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# International Conference on Hybrid Imaging (IPET 2024)

**7 – 11 October 2024, Vienna, Austria**

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# Resources. Day 2

## 1 PET-CT for the Management of Cancer Patients: A Review of the Existing Evidence

*International Atomic Energy Agency, et.al. (2021),*
*IAEA Human Health Series; (no.45); Vienna, Austria*


Abstract

The global incidence of cancer is increasing in both developed and developing countries and will become an increasing health burden in the coming decades. This rise in the cancer rate will bring with it challenges for health care systems, clinicians, and patients and their families. Technologies that improve the decision-making process and optimize treatment have the potential to benefit society as a whole. The purpose of this publication, predominantly aimed at policy makers, is to develop a consensus based on the existing evidence, on the value and the main indications of hybrid imaging using positron emission tomography (PET) combined with computed tomography (CT) in the management of patients affected by cancer. Indeed, PET–CT is considered a growing segment of the health care landscape due to the rising prevalence of non-communicable diseases, the need for early and accurate diagnostic methods, the technological developments both in hardware and software, the availability of new tracers and the acceptance in emerging markets.. Fluorodeoxyglucose (FDG) PET–CT has earned global recognition as a significant tool in the modern management of cancer patients. However, FDG has limitations in the assessment of several prevalent tumours such as prostate cancer. In addition, new therapeutic options available today in the management of cancer have underscored the need for assessing tumour characteristics other than metabolism. Therefore, there has been a pressing need for the development and clinical assessment of additional PET radiopharmaceuticals that can enable imaging and precise characterization of various aspects of a wide range of malignant tumours. While the use of PET–CT is a standard of care in oncological practice in many developed countries, it is still limited in many low- to middle-income nations. Based on these considerations, the International Atomic Energy Agency (IAEA) recognizes the need to make reliable information widely available to support Member States in the use of PET–CT. To achieve this goal, the IAEA convened an expert consultant group to review, given the latest evidence, the previous publication Human Health Series 9 (Appropriate use of FDG-PET in oncology). In the present publication, we focused our interest in highlighting the main indications of FDG and non-FDG radiopharmaceuticals in the management of cancer patients, based on the current clinical evidence. The recommendations included here to promote the optimal use of PET–CT imaging procedures in oncology considered the most recent developments of PET radiopharmaceuticals. These broad recommendations cannot be rigidly applied to all patients in all clinical settings but might be considered as a valid basis for tumour board discussions.

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# Resources. Day 2

## 2 Production, Quality Control and Clinical Applications of Radiosynovectomy agents

*International Atomic Energy Agency (2021), IAEA Radioisotopes and Radiopharmaceuticals Reports; (no.3); Vienna, Austria*


Abstract

Therapeutic radiopharmaceuticals are a major role player in today's nuclear medicine, especially for the treatment of cancer. One of the interesting and long practiced fields of their application is 'radiation synovectomy,' or in short 'radiosynovectomy'. In the last decades, the production and quality control of radiopharmaceuticals for use in radiosynovectomy has gone from simple phosphorous-32 (32P) colloids to recently developed matrixes labelled with short/medium range beta emitters. It is a well-established technique with growing applications worldwide. However, the lack of generic and peer-reviewed production, quality control and clinical application guidelines and recommendations, are a major concern for their application in human patients. Based on both, IAEA's global efforts in supporting Member States in the application of nuclear techniques in radiopharmacy and health, and on several requests from Member States as well as professional societies in recent years, formulation of an IAEA technical publication on the subject became pertinent. Currently, there is a lack of international standardized regulations of RSV production and clinical use. This publication is meant to be utilized by all involved professionals in the field by specifying ideal quality control and quality assurance procedures in the production of several radiopharmaceuticals for performing radiosynovectomy, as well as standard operation procedures needed for achieving successful therapeutic effects in patients.


