and SPECT nuclides

Prof. Kenji Shimazoe; The University of Tokyo, Japan

Multi-isotope imaging is important for investigating multi-molecule dynamics in individuals. PET and SPECT dual tracer imaging in vivo is demonstrated with a developed Compton PET hybrid camera. In nuclear medicine imaging, quantum chemical sensing, such as pH and chemical state of molecule, can be additional value to accumulation imaging. pH sensing and imaging is demonstrated with liquid state In-111 SPECT nuclide by double-photon imaging method. Recent works on multi-isotope imaging and quantum sensing with double photon imaging will be introduced.

Polarization and directional correlations of γ-rays for nuclei: Scope in PET

Prof. Pragya Das; Indian Institute of Technology Bombay, India

The spectroscopic investigation of nuclei at high spin states has led to many discoveries, e.g., exotic shapes, super-deformation, shape coexistence, and chiral symmetry. In this endeavor, the accurate spin-parity assignment to nuclear states is crucial. Many studies in the literature have focused on finding the directional correlation ratios (DCO) for the assigning spins without any polarization measurement for parity determination. The use of polarization-directional correlation (PDCO) [1] not only determines the parity, but can also easily distinguish stretched and non-stretched γ-transitions, allowing to establish both spin and parity. We have confirmed some earlier tentative spin-parities in 128I and 129Xe and modified a few of them with our new results on mixing ratios using PDCO. It is needless to mention here that a fresh understanding of the nuclear structure is required if the spin-parity of the bandhead state is changed.

We performed an experiment via the fusion-evaporation reaction – 11B (124Sn; α3n, p5n) 128I, 129Xe – using the Pelletron accelerator at the Tata Institute of Fundamental Research (Mumbai, India). The experimental set-up (INGA) consisted of 21 Compton suppressed HPGe clover detectors. The list-mode data [2] were utilized to construct the asymmetric matrix for finding PDCO. We used 90∘ detectors as polarimeters (θpil) and all other detectors as directional detectors (θdir), and followed the PDCO formalism by Droste et al. [1].

For the case of 129Xe, we assigned [3] the bandhead spin-parity 21/2+ to a 2180 keV state decaying via 604 keV γ-ray, based on only the DCO information. Our finding (21/2+) and other available results for the same state – 19/2+

by Huang et al. [4] and 19/2– by Helppi et al. [5] – were all in complete disagreement. So, it became imperative to confirm our assignment by further analyzing the PDCO data, which enabled us to establish the same state 21/2+. Moreover, there were other discrepancies, and we could resolve them by critically examining the PDCO contour plots, i.e., polarization (P) vs. DCO ratios (RDCO) for different values of mixing ratios. It was possible to distinguish stretched and non-stretched transitions. Notably, no polarization measurement existed in the literature prior to our work.

In the context of using polarization correlation of coincident γ-rays, the property of entanglement (orthogonal polarization) of annihilation photons (511 keV) has immense potential in positron emission tomography (PET). It can help classify the true coincidence events amongst the scattered, random, and multiple events. However, the research area has not been fully explored, probably because of experimental difficulties. Only a few simulation-based studies exist [6, 7]. We have also tried a preliminary study [8] with many simplified assumptions but have not yet succeeded in improving the image quality.

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Interaction of positron and positronium with gases in liquids and development of a new positron beam for advancing such fundamental studies

Prof. Farida Selim; Bowling Green State University, USA

Through the last decades positron and positronium annihilation have been powerful tools for fundamental studies in physics, chemistry, and matter. Now the recent development of novel type of positron emission tomography (PET) at the Jagiellonian University in Krakow stimulates great interest to understand positron/positronium interactions with gases dissolved in liquids and urges new research avenues in positron/positronium science. In this talk I will give an example of such research and describe the development of a new beam to advance such fundamental studies of positron and positronium in a wide range of science. I will discuss how it can be used to advance our understanding of positron and positronium physics related to medicine. Lastly, future perspectives of positron and positronium applications in medical diagnostics and therapeutic will be given.

Development of a spatial sensitive detector for positronium inertial sensing measurements

Dr Sebastiano Mariazzi; University of Trento, Italy

Co-authors: Ruggero Caravita, Lisa Glöggler, Luca Povolo, Luca Penasa, Sushil Sharma, Pawel Moskal, Roberto Sennen Brusa

Recent experiments have demonstrated the possibility to produce positronium in the long-lived 23S state (lifetime of 1142 ns) via 13S→33P [1] laser excitation followed by spontaneous [2, 3] or stimulated [4] 33P→23S transition. This excitation scheme has shown to be suitable for the production of a monochromatic source of 23S positronium [3,5].

The employment of such a source of 23S positronium has been proposed to perform the first force-sensitive inertial studies, including gravity, with a purely leptonic system [6]. In order to perform these studies, three main steps are necessary: i) a monochromatic beam of 23S positronium has to be produced, ii) the 23S beam has to cross a deflectometer/interferometer device with consequent formation of the fringe pattern and iii) the displacement of the fringe pattern determined by an external force exerted on positronium has to be detected.

