Ohrid-Workshop 6-8 September 2015

PET cameras: Principles, use a hospital & ongoing developments

(# is for15 mn) (= is for 30 mn) (= = is for 50 mn)

Time –table
31/08/15

Time	SUNDAY 6/915 : Introduction & CT, SPECT	MONDAY 7/9/15 : PET, Hybrid & Applications	TUESDAY 8/9/15 : Rad Protection & Developments
08:15 10:15	 *9:30 : Registration* *10:30*	*Session 3:* PET & Main Applications Chair : S. Petkovska *== PET Principle & History* *I. Rausch, Vienna, A* *== Clinical application of FDG PET/CT J-N Talbot , Tenon Hospital., Paris-F*	*Session 7:* Radiation Protection in MP applications Chair : P. Le Dû, *= General Risks with Radiation* *M. Medvedec, Zagreb, HR* *= Optimisation in Nuclear Medicine* *M. Medvedec, Zagreb, HR* *== Patient, Workers, Public protection & Hospital* *M. Medvedec, Zagreb, HR*
	Coffee Break	Coffee Break	Coffee Break
10 :30 12:30	*11:00* *Opening Session* Chair : D. Miladinova *# Welcome (University Rector or Dean)* *# Med. Phys. In MK, S. Petkovska, Skopje* *== Medical Imaging Review* *Y.Lemoigne, IFMP & CERN-CH* *= Interactions of biomedical oscillations* *T. Stankovski, Skopje-MK* *13/00*	*Session 4:* More PET Imaging Applications Chair : M. Zdraveska *== clinical PET/CT with other tracers* *J-N Talbot, Tenon Hospital, Paris-F* *= Research Example by Small Animal PET Y.Lemoigne, IFMP & CERN-CH* *= Varian and PET* *Varian representative in MK*	*Session 8:* PET and HEP Transfer to Medical Physics Chair : I .Rausch = shielding requirements for PET/CT *J. Haglund , Fredrikstad, NO* *== Transfer from HEP* *P. Le Dû , IEEE & IPN Lyon-F* *= Developments in PET from HEP* *L. Litov, Sofia Uni. BG*
	Lunch	Lunch	Lunch
14:15 16:15	*Session 1:* *Medical Physics in NM* Chair : Y. Lemoigne == NM Dosimetry: Diagnostic & Therapy *M. Bardies , Toulouse, F* *= Dose & risks in Iodine 131 treatment* *M. Zdraveska, Skopje-MK* *= CT: Computed Tomography* *J. Haglund , Fredrikstad, NO*	*Session 5:* *PET complements* Chair : J-N Talbot *== Pet Quality Control & Quantification* *I. Rausch, Vienna, A* *= Pet in Norway / an example* *J. Haglund , Fredrikstad, NO* *= Imaging for R. Oncology (CT, PET-CT)* *S. Petkovska, Skopje-MK*	*Session 9:* *Use of PET in Hadrontherapy* Chair : M. Medvedec *== Hadrontherapy principles* *P.R. Altieri, INFN & Bari Uni, IT* *= On line dose monitoring* *P.R. Altieri, INFN & Bari Uni, IT* *= Particle Therapy - the future* *P. Le Dû, IEEE & IPN Lyon-F*
16:30	Coffee Break	Coffee Break	Coffee Break
18:30	*Session 2:* *Medical Imaging* Chair : M. Bardies *== SPECT/CT Instrument' & Clinical App* *D. Miladinova, Skopje-MK* *= Dose Optimisation in MDCT* *V. Gershan, Skopje-MK*	*Session 6:* *Hybrids system:* PET-MRI Chair : P.R. Altieri *=== PET-MRI: Principle, Advantages&Problems* *L. Bidaut, Dundee, UK* *= Ecologic Talk* *F. Vosniakos, Thessaloniki-Gr*	*Session 10:* *Open Discussion & conclusions* *Chair: D. Miladinova, Y. Lemoigne* *With: P.A, J.H, M.M , P.LD, I.R ,S.P and other persons for very short presentations…* *End of Workshop*
19:30 20:00 23:00	*WELCOME COKTAIL* *@ st Naum Monastery*	*BANQUET*	Possibility of Transport to Skopje by Public Bus (Courtesy bus to SKP Airport Wednesday 8:00)