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## 3 Early Results of Hypofractionated Radiotherapy for Localized Prostate Cancer Patients

*Nguyễn Đình Châu, Nguyễn Xuân Kiên, Bùi Quang Biểu, Phạm Quang Trung, Lê Mạnh Đức, & Quách Ngọc Mai (2023), Vietnam Conference on Nuclear Science and Technology VINANST-15 Agenda and Abstracts; 241 p; Viet Nam (Vietnamese)*


Abstract

Objectives: To evaluate the early results of hypofractionated radiotherapy in prostate cancer patients with localized stage. Methods: A prospective, uncontrolled intervention study on 30 prostate cancer patients with stage T1-3bN0M0 underwent radical radiotherapy at 60-65Gy in 20-25 fractions with or without endocrine therapy. The Kaplan-Meier curve was used to estimate PSA control and survival rates. Evaluation of early side effects according to CTCAE 5.0 criteria. Results: Median follow-up time was 22.5 months. PSA recurrence-free survival and disease-free survival at 30 months were 92.3% and 90.0%, respectively. Most of the early lower digestive tract and urinary side effects were grade 1-2, including proctitis (40.0%), cystitis (33.4%), and enteritis (10.0%); no early side effects were grade 3 or higher. Conclusion: Hypofractionated radiotherapy in localized prostate cancer has promising results and is safe. (author)

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# Resources. Day 2

## 4 Evaluation of Scattered Radiation in a Radiotherapy Treatment for Prostate Cancer Using Proton Therapy Compared to IMRT: a Study Using the Monte Carlo Method

*Alves, Arthur S.B.Z., Machado, Ariadny T., & Xavier, Douglas A.A., et. al. (2023), Metrology 2023: CBMRI: Brazilian congress on ionizing radiation metrology, Brazil*


Abstract

Radiotherapy using proton beams, or proton therapy, represents a major advance in the field of radiotherapy and clinical research. It delivers the prescribed dose in a precise manner and causes little to no damage to nearby structures. The main source of scattered radiation to the rest of the body in this case, comes from the creation of secondary particles, mainly neutrons, due to the high energies used in this beam. Using the Monte Carlo method with an anthropomorphic voxel phantom object, this paper compared the dosimetric data obtained from a prostate cancer treatment simulation using proton therapy, with the results previously obtained from literature for a similar treatment using photon beams. The deposited neutrons doses throughout the whole body were lower than IMRT by about 49%. In the irradiation field and in the organs nearby the tumor, the neutron's absorbed dose was less than half the photon dose, while in the remaining vital organs, disregarding those in the target area, the dose of neutrons exceeded IMRT by more than threefold. However, this last set of organs away from the fields, still represents less than 10% of the whole-body scattered absorbed dose contribution in IMRT and 16% in proton therapy. (author)


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## 5 Can Pre-Therapeutic Gallium-68 DOTATOC PET/CT by SUV Measurement Predict Progression-Free Survival and Treatment Response in Patients with Metastatic Neuroendocrine Tumours of the Gastrointestinal Tract after PRRT with Therapeutic Lutetium-177?

*Pavel, Friederike Leonie (2022), Marburg University (Germany). Fachbereich Medizin*


Abstract

The present study investigated 62 patients with metastatic neuroendocrine tumours of the gastrointestinal tract who received a Ga-68-DOTATOC PET examination followed by peptide radio-receptor therapy with lutetium-177-DOTATOC at the Department of Nuclear Medicine at the University Hospital Marburg between 2014 and 2019. The analysis focused on the possible predictors of progression-free survival: Ki67, SUVmax, WHO grading, chromogranin A, primarius location, age at first diagnosis and sex. In summary, this work demonstrated the role of Ki67 as a prognostic parameter for progression-free survival in patients with metastatic GEP-NET after Lu-177-PRRT. A revision of the delineation between G1 and G2 tumours from Ki67=2% to Ki67=5% should be considered to increase prognostic significance. The SUVmax could not offer any prognostic conclusions for the collective already selected for PRRT. Chromogranin A continues to be justified as a tumour marker and progression parameter, but is not suitable for formulating a prognosis with regard to PFS. Age at first diagnosis could not predict PFS. A worse prognosis was shown for p-NET than for NET of the small intestine. Significant differences in Ga-68 memory could only be found for the variable "primarius", but not for WHO grading or the occurrence of progression. Surprising was the significant difference in PFS between men and women of the collective - the genesis of which, however, could not be conclusively clarified. In addition, tumour progression occurred more frequently in women. Prospective studies in the future should continue to investigate the possible differences between the sexes in order to be able to classify results like these.