In this work, the aforementioned steps are presented. Particular attention will be dedicated to the description of the possible detection schemes that could be used for resolving the fringe pattern displacement. Recent results in the development of a spatial sensitive detector for positronium are shown and the perspectives are discussed.

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Mirror Matter searches with the J-PET detector

Dr Elena Perez del Rio; Jagiellonian University, Poland

The Positronium system, a bound state of an electron and a positron, is suitable for testing the predictions of quantum electrodynamics (QED), since its properties can be perturbatively calculated to high accuracy and, unlike the hydrogen system, is not affected by finite size or QCD effects at the current experimental precision level. Experiments searching for invisible decays of the Ps triplet state, the ortho-Positronium (o-Ps), which mainly decays to three photons, are being conducted, since they are sensitive to new physics scenarios, e.g. mirror matter, milli-charged particles, and extra space-time dimensions.

The particular case of Mirror Matter (MM) and its search with the J-PET setup is presented in this talk.

Mirror Matter was originally proposed to restore parity violation in weak interactions, by introducing a new hidden mirror sector where parity is violated in the opposite way. This means that under certain spatial inversion the particles transform into a parity reflected new mirror state. These mirror partners would interact with Standard Model (SM) particles via gravitation, making them suitable candidates for Dark Matter. In the o-Ps system, the photons from the decay would oscillate into their mirror partners, leaving no signal in the detector. By performing a high precision measurement of the o-Ps lifetime, the accuracy of the present QED calculations can be tested and a search for the invisible decays of the o-Ps conducted. A discrepancy with the expectation from theory could indicate the presence of Physics Beyond the SM, i.e. a signal for MM.

The presented search is conducted with the novel total-body Positron-Electron Tomography (PET) scanner at the Jagiellonian University. The J-PET is a large and high precise medical imaging tool, based on plastic scintillators.

Precision tests of discrete symmetries in decays of positronium with the J-PET detector

Dr Eryk Czerwiński; Jagiellonian University, Poland

The Jagiellonian PET (J-PET) detector is the only device which enables estimation of positronium spin axis together with determination of polarization of photons from positronium annihilation on the event-by-event basis. This allows to test angular correlations in the annihilations of the lightest leptonic bound system and explore a new class of discrete symmetry odd operators that were not investigated before. Such measurement is equivalent to a search for possible violation of combined charge, parity, and time-reversal symmetries as yet another approach for a test of New Physics. Positronium, a bound state of electron and positron, as the lightest matter-antimatter system and at the same time an eigenstate of the C and P operators is an unique probe in such endeavor. With first measurements demonstrating such capabilities we are able to reach the precision of CPT and CP tests at permill level. In the talk we will describe experimental techniques and recent results of discrete symmetries tests in the decays of positronium in a whole available phase-space.

Research in Neutron Capture Therapy at University of Pavia

Prof. Saverio Altieri; University of Pavia, Italy

Boron Neutron Capture Therapy (BNCT) is an experimental radiotherapy treatment characterised by selectivity at the cellular level based on the 10B(n,alpha)7Li reaction induced by thermal neutrons; the reaction products, alpha and 7Li have a biological efficacy comparable to that of C-ions used in Hadrontherapy; and they have the added advantage of being produced directly in the tumour cells, where they release their destructive energy, without having to pass through the layers of healthy tissue overlying the tumour.

Today, the international BNCT community, after its experience with neutron from research nuclear reactors, finally has sources produced with proton accelerators via p,Be or p,Li reactions. Accelerators have the advantage of being easy to install in a clinical facility and therefore offer the possibility to treat patients in a more appropriate environment.

The University of Pavia has a long tradition in the field of BNCT based on the use of the Triga Mark II nuclear research reactor of the LENA laboratory; here in the past BNCT was applied to treat diffuse liver metastases, using the auto-transplantation technique with the irradiation of the explanted liver in the reactor's Thermal Column.

Today, preclinical research, in collaboration with INFN, many Italian Universities and international Institutions and Laboratories, is still very active on various aspects of BNCT: research into new boron carriers with in vitro and in vivo toxicity and efficacy tests, measurement of boron concentration in biological samples by alpha spectrometry, neutron autoradiography, online measurement of boron dose by SPECT and/or Compton Camera technique with CdZnTe (CZT) detectors.

UNIPV has an intense collaboration with the Centre for Oncology Hadrontherapy (CNAO) where a BNCT facility based on the TAE-TLS p-Li accelerator will be ready in a couple of years. Two treatment rooms are planned, one dedicated to patients and one to BNCT research.

In the talk, after a brief introduction to the BNCT technique, the above-mentioned topics will be presented.

