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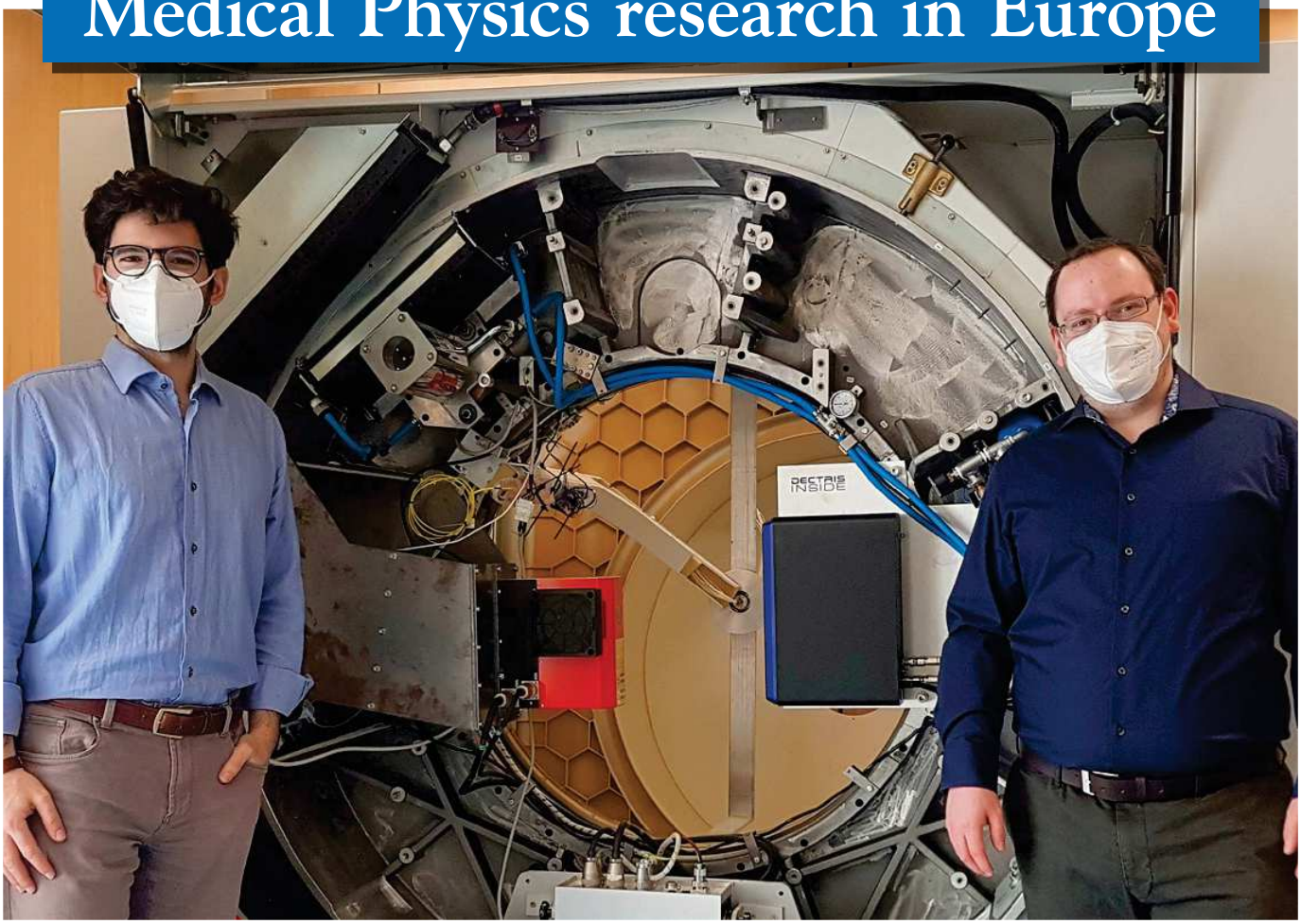

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Cover photograph shows PhD student Carlo Amato (left) and postdoctoral researcher Dr. Stefan Sawall (right), standing next to the experimental CT gantry at DKFZ in Heidelberg; the gantry is equipped with a micro focus x-ray source and a photon counting detector. See the article on page 55 of this issue.