MEDICAL PHYSICS IN MK

Sonja PETKOVSKA

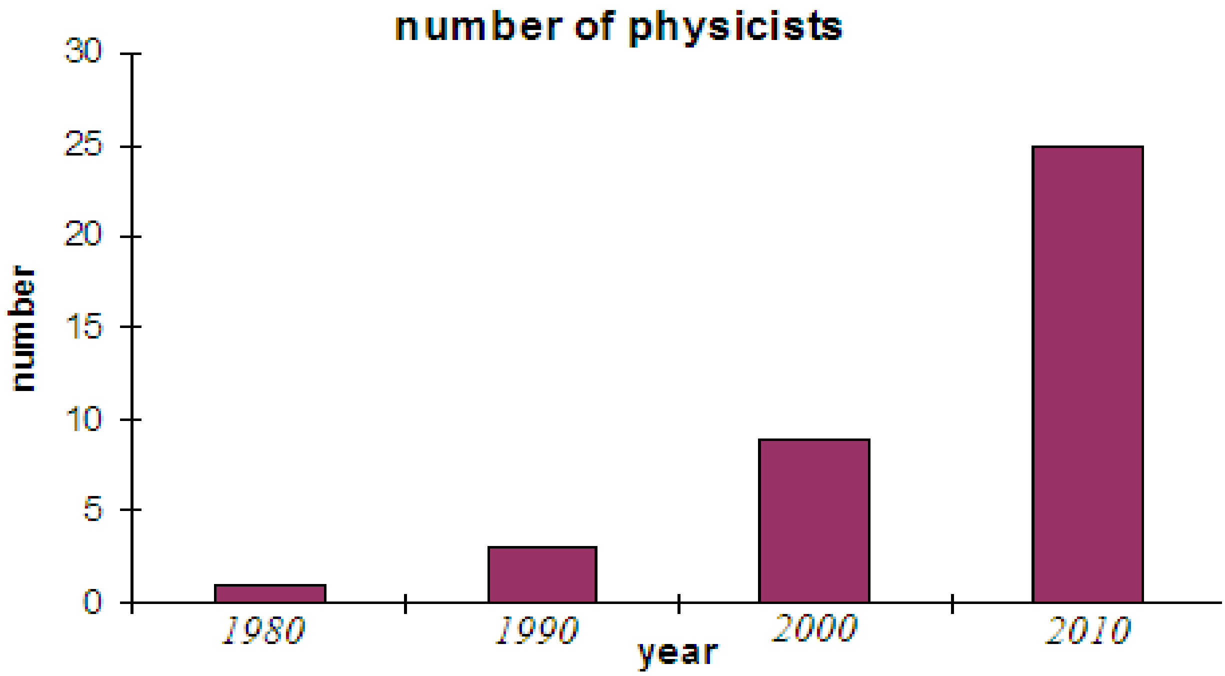
ACIBADEM Sistina, Skopje, Macedonia

A short review of several aspects concerning medical physics is presented: the undergraduate and postgraduate education in medical physics, current professional engagement of medical physicist in Macedonia and perspectives for increasing their number.

Undergraduate education in Medical Physics in Macedonia is established at the Institute of Physics, Faculty of Natural Sciences and Mathematics in Skopje. Concerning the Postgraduate education in Medical Physics, there is a nationally approved education program. Specialization for Medical Nuclear Physics in Nuclear Physics and in Radiotherapy was established on the faculty of Medicine in Skopje twenty years ago for the physicists who are already employed in clinical work or radiation protection. This kind of education is very important for the physicists because it is a connection between physics and medical practice. Trough the medical physics specialisation a basic teoretical knowledge in medicine (as anatomy, physiology etc) and applied medical physics could be achieved. Study plan and program of specialization is provided in 6 semesters.

There are 25 physicists whose professional engagement is in the field of medical physics. Twelve of them are Specialists of Medical Nuclear Physics. The Health Protection Institute, The Nuclear Medicine and Radiotherapy are the fields where the medical physicists are employed.

Despite of the fact that in the last period, the number of physicist in healthcare was rapidly increasing we can not be satisfied with the number of employees and their status nowadays.



As a conclusion, some future perspectives in this very important branch of our society are given – increasing the number of medical physicist, improving their knowledge and experience by certain training courses, involving the physicist and engineers in Master and PhD study programs related to medical physics, as well as collaboration with researchers on joint project activities. Also, the number of medical physicist in professional association has to be increased, and their activities in organizing conferences, seminars or some other meetings will benefit for promotion of medical physics profession in Macedonia

INTRODUCTION AND MEDICAL IMAGING REVIEW

Yves LEMOIGNE, PhD

IFMP Ambily, France & CERN Geneva Switzerland

The lecture presents a review of Medical Imaging which will be the main topic of this Medical Physics part of the workshop.

Five different techniques could be studied: Ultrasound, CT, SPECT, PET, MRI. Then we will see their use in Hospital.

IMAGING Exploration inside the human body is done within two purposes:

1- ANATOMICAL to see INSIDE the body at a moment (X-rays CT, MRI, Ultrasounds)

2- FUNCTIONAL to see how the body functions during a period of time (PET, SPECT, fMRI.)

There are two types of machines depending if source is OUTSIDE the body like the detectors (CT for instance) or INSIDE the body (MRI, PET or SPECT).

This lecture will present a short review of Medical Imaging techniques:

- INNOVATIVE Medical Imaging:

1- Ultrasound has been studied in last year Shkodra Workshop by Christian Cachard and Hervé Liebgott. Ultrasound are are popular because three positive points:

Real time imaging, No radiation, Relatively low cost (no special building requested).

Spectacular applications of Modern US were given in Shkodra: Innovation in US imaging, in live cardioimaging, Longitudinal motion of the carotid artery wall as a new marker of cardiovascular risk; Stenotic Internal Carotid Artery with Echo-Doppler, Transesophageal imaging, studies of the coronary arteries with insertion of a catheter,Complex motion visualization of cardiac flow (return flow)...

2- PET alone is progressively replaced to PET-CT, PET-MR... a "REVOLUTION" in Medical Imaging @Hospital (only possible from recent technical developments)

3- MAGNETIC RESONANCE IMAGING (Luc Bidaut): Well known great performance but particulary performant for: Diffusion Weighted Imaging , Diffusion Tensor Imaging; MRS could give impressive results to ANALYSE IN-VIVO what molecules are present inside the body.

4- INNOVATIVE THERAPY:

- Hadrontherapy (PA, PLD) Mainly for:Radioresistive cells, Pediatric cancer, difficult configuration of tumor ...

- Iowards online dose monitoring : "on beam" monitoring

DETECTION OF COUPLED OSCILLATIONS FROM BIOMEDICAL SIGNALS

Tomislav STANKOVSKI

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Periodicity and *oscillations* underlie many dynamical systems in biomedicine. For example the traces of oscillations can be observed in number of biomedical signals like the ECG for the heart activity, EEG for the brainwaves, laser Doppler blood flow signal for the local cardiovascular mechanisms and thorax-belt measurement of the breathing process. These oscillations can interact between each other, leading to new qualitative states like synchronization and oscillation death. In search to better understand and quantify such biomedical oscillations and their interactions, and stemming from physics, many effective methods for characterisation of different aspects of biomedical oscillations have been developed. These can include the wavelet transform for time-frequency analysis, wavelet phase coherence for detecting the coordination of the oscillations, coupling strength and directionality with conditional mutual information (transfer entropy), and dynamical Bayesian inference for evaluating dynamical mechanisms and coupling functions. The methods are demonstrated on several important biomedical *applications*. This will include a study of how a time-varying breathing frequency affects the human neurophysiological mechanisms. The cardiorespiratory coupling functions will be determined also from such time-varying breathing signals. The methods and the findings of the cardiorespiratory coupling functions are then applied to study the human ageing. Neuronal cross-frequency coupling functions are also inferred from brainwaves intervals of subjects under anaesthesia and autism.