Towards including radiation quality in proton therapy treatment planning and dosimetry

Dr Jan Gajewski; Institute of Nuclear Physics Polish Academy of Sciences, Poland

Proton radiotherapy is recognised as an effective treatment method of tumours, which allows for increased sparing of normal tissues compared to conventional radiotherapy. Further improvement of clinical proton radiotherapy can be obtained with development of advanced treatment planning and dosimetry methods. The uncertainties in the biological modelling of the radiation effectiveness pose the major limitation of this treatment modality, which increases the risk of complications caused by proton irradiations, such as the development of secondary tumours or necrosis. Therefore, one of the main challenges in proton radiotherapy is to improve the current strategies of treatment planning by accounting for radiation quality described by means of the particle stopping power (Linear Energy Transfer - LET). Nowadays, LET is not considered in the clinical routine of treatment planning and dosimetry even if its engagement would fully allow to exploit the clinical advantages of proton radiotherapy.

Within the seminar, an overview of the computational and experimental methods for proton therapy treatment planning and dosimetry, clinically used at CCB and in other proton facilities will be presented. Moreover, it will be shown how to introduce radiation quality information in proton treatment. This part includes the development of (i) dosimetrical methods based on TimePix semiconductor pixel detectors developed in the framework of the CERN Medipix collaboration and (ii) computational methods based on fast GPU-accelerated Monte Carlo codes. The inclusion of radiation quality in the treatment planning and dosimetry has the potential to improve the precision of patient treatment in proton therapy.

Safe proton radiotherapy for patients with metallic spine stabilization system

Dr Kamil Kieislewicz; Centre of Oncology, Maria Sklodowska-Curie Memorial Institute Krakow Branch, Poland

Introduction

Since the beginning of proton radiotherapy in Krakow, skull base tumors are the main sites treated here. Due to the need to deliver a high dose of ionizing radiation (70-74Gy RBE) and the close presence of critical structures, such brainstem, optic chiasm, optic nerves, the use of a proton beam creates better opportunities for dose escalation to the target volume compared to photon radiotherapy. The problem when planning such treatment is the presence of metal stabilizers in about 40% of patients, which increase the uncertainty of the planned dose deposition.

Material and methods

Acquisitions of CT layers necessary for treatment planning were performed on the Siemens Somatom Definition AS apparatus using the iMAR, an optimized iterative algorithm for reducing metal artifacts. Then, a dedicated calibration curve for the Varian Eclipse treatment planning system (HU vs. RSP) was prepared. For each patient with a stabilizer, computed tomography was additionally reconstructed in the extended HU scale to transfer the necessary information about the implant density for treatment planning algorithm. Treatment plans were also based on individually defined structures - so-called target per field (volume to be irradiated from a given therapeutic field - beam) in order to avoid fragmented areas of artifacts reconstructed in an unacceptable way. The geometry of the beams was also optimized in relation to the metal element and critical organs.

Results and conclusions

The presented procedure allowed for the safe proton radiotherapy treatment using scanning beam in over 50 patients with metallic stabilizers, which was additionally confirmed by Monte Carlo simulations with the FRED tool (Fast paRticle thErapy Dose evaluator).

Dose distribution comparison of cerebrospinal axis irradiation. Helical Tomotherapy vs. Proton Pencil Beam Scanning

Dr Bartosz Kiełtyka; The University Hospital in Krakow, Poland

Background

Radiotherapeutic treatment performed in cerebrospinal axis becomes more common in oncological practice. Central nervous system (CNS) malignant tumors are diagnosed in 1-2% of all adult patients. Most cases are regarding brain tumors in which a combined treatment is a standard of care: surgical resection, radiotherapy (RT) and chemotherapy (CHT). In clinical practice, the most frequent techniques in external beam RT are related to dynamic techniques based on a standard medical accelerator. The treatment is prepared in fractionation scheme 1.8-2.0 Gy / fraction in 25-30 fractions. Recently, tomotherapy is used to irradiate long and symmetrical types of structures, however published clinical results are sparse. Proton beam irradiation (PBI) is another treatment mode although less available in most countries. The aim of this study is to compare dose distributions in treatment plans for the cerebrospinal axis irradiation using photon and proton techniques.

Material and methods

The aim of the study is to compare dose distributions in treatment plans for the cerebrospinal axis irradiation photon and proton techniques were used to prepare RT plans. To create a photon tomotherapy plan in helical technique implemented on the Radixact apparatus, a treatment planning system (TPS) Precision, Accuray, was used. In case of proton RT planning, TPS Eclipse (Varian) was used in scanning beam mode. In this study, six treatment cases were analyzed. In both mentioned techniques the same tomographic scans and contours of the critical organs (RT Structures) were used for treatment plan preparation. used for Then the comparison of prepared plans was performed on RayStation, RaySearch Laboratories software. Dose distributions in the target and critical organs were analyzed in terms of uniformity, maximum, average, minimum dose for target and integral dose. The high dose gradient areas that represent the resilience of treatment plans to uncertainties related to patient positioning and organ mobility were also investigated. The technique of proton radiotherapy requires joining the fields. Field joints were subjected to deep analysis. Duration of treatment was also compared.