RESEARCH IN MEDICAL PHYSICS

Towards positronium imaging with total-body PET from plastic scintillators

Professors Pawel Moskal and Ewa Stępień from the Jagiellonian University in Cracow, Poland, describe their research aimed at developing new PET scanners

The Jagiellonian Positron Emission Tomography (J-PET) research group is developing cost-effective technology based on plastic scintillators for the construction of total-body PET scanners. The state-of-the-art PET systems are built from crystal scintillators arranged radially into rings surrounding a patient. The Total-Body J-PET (TB-J-PET) scanner will be constructed from modules composed of axially arranged cost-effective plastic scintillator strips read out by SiPM at the ends. The J-PET scanner may be constructed as a modular, light and portable device, enabling re-configuration of the tomographic volume, which may help to extend PET diagnosis in patients who cannot be examined by standard PET due to obesity or claustrophobia. Fig. 1 shows the prototype of the modular J-PET tomograph. Application of plastic scintillators and axial arrangement enables construction of economic PET with long axial field-of-view (AFOV), up to 2.5 m and more. This approach allows high sensitivity imaging of the whole human body, with high and uniform sensitivity over the whole patient from the brain to the feet.

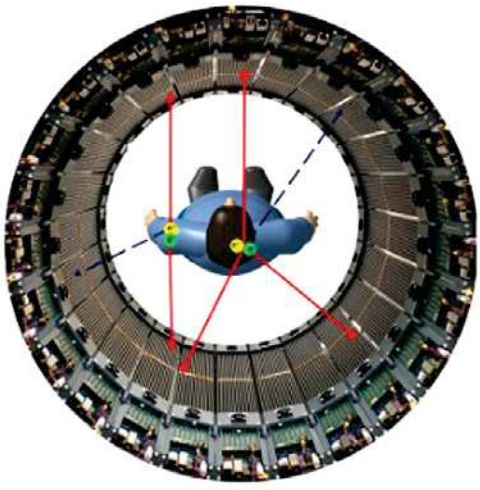

Fig. 1: Photograph of the single layer (with 50 cm axial field-of-view (AFOV)) modular J-PET prototype with superimposed representations of electron-positron annihilation in the patient's body for two and three photon events (red solid arrows) and the associated prompt gamma rays (blue dashed arrows) emitted by the β+γ radionuclide such as e.g. ^{44}Sc. The single-layer J-PET prototype with AFOV = 50 cm weighs only about 60 kg. It consists of 24 modules each built from plastic scintillator strips (black) read out at both ends by SiPMs equipped with the dedicated front-end and digitizing electronics visible in the foreground (Moskal and Stępień, 2020).

Plastic scintillators are more than an order of magnitude less expensive than crystals. In addition, in the case of TB-J-PET, the cost of electronics is proportional to the trans-axial cross section of the detector while in the case of crystal-based TB-PET they are proportional to the area of the detection cylinder. Overall, the plastic TB-J-PET may be more than a factor of five less expensive than the crystal-based TB-PET, making it a realistic cost-effective solution for broad clinical applications. The prospects and clinical perspectives of total-body PET imaging using plastic scintillators has been recently discussed in a review (Moskal and Stępień, 2020). Here we only shortly summarize the main advantages that TB-J-PET may provide for diagnostics.

High sensitivity TB-J-PET will open opportunities for application in PET scans of events with the emission of three or more photons. Some examples of multi-photon events are shown pictorially in Fig. 1. The data acquisition system of the J-PET tomograph enables detection of double, triple and in general multi-coincidence events. In particular, it enables registration and identification of two ($e^+e^- \rightarrow 2\gamma$) and three photon ($e^+e^- \rightarrow 3\gamma$) annihilations, as well as prompt gamma emitted in the case of some isotopes referred to as $\beta^+\gamma$ emitters, such as e.g. ^{44}Sc, ^{66}Ga or ^{82}Rb. In the current PET imaging procedures, prompt gammas constitute a source of unwanted background. However, these multi-photon coincidences may be useful for diagnosis. The capability of TB-J-PET to register and identify the signals from prompt gammas and from 2γ annihilations will allow for tagging the events originating from various isotopes. Therefore, in the case of the β+γ emitters, TB-J-PET may be used for simultaneous multi-tracer imaging, and for the newly-developed positronium lifetime imaging, which is a promising approach for the in-vivo assessment of tissue pathology. Recently proposed positronium imaging can deliver information complementary to the currently used SUV based parameters. During PET imaging a positron emitted by the radionuclide annihilates with the electron in the patient's body, directly or via formation of the metastable positronium atom (an atom built from an electron and a positron). In the human body, positronium atoms are formed in up to about 40% of cases of positron-electron annihilations. In tissue, the ortho-positronium mean lifetime strongly depends on the size of intra-molecular voids (free volumes between atoms), while its formation probability depends on the void's concentration. Fig. 2 shows pictorial representation of the basic processes involved in positronium imaging, with the example of examination of the prostate cancer.