NUCLEAR MEDICINE DOSIMETRY : DIAGNOSTIC & THERAPY

Manuel BARDIÈS

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Dosimetry in Nuclear Medicine is performed with dif ferent aims:

In diagnostic nuclear medicine, the objective is to document the practice, give an order of magnitude of the irradiation. The domain is that of stochastic effects. In Molecular RadioTherapy (MRT), the goal is to assess the irradiation delivered to the (tumour) target, while insuring that irradiation toorgans/tissues at risk is kept below a safety threshold. The domain is that of deterministic effects. The accuracy required for the determination of the absorbed dose is therefore different between diagnostic, where an order of magnitude of the irradiation is sufficient, and therapy, where - as in external beam radiotherapy - the best possible accuracy is looked for.

We will present current dosimetry approaches applied in both contexts. Interestingly, the computational formalism used to derive the absorbed dose is common to diagnostic and therapy, even though the level of refinement in the implementation of the formalism depends on the application. As such, the absorbed dose is not indicative of the effect of the nuclear medicine procedure (diagnostic and therapy); we will also review some of the current achievements in absorbed dose / effect relationship assessment in Molecular

Radiotherapy.

EFFECTIVE DOSE ESTIMATION AND RISK ASSESMENT IN PATIENTS TREATED WITH IODINE ^{131}I USING MONTE CARLO SIMULATION

Marina ZDRAVESKA Kochovska,

Institute of pathophysiology and nuclear medicine, Medical faculty, Skopje, Republic of Macedonia

The most frequently used radiopharmaceutical for treatment of thyroid diseases such as Thyroid Cancer and Hyperthyroidism is radioactive iodine ^{131}I. It has a very high success rate in treatment of patients with thyroid diseases and also it has been proven to be safe and relatively inexpensive treatment modality. Whenever radiation is used in the treatment of the benign or cancer diseases dosimetry is essential. The main aim of this study is to perform external measurements of dose rate after administered activity and to simulate dosimetry of internal organs and risk assessment using MCNP 4b code, either for thyroid cancer and Hyperthyroid patients. To search safety optimization in this kind of therapy, it was recognized the necessity of more accurate knowledge of dose levels received by stomach and other organs. Of great importance is to know the effective dose that will be reached in gastric and other surrounding organs such as liver, lung, bladder etc. Additional aim was to provide information to be used in the improvement of radiation therapy, radiation safety practices and improvement of the fundamentals of radiation protection as defined by ICRP: justification, optimization and application of dose limits. The significance of this research is that the dose's to internal organs can be determined and it worth to mention that such internal dosimetry calculation has been performed rare in the field of nuclear medicine. In accordance with the calculations carried out during this study and reference available in the literature that the therapy with radioiodine will be improved at the Institute of pathophysiology and nuclear medicine. Designed quality programs will be useful also for regulatory and accreditation bodies in the process of accreditation and radiation protection strategy.

INTRODUCTION TO COMPUTED TOMOGRAPHY

Julie HAGLUND

Fredricstad, Norway

With the advent of hybrid scanners in modern nuclear imaging departments, it is important to have a fundamental understanding of the CT component of the scanner. Computed Tomography is an x-ray imaging technique that produces thin slice views of the object. A planar slice of the object is defined, and x-rays are passed through it in directions that are parallel to the plane of the slice. The CT slice is a few millimeters thick and eliminates the overlapping of information that is characteristic of traditional x-ray imaging.

Modern CT scanners use a wide range fan beam of x-rays to cover the entire object being scanned. Adding arrays of detectors opposite the x-ray beam makes use of the entire beam of radiation and reduces the scan time. Image quality in CT is determined by the physical processes that govern the acquisition of the projection data and the reconstruction algorithm selected. Spatial resolution in the scan plane and perpendicular to the scan plane, noise, low contrast resolution, and radiation dose are common image quality parameters.

In the hospital setting, dose to the patient is of importance. The dose concepts CT Dose Index and Dose Length Product have been developed specifically for Computed Tomography. Dose to the patient is influenced by beam energy, x-ray tube current and time, pitch, collimation, and the size of the patient. Dose reduction methods include reducing the mAs or beam energy.

SPECT/CT INSTRUMENTATION AND CLINICAL APPLICATIONS

Daniela MILADINOVA MD PhD

Institute of Pathophysiology and Nuclear Medicine "Acad. Isak S.Tadzer", Faculty of Medicine, University "Ss. Cyril and Methodius", Skopje

Correlative imaging has been used in clinical practice, mainly for the interpretation of nuclear medicine studies where detailed anatomical information is often lacking. Software co-registration techniques suffered from technical limitations related to different geometries of the imaging equipment and differences in positioning of the patients. SPECT/CT combines the functional imaging capabilities of Single Photon Emission Computed Tomography with precise anatomical overlay of Computed Tomography images acquired sequentially, as a part of a single study.

SPECT/CT systems usually use a low dose single slice CT where both the SPECT and CT detector are mounted on the same rotating platform. The system is characterized by high spatial resolution and faster scanning time.

The increased diagnostic value of integrated SPECT correlated with CT includes: improvement on lesion detection, more precise localization of foci of uptake resulting in better differentiation of physiological from pathological uptake, characterization of serendipitous lesions and confirmation of small, subtle or unusual lesions.

SPECT/CT is useful in solving problems when the location of the activity is unclear on planar imaging, allows higher sensitivity and specificity than routine nuclear scintigraphy and obviates the need for delayed images and multi-days studies.

SPECT/CT fusion images affect the clinical management in a significant proportion of patients with a wide range of diseases. The main clinical application of SPECT/CT in routine nuclear medicine practice is in the area of bone scanning, graft infections, cardiac imaging, parathyroid imaging, lymphoscintigraphy, patients with unexplained abdominal pain, tumor and mass localization (general oncology) and especially in thyroid cancer staging.

The SPECT/CT obtained data should be used in guiding further investigations, excluding the need for further procedures, changing inter and intramodality therapy, including soon after treatment has been initiated and by providing prognostic information related to the disease.

It is expected that the role of SPECT/CT, as well as PET/CT in modifying clinical practice will continue to develop in the future and that these diagnostic tools will be the basic components of `personalized medicine`.

DOSE OPTIMIZATION IN MDCT

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The use of CT imaging has increased tremendously in recent years resulted from improved technology, such as the introduction of modern multidetector-array CT scanners and parallel increases in clinical applications of CT scanning. Several studies have suggested that, although CT is not the most common radiological examination, it is responsible for the largest radiation dose in patients. Therefore, there is a strong need to minimize the radiation dose delivered to patients and reduced the risk of radio induced cancer.