Results and conclusions

The dose distributions obtained in proton plans are much more favorable in terms of the protection of critical organs and the integral dose reduction, which is very important in case of pediatric patients reducing the risk of secondary cancer induction. On the other hand, the treatment plans prepared for the photon helical technique are characterized by a greater dose distribution homogeneity in the areas where fields needed to be joined in proton techniques. Those photon plans were proved to be less sensitive to errors resulting from the geometry of the patient's position. For both techniques similar irradiation times were obtained. Each technique has its own benefits and depending on availability might be applied in the treatment of adult CNS malignant tumors.

PET-MRI nanotheranostics with radio-labelled nanoparticles

Prof. Zdenka Kuncic; University of Sydney, Australia

In radiation oncology and nuclear medicine, the efficacy of theranostic strategies (i.e. combining treatment with diagnostic imaging) may be dramatically improved by leveraging the unique properties of nanoparticles. Due to their nanoscale size, nanoparticles can penetrate target tissues and tumour cells, and enhance physico-chemical reaction rates. In this talk, I will discuss the opportunities presented by superparamagnetic nanoparticles, which, when labelled with suitable radioisotopes, offer a means for realising PET-MRI theranostics. I will present results on a novel chelate-free technique for radio-labelling superparamagnetic nanoparticles with clinically relevant isotopes and discuss how such nanoparticles can improve the overall image quality of PET-MRI. I will also discuss how radio-labelling superparamagnetic nanoparticles with therapeutic isotopes presents an opportunity for enhancing internal targeted radiotherapy by leveraging MRI guidance and nanoparticle radio-enhancement effects.

Compartmental models – a useful tool for medical therapy and diagnosis

Prof. Aleksandra Jung; AGH University of Science and Technology, Poland

Among many computational methods, compartmental models are still attractive for many applications in medicine, both in the fields of therapy and diagnosis. Below relevant examples are presented, they are based on literature and own research results.

Kinetics models based on differential equations are common for dose estimation in extracorporeal therapies. Hemodialysis adequacy considers methods based on experimental data providing to different measures like Kt/V or equivalent renal function. This can be improved by adding additional dialysis adequacy indices tested by numerical simulations. Mathematical models may accurately reproduce the clinical data of adequacy markers like urea or creatinine. In extracorporeal liver support therapies (ELS) considerable efforts focus on dose parameter estimation, correct identification of compartment volumes and transfer coefficients parameters. A limited amount of clinical data in this case can be resolved by combined models of kinetics of the two substances: bilirubin and urea. Building new models for ELS may also be partially supported by the use of physiological models of bile acid kinetics previously described in the literature.

The outcome of the model depends on its structure, parameters and initial conditions. Therefore, it is necessary to investigate the sensitivity of applied parameters, especially when the number of observation points is limited as it facilitates to decide the sampling rate in clinical practice. The accuracy of the parameter estimation may be improved if the sampling time is selected individually for each patient near the peak values of the sensitivity. This is beneficial both for the individualization of therapy assessment for a single patient and for the preparation of a new complete clinical trial protocol.

Compartment models describing the kinetics of radiolabeled substances are successfully used to support PET and SPECT imaging diagnostics where radiopharmaceuticals are used routinely. The results of the mathematical model allow, in this case, to obtain additional detailed diagnostic information. Models are also useful for comparing the diagnostic value of PET and SPECT tests, for distinguishing malignant neoplasms from inflammations or other benign changes, for assessing the diagnostic value of new radiopharmaceuticals or for assessing the impact of disturbances on the results of estimated physiological parameters. Additionally, they are applied to evaluate the results of magnetic resonance imaging or to differentiate the severity of Helicobacter pylori infection based on the result of a C-14 labeled urea breath test.

Last but not least, a clinically important area of application of this type of models is the assessment of radiological exposure during radiopharmaceutical exams, but also in the assessment of the accumulation of selected elements in our body, e.g. lead.

In each of the above-mentioned applications, the key is to define the initial assumptions and to properly adjust the complexity of the model to the amount of available experimental data and then to verify the model. Despite their limitations compartmental models can be used to identify meaningful physiological parameters helpful in making the correct diagnosis or selecting the appropriate therapeutic dose.

Mesoporous silica carriers for controlled drug release

Dr Radek Zaleski; Maria Curie-Skłodowska University, Poland

One of the most important challenges in modern medicine is to ensure the desired course of delivery of active pharmaceutical ingredients (APIs) to the patient’s body. Therefore, many studies are devoted to new delivery systems that can control both rate and period of drug delivery as well as the place of their administration. An important factor to consider when designing controlled release systems is the solubility of the API in the aqueous environment. Using an appropriately designed carrier allows to control the infiltration of the dissolving medium into the system, resulting in a modification of the release of API. Among others, the carriers suitable for achieving this goal are porous matrices, in which a solid dispersion of the drug is formed.

The ordered mesoporous silica SBA-15 (carrier) and diclofenac sodium (API) were used to develop a controlled drug release system. The release rate of diclofenac sodium was tested in vitro to evaluate the suitability of this system for API release control. For tabletted SBA-15, it was possible to achieve a release course close to the desired linear release profile with release of about 50% API after 24 hours.