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# Resources. Day 2

## 6 Investigation of the Diagnostic Impact of Dual-Time PET/CT with PSMA Ligands in Prostate Carcinoma and with DOTATOC in Neuroendocrine Tumours

*Ottenthaler, Stefan (2022), Marburg University (Germany). Fachbereich Medizin*

Abstract

In the present study, the diagnostic impact of dual-time PET/CT examinations with Ga 68-DOTATOC in neuroendocrine tumours and Ga 68-PSMA in prostate carcinoma was investigated by means of retrospective data analysis. The aim was to show whether the biphasic approach provides a diagnostic benefit. Methodologically, a total of 194 data set pairs of said dual-time PET/CTs were re-examined under the control of an experienced nuclear medicine specialist. The findings of the first image were compared with the findings of the review of both images. Cohen's kappa was used to calculate the randomly adjusted agreement between the two types of examination. The endpoint was the comparison of sensitivity and specificity of the simple versus the biphasic examinations. If available, histological confirmation was used as the gold standard; otherwise, if possible, the patient's history over the following 2-5 years using clinical radiological findings was used as the reference standard. The direct comparison of the pairs of findings showed clear differences between the two groups: Almost half of all DOTATOC cases and about one third of all PSMA examinations showed a change in findings due to the second admission, of which 45.5% (NET) and 66.7% (PCa) showed TNM-relevant changes in findings. Among the NET cases, there was a strong, relative clustering of changes in findings in pancreatic and intestinal lesions. This clustering was statistically significant compared to the average of all NET changes. The calculated kappa values of both groups showed only moderate agreement between the pairs of statements, which conversely can be understood as an indication of a relatively large difference in statements. For the PSMA recordings, there was a significant increase in sensitivity and specificity from 81.8% to 95.7% and 66.7% to 100%, respectively. (95%-CI: from 61.5-92.7% to 79.0-99.2% and from 39.1-86.2% to 74.1-100%, respectively). However, due to the lack of sufficient cases with histological or clinical-radiological reference, no statistical significance was found for this. However, for the examinations of NET patients, a statistically significant improvement in sensitivity from 53.3% to 93.3% (95%CI 39 - 67.1% and 82.1 - 97.7%, respectively) and in specificity from 54.6% to 86.4% (95%-CI 34.7 - 73.1% and 66.7 - 95.3%, respectively) could be demonstrated.

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# Resources. Day 2

## 7 Combined Photon-Carbon Ion Radiotherapy Treatment Planning

*Bennan, Amit Ben Antony (2021), Heidelberg University (Germany). Medizinische Fakultät*

Abstract

Carbon ion therapy is a promising treatment modality that is not widely accessible to patients due to limited resources and a high cost of treatment. Therefore, it is necessary to consider mixed modality treatments where carbon ions are utilized in combination with the more widely available and accessible, photon therapy. In contemporary clinical combined treatments, photon fractions and carbon ion fractions are separately optimized and simply accumulated based on the RBE weighted dose. Such a "naive" combination does not fully exploit physical and radiobiological advantages emerging from the interplay of both modalities. Carbon ions excel at delivering high RBE conformal dose to the target volume and avoid delivering dose to distal healthy tissue. Photons, besides generally larger integral dose, have a lower RBE and are desirable to irradiate target subvolumes that are adjacent to healthy tissue or have healthy tissue infiltrated by tumour tissue, due to the greater fractionation potential. This thesis presents a novel method to exploit these differences by simultaneously optimizing photon and carbon ion fluence contributions in order to answer the question: what is the ideal combined photon-carbon ion fluence distribution given a specific fraction allocation between photons and carbon ions? The joint optimization framework allows for the synergistic optimization of photon-carbon ion treatments based on the cumulative biological effect, incorporating both the variable RBE of carbon ions and the fractionation effect within the linear quadratic (LQ) model. As a part of this study, the joint optimization workflow was implemented within the open source treatment planning toolkit matRad. Joint optimization strategies yield individually non-conformal photon and carbon ion dose distributions that cumulatively deliver a homogeneous conformal biological effect distribution in the target volume. Compared to conventional combined treatments, joint optimized treatments exhibit better conformity and better sparing of critical structures through a spatial redistribution of dose between modalities and a non-uniform fractionation schedule within the target volume.