Dose optimization can be achieve by several methods, such as recently developed new tools and features in MDCT, then by adjustment of exposure parameters according to patient size, clinical needs, or type of examination, etc.

Education and training of clinical staff in the scanner performances and available dose reduction tools play important part towards dose optimization.

Although the Dose Reference Levels or implemented patients dosimetry procedures do not provide dose optimized examinations by themselves, they may have a significant influence over dose reduction actions.

Our findings suggest that CT examinations in Republic of Macedonia are performing by using of default protocols installed by manufactures or their local representatives. In addition, the CT protocols are not optimized, neither in terms of clinical needs nor in terms of diagnostic image quality.

POSITRON EMISSION TOMOGRAPHY – HISTORY AND PRINCIPLES

Ivo RAUSCH

Medical University Vienna, Austria

The discovery of radioactivity in the late 1890's by Henry Bequerel was the starting point of a wide range of new discoveries and application. One of those was the development of the radioactive tracer principle by George de Hevesy in 1911 which led to the first experiments using a radioactive tracer in humans in 1923. In the following decades the field progressed e.g. with the discovery of the positron or the development of cyclotrons and nuclear reactors. This made it possible to produce artificial radioactive sources in a large amount.

In 1951 Wrenn and colleges published the first application of positrons for brain tumours using coincident detection of the annihilation photons. This was the birth of the technique used in positron emission tomography (PET) and finally led to the development of the first PET scanner in 1975.

A PET relies on the simultaneous detection of two photons traveling in opposing direction originating from positron annihilation. Hence, if these two photons are detected, it is evident that the annihilation has taken place somewhere on a line (also referred to as line of response (LOR)) between the two detectors. In PET coincident photons are detected in a ring geometry or by extended opposing detector arrays from various angles around a positron source. A set of parallel LORs correspond to the projection of the activity distribution from a certain angle. Thereby, it is possible to reconstruct an image of the measured activity distribution using tomographic reconstruction technics.

In a real setting, photons traveling through an extended object are attenuated according to the properties of its material. One big advantage of coincidence detection is that the probability of attenuation is solely dependent on the attenuation probability across the whole object along the respective LOR. This can be measured using a rotating transmission source e.g. a Ge/Ga 68 source or by computed tomography, used to correct attenuation of the annihilation photons.

Therefore, PET is principally able to quantitatively measure an activity distribution in an extended object.

CLINICAL APPLICATIONS OF FDG PET/CT

JN TALBOT

Nuclear Medicine department, Hôpital Tenon and Université P&M Curie, Paris, France

18F-fluorodeoxyglucose (FDG) is a radioactive analogue of glucose suited for positron emission tomography (PET) imaging. It permits to image and quantify the intensity of the glucose uptake and metabolism by the tissues, aiming to detect and characterise lesions. The foci of FDG uptake can be localised anatomically thanks to the hybrid image acquisition and fusion with CT, in the great majority of nuclear medicine centres, or with MRI in some advanced nuclear medicine centres. A search in PubMed limited to applications in humans retrieved 16000 references since 1983 using “FDG PET” as keywords and 8220 references using “FDG PET/CT”.

The approach of PET/CT imaging with FDG is a non-specific molecular imaging since an anomaly in glucose uptake and metabolism will not be specific of a precise pathology, even though the intensity of this uptake is an element of probability. This may be seen as a drawback but it is also a strength in routine practice: one single tracer, FDG, may be used in a large number of clinical settings and in the majority of patients.

The most widely used clinical application of FDG is imaging of cancer. Most cancers, in particular the aggressive ones, take-up FDG more intensely than the surrounding healthy tissues. FDG PET/CT is now recommended in various clinical guidelines, taking into account not only the organ with the primary cancer but also the histologic type of cancer and its differentiation (e.g. in pancreas cancer, FDG is effective in case of adenocarcinoma but not in case of well-differentiated neuroendocrine tumour) and the context (FDG may not be indicated to stage a cancer in case of a small primary tumour but very effective to detect its occult biochemical recurrence).

The recommendations of the Guidelines on the use of FDG depend on the context and the date when it has been issued. The “core” summary of product characteristics (SmPC) of FDG, an official document of the European Medicines Agency (EMA), lists the main FDG indication as follows:.

Several other clinical applications of FDG have been proposed and for a few recommended by some clinical societies, such as: monitoring treatment of GIST tumours, selection of patients with hepatocellular carcinoma for liver grafting, monitoring treatment of tuberculosis, differential diagnosis of dementia …

Oncology

<u>Diagnosis</u>

Characterisation of solitary pulmonary nodule

Detection of cancer of unknown origin, revealed for example by cervical adenopathy, liver or bones metastases

Characterisation of a pancreatic mass

<u>Staging</u>

Head and neck cancers including assistance in guiding biopsy

Primary lung cancer

Locally advanced breast cancer

Oesophageal cancer

Carcinoma of the pancreas

Colorectal cancer particularly in restaging recurrences

Malignant lymphoma

Malignant melanoma, Breslow >1.5 mm or lymph node metastasis at first diagnosis

<u>Monitoring of therapeutic response</u>

Malignant lymphoma

Head and neck cancers

<u>Detection in case of reasonable suspicion of recurrences</u>

Glioma with high grade of malignancy (III or IV)

Head and neck cancers

Thyroid cancer (non-medullary): patients with increased thyroglobulin serum levels and negative radioactive iodine whole body scintigraphy

Primary lung cancer

Breast cancer

Carcinoma of the pancreas

Colorectal cancer

Ovarian cancer

Malignant lymphoma

Malignant melanoma

Cardiology

Evaluation of myocardial viability in patients with severe impaired left ventricular function who are candidates for revascularisation when conventional imaging modalities are not contributive.

Neurology

Localisation of epileptogenic foci in the presurgical evaluation of partial temporal epilepsy.

Infectious or inflammatory diseases

<u>Localisation</u> of abnormal foci guiding the aetiologic diagnosis in case of fever of unknown origin

<u>Diagnosis of infection</u>

Suspected chronic infection of bone and/or adjacent structures: osteomyelitis, spondilitis, diskitis or osteitis including when metallic implants are present

Diabetic patient with a foot suspicious of Charcot's neuroarthropathy, osteomyelitis and/or soft tissue infection

Painful hip prosthesis

Vascular prosthesis

Fever in an AIDS patient

<u>Detection of the extension of inflammation</u>

Sarcoidosis

Inflammatory bowel disease

Vasculitis involving the great vessels

<u>Therapy follow-up:</u>

Unresectable alveolar echinococcosis, in search for active localisations of the parasite during medical treatment and after treatment discontinuation.