Further improvement of the release system requires insight into the course of API release through its detailed study. The distributions of diclofenac sodium within the carrier were studied for systems before release and after various release times. Scanning electron microscopy (SEM) coupled with energy dispersive spectroscopy (EDS) was used to determine the morphology and the spatial distribution of the elements. Free volumes ranging in size from angstroms to nanometers were characterized with nitrogen adsorption and positron annihilation lifetime spectroscopy (PALS). The results obtained with these techniques allow to infer how the microstructure of the carrier-API system influences the drug release.

Polymer and composite carriers for controlled drug release

Dr Marek Gorgol; Maria Curie-Sklodowska University, Poland

Delivering of the active pharmaceutical ingredients (APIs) to the organism in the desired manner is a great challenge. Therefore, it is important to develop and investigate new systems, allowing to control both the rate and the period of drug delivery. In such systems, the carrier, in which API is dissolved, can and should be designed and/or modified in a way which allows to control the infiltration of the dissolution medium into the system, resulting in a modification of API release. The porous matrices seem to be suitable carriers for this purpose, as a solid dispersion of the drug can be formed inside of them.

Several solid API dispersions have been developed with diclofenac sodium as API and porous carriers such as mesoporous polymers: poly(trimethylolpropane trimethacrylate) (poly(TRIM)), and commercially available Amberlite® XAD7HP as well as polymer-silica composites [1]. Additionally, selected carriers were modified by functionalizing with 3-aminopropyl groups or tableting by mechanical compression.

The rate of the diclofenac sodium release from each of solid dispersions was examined in vitro to assess their usefulness for the controlled release. The use of XAD7HP with small amount of API and poly(TRIM) functionalized with 3-aminopropyl groups as porous carriers gave satisfying results, with the drug release profile quite close to linear, Unfortunately, good release profiles were obtained at the expense of reducing the amount of released API from nearly 100% to about 50% after 24 hours. It is also worth to mention, that increasing the amount of diclofenac sodium added into XAD7HP caused nonhomogeneous distribution of API inside a carrier and gave non-satisfying results in the release profile.

To better understand the course of the drug release, the initial distribution of diclofenac sodium within the carrier for each solid dispersions as well as the distribution of remaining diclofenac sodium after various release times for selected samples were studied. The morphology and the spatial distribution of the elements in sample cross-sections were determined with scanning electron microscopy (SEM) coupled with energy dispersive spectroscopy (EDS). The porosity of the investigated systems was characterized with classic low-temperature N2 adsorption porosimetry and positron porosimetry based on positron annihilation lifetime spectroscopy (PALS).

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Unsupervised learning for pixel mask clustering and cluster tracking in LHCb's Velopix sensor calibration

Maciej Majewski; AGH University of Science and Technology, Poland

The VELO detector is one of the core elements of the LHCb spectrometer. Its upcoming upgrade will consist of a new type of Velopix sensor. It branches from a Medipix family of silicon pixel matrix sensors. One of its operational challenges with future data taking at the Large Hadron Collider will be the ability to detect faulty (masked) pixels and monitor them. In this work, we propose a method for clustering the faulty pixels and tracking the progression of the clusters in time. We compare two methods of clustering (DBSCAN and OPTICS) and their influence on the proposed tracking method, using a simulated dataset of masked pixels.

3D printed lightweight and modular lithium-ion Uninterruptible Power Booster for medical devices

Gabriel Moskal; Jagiellonian University, Poland

Advanced devices for diagnostics and medical therapy require a constant and stable power source. The disadvantage of commonly used uninterruptible power supply (UPS) is the heavy weight[1], centralization and the need to use specially prepared rooms and dedicated electrical installations. The aim of the presented research is to prepare a safe, economic and modular Uninterruptible Power Booster (UPB). A UPB can increase the insufficient power output of the mains supply, guaranteeing power for the pre-planned time. Low price and modularity are possible due to the use of 3D printing and Li-ion cells, which will allow the construction of UPB installed in the immediate vicinity of the protected device. Among available technologies of chemical energy storage, Li-ion cells are characterized by high gravimetric and volumetric energy density[1]. Currently, liquid electrolytes(LE) are used in Li-ion cells, which have good ionic conductivity, but are flammable, toxic and sensitive to lithium dendrite overgrowth, which may lead to an internal short circuit and damage to a given module. For safety reasons, a much better solution than LE would be solid electrolytes(SE), which would not be flammable and hazardous to the environment. Due to the fact that SE constitute a barrier to lithium dendrites, they can extend the working time of li-ion cells[2]. Currently, there is no known material that would fit well as a SE for li-ion cells. There are several materials under development, but they are not ready for industrial applications[3,4].This presentation concerns the research conducted on SE, synthesized with the use of cheap, environmentally safe materials. For this purpose, syntheses of materials based on silicon glass and polysaccharides were performed. Methods of syntheses and the results for measuring the ionic conductivity of the tested electrolytes and an example UPB for J-PET mobile tomograph will be presented[5,6]. The use of this solution with stationary devices will allow to reduce electricity costs by loading the energy storage using a less expensive night tariff, and then using the collected energy during the day, and also to install the device in a room without access to a UPS system.