## 8 Effectiveness of Therapeutic Radionuclides in Targeted Treatment

*Vlk, Martin (2022), 43. Days of Radiation Protection, 2022. Books of presentations and posters. Slovakia: Slovenska zdravotnicka univerzita; 851 p; (Czech, English)*

Abstract

In the last decade, preclinical research in the field of targeted radionuclide therapy began to focus on Auger emitters and emitters undergoing one or more cascaded alpha transformations with the simultaneous emission of both beta and gamma radiation - the so-called 'in vivo' generators. ---- In common clinical practice, 131I (T1/2 8.05 days) and 177Lu (T1/2 6.65 days) have been used in targeted therapeutic applications for many years. From February 2021, in the Czech Republic, it is available for the treatment of inoperable or metastasizing, well-differentiated (G1 and G2) gastroenteropancreatic neuroendocrine tumors (GEP-NET), which progress on treatment with somatostatin analogues and in which the excessive presence of somatostatin receptors on the surface of the tumor is confirmed by scintigraphy. --- The clinical efficacy of 177Lu against prostate cancer has also been studied and confirmed. In connection with PSMA and GEP-NETs, the possibilities of using alpha emitters, e.g. 225Ac and 213Bi, were investigated. Actinium-225 (T1/2 10 days, α 5.8 MeV) and its daughter radionuclide 213Bi (T1/2 45 min, a 5.8 MeV (2.1%), β- 1.4 MeV (98%) ) are studied in several clinical studies and preclinical research. ---- Compared to beta emitters,

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# Resources. Day 2

**9**

which are used in therapy for a significantly longer period of time, the mass of emitted a particles is about 7000 times greater than β-particles. At the same time, the energy of a-particles is 10-30 times greater than β-particles: a typically 4-8 MeV and β- approximately 0.2 - 2.25 MeV. The linear energy transfer LET of a-particles is about 100 times greater than that of β-particles. For alpha particles with energies of 4-8 MeV, the LET in the tissue is about 100 keV/micrometer, towards the end of the path in the Bragg maximum it can locally increase to 300 keV/μm. For β-particles with typical energies of hundreds of keV, the LET is only about 0.2 keV/micrometer. However, the effective range of a-particles in the tissue is considerably shorter than that of μ-particles. For a, the range is about 2 - 5 cell diameters, for β - hundreds of cell diameters. Auger emitters are touted as potential competition to beta emitters. Research attention is mainly devoted to the study of 161Tb, which is currently produced at the LVR-15 reactor at the CVR UJV. Assessment of the biological effectiveness of the above-mentioned radionuclides, determination of MTD, blood count and kidney function are, in connection with dosimetry, key parameters for determining the effectiveness and safety of therapy. The aim of the lecture is to show the available preclinical and clinical data from the application of radiopharmaceuticals with the mentioned radionuclides, to try to compare their biological effectiveness and to present possible trends for the future.