Clinical studies aiming to demonstrate the utility of FDG PET/CT are still ongoing in many clinical applications.

RESEARCH EXAMPLE WITH SMALL ANIMAL PET

Yves LEMOIGNE, PhD

IFMP Ambilly, France and TERA Foundation Novarra, Italy

Biomedical research needs a precise quantification of biological parameters and PET can provide them.

As example, the speaker refers to an experience of neurotransmission in the brain of a rat. The aim was to study the binding of serotonin, in fact quantifying 5-HT1A receptors interactions in rats. Serotonin is involved in various physiological functions and behaviour like anxiety, depression (to fight against)

This will :

1- Rely on backgrounds and mathematical modeling (basics of pharmaco-kinetics); establish the need for dynamic imaging (i-e change in a given period of time); role of mathematical models.

2- Discuss the principles of the experiment and data analysis from micro-PET: measurement of the density of 5-HT1A receptors expressed in pico-mol by ml in the hippocampus area of a rat brain.

PET - QUALITY CONTROL AND QUANTIFICATION

Ivo RAUSCH

Medical University Vienna, Austria

The main purpose of a Positron Emission Tomography (PET) examination is to obtain a quantitative evaluation of a specific metabolic process. To obtain this a quality management system (QMS) has to be set up. A QMS is a program that controls how quality is maintained and ensured throughout an organisation. It consists mainly of Quality Assurance (QA), a concept of actions which ensures that certain requirements are met, and Quality Control (QC) to monitor the procedures and the performance of a system.

Quantification in PET is not only a matter of proper PET system performance. The outcome of a study is influenced by various factors related to technical, biological and physics related factors. QA in the case of PET should incorporate standardised operation procedures (SOP) for the whole work flow. It start with the instruction to the patient prior to the day of examination (e.g. special diet before an FDG study). Further on, it should include SOPs for patient handling (e.g. tracer / disease specific uptake times) as well as instructions on standardized acquisition and reconstruction protocols. And lastly SOPs for a standardized evaluation of the studies.

One important part of the whole workflow is to ensure the proper function of the PET system itself. This is achieved by proper QC and eventual corrective actions. QC of the system consists of initial tests as part of the acceptance testing after installation and routine QC procedures. Acceptance testing is performed to check if the system meets the specifications provided by the vendor. It follows standardized measurements like described in the NEMA-NU2 standard and consists, for example, of measuring the spatial resolution, sensitivity, count rate performance and image quality. Furthermore, this measurement serve in the following as reference for future testing.

During operation of a PET, routine QC procedures have to be performed. This tests should be simple and specific to the imaging system and sensible to system changes. For this procedures it is essential to properly document the results to estimate the long-time behaviour of the system. Lastly, there should be SOP defining thresholds for the results of the tests and defined corresponding actions if this thresholds are exceeded.

PET IN NORWAY, AN EXAMPLE

Julie HAGLUND

Fredricstad, Norway

The challenge of installing and starting clinical operations of PET/CT in a hospital requires cooperation from a multidisciplinary team. This is well described by the AAPM Task Group 108 and IAEA [1,2]. When not only the PET/CT modality is new to the department, but also the entire hospital facility is new, even greater efforts are required in order to successfully begin clinical activity. At the new Østfold Hospital Kalnes, the decision to install a PET/CT in the nuclear medicine department required starting from scratch in every possible way. The decision to install a PET/CT was made after designing and planning a room for SPECT/CT, which meant modifying the physical buildings of the new hospital during a late phase of construction. Shielding had to be increased in order to accommodate positron annihilation radiation energy. Østfold Hospital Kalnes had the opportunity to choose among three manufacturers of PET/CT machines. In order to decide which machine to purchase, extensive research and evaluation by a multidisciplinary team was necessary. The team had to choose a machine that will be suitable for the present and future ambitions of the hospital. The staff of the nuclear medicine department is well experienced in clinical SPECT/CT, but nobody had previously worked with PET/CT. Training became a critical part of preparing for the installation and clinical implementation of a new modality. Department seminars highlighted radiation safety and clinical PET/CT protocols, and visits to other hospitals were made in order to observe clinical routines and quality control procedures. Since Østfold Hospital Kalnes is not a university hospital and is completely new to PET/CT, it was decided to join the EARL FDG quality assurance program from the European Association of Nuclear Medicine. Participation in EARL will enhance confidence in both the staff and the public because accreditation shows that the department performs PET/CT studies at a level that is comparable to university hospitals that have a long clinical history with clinical PET/CT. The program will also increase possibilities for collaboration and research.

[1] Madsen MT, Anderson JA, Halama JR, Kleck J, Simpkin DJ, Votaw JR, et al. PET and PET/CT shielding requirements AAPM Task report 108, Med Phys2006;33:4–15.

[2]International Atomic Energy Agency, Radiation Protection in Newer Medical Imaging Techniques: PET/CT, Safety Reports Series No. 58, IAEA , Vienna (2008).

IMAGING FOR RADIATION ONCOLOGY – CT, PET-CT

Sonja PETKOVSKA

ACIBADEM Sistina, Skopje, Macedonia

Abstract: Radiation therapy plays an important role for treatment of cancer patients. Precise and accurate localization of radiotherapy targeted to the PTV is critical for optimizing the therapeutic ratio, by maximizing the radiation dose delivered into volume of interest and limiting the radiation dose into normal tissues. Computed tomography (CT) is the primary modality for image-based treatment planning, but conventional anatomic imaging with CT has limited sensitivity to identify distinctly the anatomic borders of the tumor. Integration of multimodality imaging data for radiotherapy treatment planning is beneficial and indispensable for perfect delineation.

Functional imaging with PET can provide information that can influence RT planning, it can reveal targets that are not well visualised by CT/magnetic resonance (MR) structural imaging. Physiological and molecular information about the tumour can be incorporated into RT planning trough CT and PET-CT images registration. Thus improving the accuracy of clinically relevant radiotherapy target definitions and dose delivery. Furthermore, the imaging of biologic inhomogeneities within sub volumes of the tumour may offer the possibility to adapt doses to local differences in radiosensitivity. is required.