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The charm of charm

Jakub Ryżka; AGH University of Science and Technology, Poland

The existence of CP violation in charm particle decays has been elusive for a long time for experimentalists and has been observed for the first time in 2019 in the LHCb experiment. During the LHC Run 1 and Run 2, the LHCb collaboration collected huge data samples on a scale never seen before. These data enable the most sensitive searches for CP violation ever performed. These measurements are interpreted as precise tests of the Standard Model. In the presentation, the latest results achieved in charm decays will be reviewed and two innovative model-independent techniques (Kernel Density Estimation and Energy test) for searching for CP violation in charm baryons will be discussed.

Preliminary results of determining Modular J-PET spatial resolution

Faranak Tayefi Ardebili; Jagiellonian University, Poland

Modular J-PET is the latest prototype of the Jagiellonian-PET, based on long plastic scintillator strips [2]. The modularity of this prototype allows for cost-effective imaging of multi-photon annihilation and positronium imaging, straightforward assembly, and portability [1-3]. Moreover, due to the low weight of a scanner, it is possible to perform an examination with a static bed and mobile detection system closing on the patient from its side, which cancels the need for large rooms in clinics [1-3].

The Modular J-PET consists of 24 modules which are arranged in regular 24-sided polygons circumscribing a circle with a diameter of 73.9 cm [4]. Each module was built out of 13 scintillator strips placed next to each other with a length of 50 cm and a cross-section of 6 mm × 24 mm, read out of scintillation light on both ends is done by an analog Silicon Photomultipliers (SiPMs). This study presents preliminary results of the spatial resolution measurement of the Modular J-PET tomograph performed with Na source placed at various positions inside the detector according to the NEMA_NU 2-2018 standards [5]. The collected data were analyzed using a specialized software program called the J-PET Framework, which is based on the C++ architecture [6]. Experimental data were verified with the GATE simulations [7]. In simulations of the Modular J-PET spatial resolution, a back-to-back gamma source was simulated in the same position as used in the experiment [8]. The results of the simulation were reconstructed with the QETIR package.

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129m,131m,133mXe – for gamma-MRI, a novel medical imaging technique

Mateusz Chojnacki; CERN, Switzerland

Gamma-MRI is a future imaging modality that should allow the simultaneous exploitation of the sensitivity of gamma-ray detection (SPECT) and the spatial resolution and flexibility of MRI [1]. The approach uses, like in SPECT, gamma-emitting nuclei, which are highly polarized and thus exhibit anisotropic gamma-ray emission, whereas their spins are rotated by rf pulses, like in MRI. The signal in gamma-MRI is the change in the ratio of gamma rays emitted longitudinally and transversally to the spin (and magnetic field) direction [2]. The first nuclei used in the project are 11/2− spin isomers 129mXe (T1/2=8.9 days), 131mXe (T1/2=11.8 days) and 133mXe (T1/2= 2.2days).

The efficient production and purification of the 129m,131m,133mXe is one of the first milestones in the gamma-MRI project. This contribution will present two main methods of production tested so far: neutron irradiation of enriched stable 128Xe (product: 129mXe) and 130Xe (product: 131mXe) in the RHF reactor at Intitute Laue-Langevin (ILL; Grenoble, France) and at the MARIA reactor in the National Centre for Nuclear Research (NCBJ; Świerk, Poland), and ion-implantation of 129m,131m,133mXe into gold foils at the ISOLDE facility in CERN (Switzerland). Both methods provide high values of xenon isotopes activities that can be extracted efficiently and used in polarization experiments.

The presentation will give a brief introduction to the gamma-MRI technique and will mention the different elements of this EU-funded project. It will then concentrate on the work performed at the CERN, namely production and purification of the Xe isomers.

The development of the QETIR image reconstruction software for the Total-Body J-PET application

Meysam Dadgar; Jagiellonian University, Poland

The unique features that PET scanners have provided to the specialists in diagnosing diseases and investigating the physiology of the body have facilitated the development of a more advanced generation of tomographs in order to improve their performance, called Total-Body PET scans.

Due to the larger AFOV, TB PET scanners provide more extensive detection coverage around the patient's body. They have significantly increased the probability of detecting photons emitted from the patient's body. This issue has increased the sensitivity of TB PETs and enhanced their accuracy in detecting and locating tumors with smaller dimensions. This unique feature can increase the chances of saving the patient by detecting tumors in the early stages.

Along with the numerous advantages of developing TB PETs, the construction cost and maintenance of these systems, due to a large number of electronic components and detectors, have become one of the biggest obstacles to their widespread use in diagnostic and research centers.

J-PET collaboration at Jagiellonian University, as one of the leading research groups in developing cost-effective larger AFOV PET based on plastic scintillators, has been able to introduce a new generation of the systems mentioned above by overcoming the existing limitations.