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**10**

## Development of a Low-Cost System for Respiratory Monitoring of Patients During Radiotherapy Treatment of Breast Cancer

*Reis, R.G., Oliveira e Silva, L.F., Moreno, C.S., Luz, G.V.S., & Ferreira, T.T. (2022), Proceedings of the 26 Brazilian congress on medical physics; 9 Latin American Congress on medical physics; 177 p; Brazil (Portuguese)*

Abstract

In Brazil, breast cancer is the most common malignancy among women, accounting for approximately 30% of cases. Adjuvant radiotherapy has a significant impact on the treatment of this disease. Studies point to the benefits of using techniques with respiratory control in the treatment of left breast cancer, with a potential reduction of doses of radiation in the lung and heart. This work presents the design development of a low-cost respiratory control system, to perform treatments using the voluntary deep inspiration technique (DIBH). Tests of linearity, constancy, response time, reproducibility, and accuracy, were performed to validate the proposed system. The linearity and accuracy tests showed R2 values of 0.9999 and standard deviation (SD) ±0.5 mm, respectively. In the constancy test, it was found an average value of 199 mm (nominal value of 200 mm) and SD of ±0.5 mm. The reproducibility test showed an average value of 199 (±0.8) mm (nominal value of 200 mm). System response time was less than 1 second. The results indicate that the system sensitivity is adequate, as the device was able to notice changes in the setup of 1.0 (±0.8) mm. The respiratory management system developed was proven promising to be used in radiotherapy of left breast cancer, using the DIBH approach. The technology is in the patenting phase, and further details cannot be included in this work. (author)

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# Resources. Day 2

## 11 Preliminary Study on Radiosensitivity in Human Peripheral Blood Lymphocytes of Breast Cancer Patients Before Radiotherapy

*Pham Ngoc Duy, Tran Thanh Mai (2021), Vietnam Conference on Nuclear Science and Technology VINANST-14 Agenda and Abstracts; 246 p; Viet Nam*


### Abstract

Chromosome aberrations induced by DNA damages in G2 phase of cell cycle is expected to be used to assess the individual radiosensitivity. In this study, human peripheral lymphocyte from 12 healthy donor and 14 breast cancer patients samples were cultured in vitro and irradiated by X-ray with the doses of 0.5; 1.0; 2.0 Gy at 69 hours after the beginning of culture. The cells continued to be treated with 4 mM caffeine, cells harvesting and scoring for the chromatid break frequency in the samples with and without caffeine treatment. IRS value showed that 12/12 healthy control persons and 11/14 patients were in normal range of radiosensitivity, 2/14 patients were in radioresistant and 1/14 patients was in radiosensitivity. The results indicated that this method has potential been applied in assessing individual radiosensitivity, especially for cancer patients before radiotherapy. (author)


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## 12 Cancer and Different Treatment Modalities

*Cyrus, A. Assadi (2023), Republican Scientific and Practical Conference 'Innovative development of science' with the participation of international organizations Proceedings; 303 p; Tajikistan*


### Abstract

Understanding Cancer means knowing it is more than one disease. Although there are many types of Cancer, they all start because of uncontrolled growth of abnormal cells. Normal cells grow, divide and die in an orderly fashion. Because cancer cells continue to grow and divide, they outlive normal cells and form new abnormal cells. Cancer cells develop because of damage to DNA, which directs all activities in each cell. When DNA becomes damage, the body is usually able to repair it. In Cancer cells, however, the damaged DNA is not repaired. People can inherit damaged DNA., which results in approximately 10% of all cancers. More often, though, a person's DNA becomes damaged by exposure to something in the environment or random cellular events. Most cancers originate almost anywhere in the body and usually form as a solid tumor. Other such as Leukemia and Myeloma, are sometimes referred to as liquid tumors. These Cancer cells involve the blood and blood forming organs (bone marrow) and circulate through only tissues, where they grow. The different types of cancer include Carcinoma, Sarcoma, Lymphoma and Leukemia. The place where a Cancer starts is called the primary site. From there it can spread (Metastasis) to other parts of the body. Regardless of where a Cancer may spread, it is always named for the place it began. For instance, breast cancer that spreads to the liver is called metastatic breast cancer, not liver cancer. Different types of cancer can behave very differently. For example, lung cancer and breast cancer are different disease that grow at different rates and responds to different treatments. That is why people with cancer need treatments that's is aimed at their particular type of cancer. (author)