To be able to use PET-CT for tumor delineation, the position of the patient is crucial. All set-up and patient positioning tools currently used in the radiation oncology department on simulators and linear accelerators should be equally conscientiously used in the PET suite when images are acquired for treatment planning. All quality controls required in the radiation therapy process, particularly those for geometrical alignment between all parts of the radiotherapy chain, must also include the PET scanner.

PET/MR: Principles, Applications, Evolution...

Luc BIDAUT, PhD

Fife-Tayside, Scotland, UK

Osman Ratib, MD, PhD
Geneva, CH

Advanced imaging can be simply depicted as a mix of multidimensional, multimodal and parametric imaging. Multidimensional (e.g. 3D) biomedical imaging initially stemmed from the availability of tomography equipment and data sets, which can then accurately depict the volume of a patient's body, either directly or through stacks of individual slices. Such information can be used either for a diagnosis or for the planning, simulation and monitoring of an intervention.

Multimodality and multiparametric imaging stemmed from the complementarity of information brought up through anatomical (e.g., CT and MR) and functional (e.g., PET, SPECT) modalities. Such advanced approaches were much facilitated by the advent of hybrid imaging equipment in recent years. After PET/CT and SPECT/CT, PET/MR is the latest instance of hybrid imaging to be deployed in the clinic. Compared to CT, MR provides exquisite contrast in soft tissues through non-ionising means. This relative strength for anatomical imaging can present challenges when MR is also to be used for correcting PET shortcomings in relation to the propagation of radiation, which CT is also based upon and thus intrinsically more suited to provide. For some time now, various commercial designs of PET/MR scanners have been available to the community and moved through their stride at various translational sites to assess not only what they can uniquely provide for research and clinical applications, but also their potential weaknesses and best ways to address them. This presentation will summarise the principle and design of PET/MR scanners, exhibit a few current and future applications while comparing PET/MR results to other hybrid modalities through a few selected cases, and finally provide a glimpse at near future PET/MR developments and likely evolution.

GENERAL RISKS WITH RADIATION

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Risk is the effect of uncertainty on objectives. An effect is a positive or negative deviation from what is expected, and an uncertainty is a state or condition that involves a deficiency of information and leads to inadequate or incomplete knowledge or understanding. Radiation risks is detrimental health effects of exposure to radiation (including the likelihood of such effects occurring), and any other safety related risks (including those to the environment) that might arise as a direct consequence of exposure to radiation, the presence of radioactive material (including radioactive waste) or its release to the environment, or a loss of control over a nuclear reactor core, nuclear chain reaction, radioactive source or any other source of radiation. Ionizing radiation can cause damage to the living matter. This damage occurs through the change in chemical properties of molecules in the living matter following exposure to radiation. Since the basic structure of living matter is a cell, the interaction of ionizing radiation with living matter is basically an interaction with the cell, and with the structures and molecules in different cell components. This can cause damage to the most important target in the irradiated cell - the deoxyribonucleic acid (DNA) molecule. However, the most of damage is readily repaired by the cell. If it is not, it can result in cell death. Alternatively, if the DNA damage is repaired erroneously, it can result in an alteration leading to cancer induction or hereditary changes. Several factors affect cell survival, such as radiation quality, radiation dose and dose-rate, dose fractionation, types of cells, radioprotectors/radiosensitizers, temperature, etc. Stochastic effect is a radiation induced health effect, the probability of occurrence of which is greater for a higher radiation dose and the severity of which (if it occurs) is independent of dose. Stochastic effects may be somatic effects or hereditary effects, and generally occur without a threshold level of radiation dose. Examples include solid cancers and leukaemia. Deterministic effect is a health effect of radiation for which generally a threshold level of radiation dose exists, above which the severity of the effect is greater for a higher radiation dose. The level of the threshold radiation dose is characteristic of the particular health effect but may also depend, to a limited extent, on the exposed individual. Examples of deterministic effects include erythema and acute radiation syndrome (radiation sickness). Such an effect is described as a severe deterministic effect if it is fatal or life threatening or results in a permanent injury that reduces quality of life. Deterministic effects are also referred to as ‘harmful tissue reactions’. Both stochastic and deterministic effects are important in radiation protection. The main objective in radiation protection must be to avoid deterministic effects and to reduce the probability of stochastic effects to as low as reasonably achievable (ALARA) level.

RADIATION PROTECTION OPTIMIZATION IN NUCLEAR MEDICINE

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Radiation protection and safety is the protection of people from harmful effects of exposure to ionizing radiation or due to radioactive material and the safety of sources, including the means for achieving this, and the means for preventing accidents, and for mitigating the consequences of accidents if they do occur. Radiation protection and safety is concerned with both radiation risks under normal circumstances and radiation risks as a consequence of incidents, as well as with other possible direct consequences of a loss of control over any source of ionizing radiation. Safety measures include actions to prevent incidents and arrangements put in place to mitigate their consequences if they were to occur. The practice of diagnostic and therapeutic nuclear medicine involves the use of unsealed radioactive sources of ionizing radiation. Thus, the potential risks associated with internal and external radiation exposures must be weighed against the benefits to the patients and the society. This requires that the right procedure with the right radioactivity is applied to the right patient at the right time. Three main general principles of radiation protection are justification, optimization and dose limitation. Optimization of radiation protection and safety is the process of determining what level of radiation protection and safety would result in the magnitude of individual radiation doses, the number of individuals subject to public or occupational radiation exposure (members of the public, workers), and the likelihood of radiation exposure being as low as reasonably achievable (ALARA), with physical, technical, economic, social, environmental and other factors being taken into account. This means that the level of radiation protection should be the best possible under the prevailing circumstances. The optimization of protection and safety of individuals subject to medical exposure (patients, carers and comforters of patients, volunteers as part of a programme of biomedical research) is the management of the radiation dose to the patient commensurate with the medical purpose. This principle shall be applied not only in terms of effective dose but also, where appropriate, in terms of equivalent doses, as a precautionary measure to allow for uncertainties as to health detriment below the threshold for tissue reactions. Radiation dose constraints and reference levels are used for optimization of protection and safety, the intended outcome of which is that all exposures are controlled to levels that are ALARA. Radiation dose constraints are applied to occupational exposure and to public exposure in planned exposure situations. Radiation dose constraints are set separately for each source of ionizing radiation under control and they serve as boundary conditions in defining the range of options for the purposes of optimization. Radiation dose constraints are not radiation dose limits, and exceeding a radiation dose constraint does not represent non-compliance with regulatory requirements, but it could result in follow-up actions. It is of paramount importance that the medical exposure leads to the required outcome. The government or regulatory body shall establish and enforce requirements for the optimization of radiation protection and safety, and registrants and licensees shall ensure that radiation protection and safety is optimized. A phrase ‘radiation protection and safety is optimized’ means that optimization of radiation protection and safety has been applied and the result of that process has been implemented. Optimization is a prospective and iterative process that requires both qualitative and quantitative judgements to be made. The role and the importance of medical physics and biomedical engineering experts in the process of optimization of radiation protection and safety in nuclear medicine are crucial.