Besides the hardware challenges in the construction of TB PET systems, the demand to develop image reconstruction software that can support these complex systems was felt due to the significant differences between these systems and current clinical tomographs.

In addition to the cases mentioned above, in TB J-PET, due to the utilization of dual-layer configuration and large AFOV, most of the image reconstruction software are not able to support it.

The Medisip group developed QETIR (Quantitative Emission Tomography Iterative Reconstruction) at Gent University as a flexible software that has overcome the existing challenges in TB PETs image reconstruction.

The main aim of this study is to investigate the performance of QETIR image reconstruction software in J-PET scanners with different AFOVs, and single and multi-layer configurations.

10ps Time-of-Flight PET scanner: From Hope to Practice

Prof. Paul Lecoq; CERN, Switzerland

The future generation of radiation detectors is more and more demanding on timing performance for a wide range of applications, in particular for time-of-flight (TOF) techniques in PET cameras.

There is in particular a consensus for gathering Europe's multi-disciplinary 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.

The possibility to reach 10 ps time-of-flight resolution at small energies, as required in PET scanners, although extremely challenging, is not limited by physical barriers.

This talk will show how progress in nanotechnologies open new perspectives for the development of meta-scintillators, a new class of multifunctional multi-intelligent scintillators.

Indeed, a number of disruptive technologies, such as multifunctional heterostructures, combining the high stopping power of well know 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, open the way to new radiation detector concepts with unprecedented performance.

Optimization study of a muon tomography system for imaging of nuclear waste containers

Dr Anzori Georgadze; Kiev Institute for Nuclear Research, Ukraine

The important parameters of nuclear waste have to be determined for its classification and selection of optimal disposal option. For the non-destructive characterization of nuclear waste muon scattering tomography techniques can be used to image the contents of an enclosed volume by measuring the scattering angle of cosmic ray muons as they pass through a nuclear waste container using particle tracking detectors. In this paper we present an optimization study of a muon tomography detector to obtain its parameters for best performance. Using Geant4 combined with Cosmic-ray shower generator (CRY) we have studied two detector geometries to compare their efficiency of detection and reconstruction of high-Z materials. One of detector design consist of muon two tracking detectors placed on top and bottom sides of nuclear waste container and another one represents closed up design when muon trackers are surrounding container from four sides. The results of POCA reconstruction of 10 cm cubic size object of high-Z material encapsulated in a concrete matrix indicate that detector design with tracking detectors on four sides around container demonstrate slightly better performance comparing to detector design with two tracking detectors on top and bottom. On the other hand, tomography system with muon trackers on top and bottom sides can be more universal allowing changing the distance between planes and measuring nonstandard nuclear waste.

Comparative studies of plastic scintillator strips with high technical attenuation length for the total-body J-PET scanner

Dr Łukasz Kapłon; Jagiellonian University, Poland

Co-author: on behalf of the J-PET Collaboration

Plastic scintillators are used in many applications connected with advanced medical devices, for example in novel multiphoton J-PET scanners with positronium imaging capability [1, 2], and in plastic scintillation dosimetry [3].

In the first part of the lecture, results from measurements of transparency of commercially available plastic scintillators will be presented [4]. Purpose of the research is to select the best type of scintillator for the total-body J-PET scanner construction. Emission spectra, transmission spectra and technical attenuation length (TAL) values of six types of plastic scintillators with dimensions 6 mm × 24 mm × 1000 mm will be discussed. General purpose, blue-emitting plastic scintillators with low attenuation of visible light were tested: polyvinyl toluene-based BC-408, EJ-200, RP-408 and polystyrene-based Epic, SP32 and UPS-923A. The emission spectra of the investigated scintillators have maxima ranging from 420 nm to 429 nm. The BC-408 and EJ-200 scintillators have the highest transmittance values of about 90% at the maximum emission wavelength (measured through a 6 mm thick scintillator) and the highest TAL values up to about 200 cm, allowing building of long modules for total-body J-PET scanner.

In the second part of the talk, results from the research of blue- and green-emitting polystyrene-based plastic scintillators for scintillation dosimetry applications will be presented [5]. Anthracene, coumarin and perylene fluorescent dyes were used as wavelength shifters [6]. Emission maxima of manufactured green-emitting polystyrene scintillators are in range from 484 to 525 nm. The concentrations of the BPBD ultraviolet dye and Solvent Green 5 green fluorescent dye, influence the light output, rise and fall times, and the emission spectra of the scintillator samples.

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PET/CT and SPECT/CT in preclinical research: Systems and applications

Prof. Sibylle Ziegler; Ludwig-Maximilian University of Munich, Germany

PET and SPECT are truly translational since the same methods can be applied in animals and in clinical studies. Owing to the small structures, dedicated instrumentation is needed for mouse and rat imaging, while large animal models can be investigated using clinical systems. Some new detector concepts have been introduced first in preclinical systems before scaling up to clinical systems. Biodistribution and biokinetics of novel radioactively labelled tracers are studied in rodents before translating into patient use. Multi-tracer longitudinal measurements can be performed for characterizing disease models or assessing the effect of interventions. In addition, similar quantitative image analysis methods can be applied in preclinical models before translating to the clinical case.