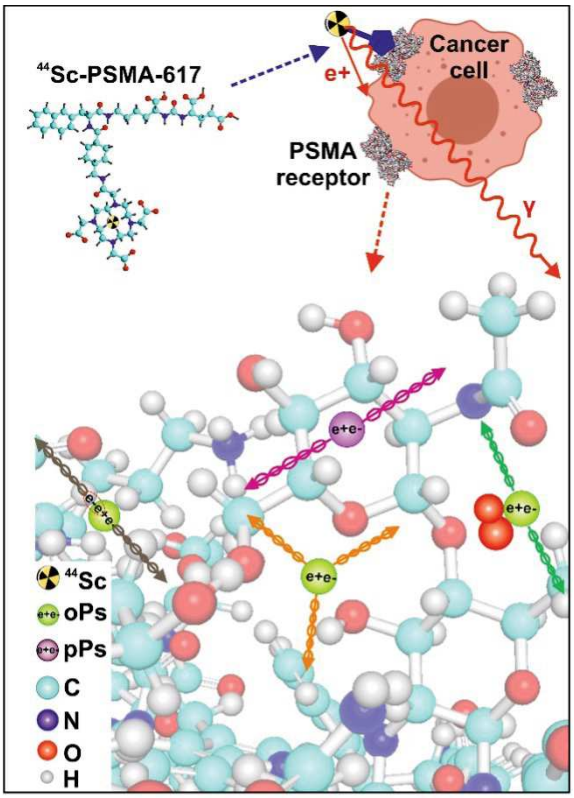

Fig. 2: Pictorial representation of the basic processes involved in the "positronium imaging" using the example of examination of the prostate cancer. The prostate-specific membrane antigen (PSMA-617 ligand) labeled with radionuclide ^{44}Sc attaches to the PSMA receptors highly expressed in prostate epithelial cells. ^{44}Sc isotope emits positron (e+) and prompt gamma (γ) via following process: 44Sc → 44Ca* e+ ν → 44Ca γ e+ ν. Positron interacting with electrons may form positronium atoms (indicated as oPs or pPs) inside cell molecules including intermolecular voids in PSMA receptors as indicated in the lower part of the sketch. Prompt gamma may be detected in the tomograph to give the signal about the time of positronium formation. Arrows indicate photons originating from the annihilation of para- and ortho-positronium inside free space between atoms (magenta and orange arrows), respectively. Black arrows indicate annihilation of ortho-positronium through the interaction with the electron from the surrounding molecule and green arrows illustrate photons from the conversion of ortho- into para-positronium via interaction with the oxygen molecule and subsequent decay of para-positronium to 2γ (Moskal and Stępień, 2020).

The main objectives of the J-PET group for the coming years are the construction of the TB-J-PET and elaboration of the combined (i) dynamic SUV imaging, (ii) kinetic parametric imaging, and (iii) positronium imaging which may serve as a biomarker enabling not only detection of the presence of diseased tissues, but also allowing to distinguish among the inflamed, infected, and cancerous tissues and permitting assessment of the grade of cancer malignancy.

The TB-J-PET project is led by Prof. Pawel Moskal (imaging technologies development) and Prof. Ewa Stępień (preclinical bio-medical studies) and is carried out by an interdisciplinary group from the Jagiellonian University, the University Hospital in Cracow, National Centre for Nuclear Research, Institute of Nuclear Chemistry and Technology, Heavy Ion Laboratory at the University of Warsaw, and the Medical University of Warsaw. It interfaces technologies from a variety of disciplines including biology, biophysics, computer science, electronics, engineering, physics, medical physics and medicine. J-PET is seeking new candidates for the research positions offering competitive salaries.

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Prof. Pawel Moskal is an inventor of positron emission tomography based on plastic scintillators and method of in-vivo pathology based on positronium imaging. He is Professor of physics and the head of the Cluster of Nuclear Physics Departments as well as the head of the Department of Particle Physics and Applications at the Jagiellonian University and serves as a Member of the Committee on Medical Physics, Radiobiology and X-Ray Imaging, Polish Academy of Sciences.

Prof. Ewa Stępień is the head of the Medical Physics Department at the Jagiellonian University and serves as a president of the Experimental Cardiology section of Polish Society of Cardiology and a member of the Committee of Physiological and Pharmaceutical Sciences of Polish Academy of Sciences. She received the 2nd award from the Polish Ministry of Health and Social Security named "Evidence Based Medicine in practice".