PATIENT, WORKER AND PUBLIC RADIATION PROTECTION IN HOSPITAL

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Medical radiation exposure is exposure to radiation incurred by patients for the purposes of medical or dental diagnosis or treatment, incurred by carers and comforters of the patients, or incurred by volunteers subject to exposure as part of a programme of biomedical research. A patient is an individual who is a recipient of services of health care professionals and/or their agents that are directed at health promotion, prevention of illness and injury, monitoring health, maintaining health, and medical treatment of diseases, disorders and injuries in order to achieve a cure or, failing that, optimum comfort and function. Carers and comforters are persons who willingly and voluntarily help (other than in their occupation) in the care, support and comfort of patients undergoing radiological procedures for medical diagnosis or medical treatment. Occupational radiation exposure is radiation exposure of workers incurred in the course of their work. Worker is any person who works, whether full time, part time or temporarily, for an employer and who has recognized rights and duties in relation to occupational radiation protection. Public radiation exposure is exposure to radiation incurred by members of the public due to sources of ionizing radiation in planned, emergency or existing radiation exposure situations, excluding any occupational or medical radiation exposure. For protection and safety purposes, member of the public is any individual in the population except when subject to occupational exposure or medical exposure. For the purpose of verifying compliance with the annual radiation dose limit for public exposure, this is the representative person. Radiation dose limits for planned radiation exposure situations, i.e. situation of radiation exposure that arises from the planned operation of a source of ionizing radiation or from a planned activity that results in an radiation exposure from a source, in case of occupational radiation exposure of workers over the age of 18 years are: an effective dose of 20 mSv (milli Sievert) per year averaged over five consecutive years

(100 mSv in 5 years) and of 50 mSv in any single year; an equivalent dose to the lens of the eye of 20 mSv per year averaged over 5 consecutive years (100 mSv in 5 years) and of 50 mSv in any single year; an equivalent dose to the extremities (hands and feet) or the skin of 500 mSv in a year. Additional restrictions apply to occupational exposure for a female worker who has notified pregnancy or is breast-feeding. For occupational radiation exposure of apprentices of 16 to 18 years of age who are being trained for employment involving radiation and for radiation exposure of students of age 16 to 18 who use sources of ionizing radiation in the course of their studies, the dose limits are: an effective dose of 6 mSv in a year; an equivalent dose to the lens of the eye of 20 mSv in a year; an equivalent dose to the extremities (hands and feet) or the skin of 150 mSv in a year. Radiation dose limits for planned radiation exposure situations in case of public exposure are: an effective dose of 1 mSv in a year; in special circumstances (for example, in authorized, justified and planned operational circumstances that lead to transitory increases in radiation exposures), a higher value of effective dose in a single year could apply, provided that the average effective dose over five consecutive years does not exceed 1 mSv per year; an equivalent dose to the lens of the eye of 15 mSv in a year; an equivalent dose to the skin of 50 mSv in a year. In context, radiation dose limits do not apply to medical radiation exposures. Verification of compliance with radiation dose limits specified here apply to the sum of the relevant radiation doses from external radiation exposure in the specified period and the relevant committed radiation doses from radioactivity intakes in the same period. The period for calculating the committed radiation dose shall normally be 50 years for radioactivity intakes by adults and up to age 70 years for radioactivity intakes by children.

SHIELDING REQUIREMENTS FOR PET/CT

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Whether installing PET/CT in an existing department or building a new facility, shielding for PET/CT is complicated and expensive [1]. The energy of positron annihilation radiation is greater than the energy of radiation used with other diagnostic imaging modalities. National regulatory limits dictate the annual radiation exposures for uncontrolled and controlled areas, and it is necessary to consider not only areas immediately adjacent to the PET/CT, but also areas above and below the facility. Barrier shielding must be determined for floors, ceilings, and adjacent walls. The short half-life of PET radionuclides and movement of injected patients within the department are also factors that must be considered when planning a PET/CT installation. Various materials can be used in order to shield positron annihilation radiation, and choices should be cost effective and practical. Effective planning for the installation of a PET/CT will include a medical physicist, workers from the nuclear medicine department, an architect, and the PET/CT manufacturer. Methods for estimating the shielding required for PET/CT take into consideration decay of the radionuclide, attenuation in the patient, and the examination protocol.

[1] Madsen MT, Anderson JA, Halama JR, Kleck J, Simpkin DJ, Votaw JR, et al. PET and PET/CT shielding requirements AAPM Task report 108, Med Phys2006;33:4–15.

IEEE NPSS Distinguish Lecturer

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This is a set of two lectures that have the objective of discussing technology transfer from basic research in High Energy Physics to practical applications. The lectures can be optimized as single 'lectures' or combined/extended as 'summer school' type lectures. Technology transfer needs to be promoted actively outside the fundamental physics community for the benefit of society. High Energy Physics is not only hunting the Higgs, but has some experience in technology transfer. It is not simple and need a very 'open minded' point of view. It can help attract a new generation of young students. Understanding the problems between collaborative partners is essential. Medical doctors need to be educated about new technologies; physicists are sometime arrogant by thinking that they already have the final solution and forgetting the reality of the medical clinical world; and for industrial and commercial companies, this is always a financial concern at the end. Successful technology transfer can result in an extension of established applications and an improvement of current performance levels and finally a more beneficial cost/benefit ratio.