In this presentation, an overview on specific instrumentation for animal imaging will be given, together with examples of preclinical imaging studies performed in our lab with specific focus on specific tracer applications in neurology and beta-cell transplant research.

Designed Protein Cages: Current State and Potential Medical Applications

Prof. Jonathan Heddle; Malopolska Centre of Biotechnology, Poland

Designed proteins offer us the potential of matching or exceeding the capabilities of nature's own naturally-occurring protein nanomachines which demonstrate a wonderous array of properties. Protein cages are hollow, typically spherical nanoscale protein assemblies which in nature have multiple uses such as materials storage, genome delivery (viruses) and catalysis (enzymes). As such it is attractive to design and produce artificial cages with properties such as multiple antigen display on the exterior for use as vaccines, and the ability to protect and carry therapeutically useful macromolecules in the interior for use as drug delivery systems. Making such systems programmable is a desirable feature and requires finding a way of opening such cages on demand to release cargo when and where required. In this presentation I will give an overview of the field and our own progress in producing a programmable artificial protein cage.1,2,3,4,5,6

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Perspectives of preclinical research in Bialystok Center of Molecular Imaging

Prof. Anna Gromotowicz-Poplawska; Medical University of Bialystok, Poland

Bialystok Center of Molecular Imaging (BCMI) is one of the key elements of the new project of the Innovative Research Center for the Prevention of Civilization Diseases and Individualized Medicine (CBI PLUS), that is now proceeding by the Medical University of Bialystok (MUB). This will be the first laboratory for the synthesis and quality control of radiopharmaceuticals in the region and the first PET/MR preclinical research center in Poland. The main goal of BCMI is to develop new radiopharmaceuticals for the early diagnosis and treatment of civilization diseases. This will be supported by the preclinical and clinical research with the innovative molecular imaging technique application. The BCMI labs will follow the GMP and GLP procedures. At the moment, the construction of the BCMI is underway. The GMP documentation has already been prepared and the purchase of the hot cell, synthesis unit, 68Ge/68Ga generator and quality control system is ongoing. In the preclinical research labs the PET/MR and SPECT/CT scanners for small animals will be installed. The configuration of systems will allow for a whole body scan, brain, heart, lung and amdominal imaging in preclinical research in the field of oncology, neurology, cardiology and metabolic diseases. The animal scanners will be a part of the unique imaging system that is already used in the MUB (i.a. human PET/MR hybrid system), thus providing the translational research. BCMI will increase opportunities for collaboration and conducting multicentre research as well as international projects. The entire BCMI installation should be completed in mid-2023.

Proteomic profiling of extracellular vesicles derived from pancreatic beta-cells cultured under hyperglycemia

Carina Rząca; Jagiellonian University, Poland

Cargo carried by extracellular vesicles (EVs) is considered as a promising diagnostic marker, especially proteins [1,2]. EVs can be divided according to their size and way of biogenesis into exosomes (diameter <200 nm) and ectosomes (diameter <200 nm) [1].

First step of this study was characterization of EVs sample [2]. Using Tunable Resistive Pulse Sensing (qNano) size distribution and concentration were measured. The mean size of exosomes was 135±15 nm, and ectosomes 210±17 nm. TEM images also confirmed the size of EVs and the purity of prepared samples. In the present study, a nano liquid chromatography with tandem mass spectrometry (nanoLC-MS/MS) was used to profile and compare the protein content of ectosomes and exosomes secreted by pancreatic beta cells (1.1B4) grown under NG (5 mM D-glucose) and HG (25 mM D-glucose) conditions. The EVs samples were lysed, and proteins were denaturated, digested, and analyzed using a Q-Exactive mass spectrometer coupled with the UltiMate 3000 RSLC nano system (Thermo Fisher Scientific) The LC-MS/MS data were searched against SwissProt Homo sapiens database using MaxQuant software and protein quantitation was done by the MaxLFQ algorithm. Statistical analysis was carried out with Perseus software. Further bioinformatic analysis was performed using the FunRich 3.1.4 software with the UniProt protein database and STRING [3, 4, 5].

As a result of the tandem mass spectrometry analysis more than 1,000 proteins were identified and quantified in each sample. The average number of identified proteins in exosomes and ectosomes was 1,397 and 1,697, respectively. Label-free quantitative analysis showed that exosome and ectosome protein composition differed significantly between those isolated under NG and HG conditions. Many pathways were down-regulated in HG, particularly the ubiquitin-proteasome pathway. In addition, a significant up-regulation of the Ras-proteins pathway was observed in HG.

Our description of EVs protein content and its related functions provides the first insight into the EV interactome and its role in hyperglycemia development and diabetic complications. The results also indicate the applicability of some of these EVs proteins for further investigation regarding their potential as circulating in vitro biomarkers [6, 7, 8].

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