These lectures are intended to give a flavor of the value of Particle Physics: can we use the state-of-the-art technologies, tools and techniques developed for fundamental physics experiments using radiation detectors in the field of High Energy Physics (HEP) for other applications of interest to society?

High energy and particle physics has considerable acquired knowledge, expertise and resources that can, when transferred in a realistic way, significantly impact other fields of applications like the practice of medical imaging for diagnostic and therapy, safeguarding homeland security, environmental sciences and severe nuclear accident monitoring. http://ieee-npss.org

APPLICATION OF FUNDAMENTAL PHYSICS INNOVATIVE TECHNIQUES AND TOOLS TO BIOMEDICAL IMAGING.

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This overview introductory talk "from basic science to the human reality" intends to show how successful technology transfer between fundamental research in Particle Physics and other fields of applications can be achieved using specific examples.

Using as input the recent advance of HEP state-of-the-art techniques and tools in detectors developments like solid-state and gaseous detectors, calorimeters, photodetectors, read-out electronics and simulations, this talk will provide examples of some direct applications in medical and molecular imaging like Positron Emission Tomography (PET), Computed Tomography (CT), X-Ray imaging and many others.

DEVELOPMENTS IN PET FROM HEP

Leandar LITOV

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High energy physics is the main source of new imaging technologies in the medicine, PET being one of the most prominent examples. The influence of the new developments in the PET technology will be demonstrated on the example of PET detector based on Resistive Plate Chambers (RPC). RPC are gaseous parallel plate detectors for charged particles that are widely used in large-scale high energy physics experiments as fast trigger detectors for muon spectrometers. The RPC's main advantages are the high time and spatial resolution, their ability to work in strong magnetic fields and the possibility to construct inexpensive large area detectors (~2-3 square meters). Transforming the resistive plate chambers from charged-particle into gamma-quanta detectors opens the way towards their application as a basic element of a hybrid imaging system, which combines positron emission tomography with magnetic resonance imaging in a single device. Results towards the development of a hybrid imaging system based on multigap glass resistive plate chambers are present. The detector design is chosen after detailed GEANT based simulations. A special care is taken to decrease the efficiency for Compton scattered photons, while keeping relatively high efficiency for 511 keV photons. RPC technology allows building a device with a large field of view, increasing drastically the geometrical acceptance in comparison to the standard devices. The RPC's excellent position resolution for the gamma quanta impact point and the time-of-flight measurement accuracy will allow reconstruction of the image with precision better than 1 mm. The first prototypes have been build and tested. The detector prototypes and the test set-up will be presented as well as the simulation and test results.

HADRON THERAPY PRINCIPLES

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Hadron therapy is increasingly considered the best radiotherapy for cancer due to its superior dose distribution. Compared to photons or electrons used in the conventional radiation therapy, the hadrons (mainly protons, neutrons and light ions) have a depth dose profile such that the energy is released to the tumor target with a high accuracy, while avoiding the surrounding healthy tissues.

The aim of this talk is to give an overview of the hadron therapy starting from the history of such a therapeutic treatment. The basics physics of the hadron therapy will be described as well as the biological properties, in order to show the advantages of protons and carbon ions with respect to X-rays in radiation oncology. The main technical aspects of a hadron therapy facility will be shown, as well as the status of hadron therapy in the world. Finally the future challenges in this multidisciplinary research field will be introduced.

ON LINE DOSE MONITORING

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Hadron therapy is nowadays the most precise modality of external radiation therapy. Unlike the particles used in the conventional radiation therapy (photons or electrons), the hadrons (mainly protons, neutrons and light ions) can penetrate through the body and deposit most of their kinetic energy at the end of their path, giving rise to the *Bragg Peak*. Since hadron therapy is very sensitive to uncertainties during planning and dose delivery, it is imperative to know the exact location of the dose deposition to ensure the tumor target, and not the surrounding healthy tissues, is being irradiated. Positron emission tomography (PET) imaging, i.e. imaging of the activation of the patient's tissue by the hadron beam, is a promising tool for monitoring the distribution of the dose deposited in the patient from the therapeutic beam.
The aim of this talk is to give an overview of the physical properties of hadron therapy dosimetry based on PET and of the technical results achieved. The role of Monte Carlo simulations for the dose distribution prediction will be discussed and finally the future developments will be introduced.

CHALLENGE OF PARTICLE IMAGING FOR HADRONTHERAPY

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This is the Treatment of cancer tumor by particles like protons or light ions is now becoming very common using hadron therapy accelerators. However, the patient dose optimization, delivery, and monitoring during the treatment are some of the main issues of this technique. The scope of this lecture is to summarize the « state of the art » of technology developments imposed by the various needs and constraints associated with the real-time dosimetry measurement and control around the patient. It will be illustrated by some R&D developments coming mainly from the High Energy Physics (HEP) community. This presentation will cover various topics including detection and tracking of organ motion, advanced technologies for a dedicated in-beam hadron PET for dose quantification, and recent developments in Proton Computed Tomography.

Radiation therapy is one of the cornerstones of modern cancer treatment. With increasing frequency, more than 50 % of tumor patients are irradiated, either as the exclusive form of treatment or in combination with other modalities, like surgery or chemotherapy. The central challenge of radiotherapy is to destroy the tumor completely, while saving the surrounding healthy tissue. In some delicate therapeutic cases, e.g. for compact, deep-seated, radio-resistant tumors growing in close vicinity to organs at risk, these objectives cannot be reached by the state-of-the-art radiotherapy technology that relies on hard photon or electron beams delivered by compact electron linear accelerators. Therefore, proton and light ion (e.g. carbon) beams have become more and more important due to their favorable physical and radiobiological properties. With a growing number of facilities in operation, the last five years have seen the development of new accelerator systems, advances in beam delivery and dose monitoring techniques, and increased clinical applications. The most significant recent advance in proton therapy has been the implementation of scanning techniques, in which a narrow proton beam is scanned throughout the target volume. This ability to "paint" the dose has opened up the possibility of performing intensity-modulated proton therapy. Proton Computed Tomography (PCT) has the potential to improve the accuracy of dose calculations for proton treatment planning, and will also be useful for pretreatment verification of patient positioning relative to the proton beam. Another innovative possible future development could be online imaging during proton beam delivery, enabling real-time adjustment of treatment.