PHYSICS *for* HEALTH *in* EUROPE *workshop*

Towards a European roadmap for using physics tools in the development of diagnostics techniques and new cancer therapies

2-4 February 2010

CERN - Switzerland

Charged particles in therapy and space
Radioisotopes in diagnostics and therapy
Prospects in medical imaging
Novel technologies in radiation therapy

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PHYSICS *for* HEALTH *in* EUROPE

Physics for Health in Europe Workshop

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Table of contents

Radiobiology in therapy and space science

Oral Communications

Early events in the formation of genetic damage by heavy ions – G. TAUCHER-SCHOLZ (GSI) ... 2

The Space Radiation Environment - Constituents, Characteristics, and Models – P. NIEMINEM (ESA) ... 2

A proposal for an experimental facility at CERN for research in hadron-therapy – M. SILARI (CERN) ... 3

The Monte Carlo Code FLUKA in Ion Therapy: Status and Outlook – G. BATTISTONI (INFN Milano) ... 3

Treatment plans in particle therapy – M. KRAEMER (GSI) ... 4

The INFN Treatment Planning System Project – A. ATTILI (INFN) ... 4

Syncrotron Radiation Therapy: a promising alternative to treat brain tumors – Y. PREZADO (ESRF) ... 5

Posters

Solid-state detector and radiobiological response in clinical particle beams: numerical comparison of amorphous track models – S. GREILICH (DKFZ) ... 8

Energy Transfer, DNA Normal Modes of Vibration, Bubbles and DNA Damage – F. TORRENS (U. Valencia) ... 8

The calibrated electroporation for express-diagnostics of latent damages of red blood cells membranes under the action of ionizing radiation – A. CHERNYSH (Inst. General Reanimatology, Moscow) ... 9

Development of carbon therapy set up at LHEP JINR –S. MOVCHAN (JINR) ... 9

Experiments on application of high power microwave radiation to biomedicine using the JINR free electron maser – S. TYUTYUNNIKOV (JINR) ... 10

The Legnaro SPES-BNCT project – P. COLAUTTI (LNL-INFN) ... 10

Accelerator based epithermal neutron source for boron neutron capture therapy – S. TASKAEV (Budker Inst. Nuclear Physics) ... 11

Antiproton Cancer Therapy - Current Status and Future Plans – M. HOLZSCHEITER (MPI) ... 11

BNCT (Boron Neutron Capture Therapy) – M. PREST (U. Insubria & INFN) ... 12

Binary therapy using gold nano-particles to enhance photon deposited dose – F. VAN DEN HEUVEL (U. of Leuven) ... 12

Relative biological effectiveness and inactivation cross section for CHO-K1 cells irradiated by different ions – Z. SZEFLINSKI (U. of Warsaw) ... 13

Analysis of radiobiological mechanisms in cells exposed to light ion irradiation – H. PISAKOVA (AS CR) ... 13

Use of fission neutrons for medical therapy and radiobiological studies – F. WAGNER (FRM II) ... 14

R&D in novel simulation methods – M.G. PIA (INFN Genova) ... 14

Voxel based pathomechanistic models for TCP (tumour control) and NTCP (normal tissue complication) – R. MUELLER (DGMP; AAPM; DEGRO) ... 15

Malignant Induction Probability (MIP) Maps for X-ray and Particle Beams – C. TIMLIN (U. of Oxford) ... 15

Ion Beams for Radiotherapy – O. JÄKEL (Heidelberg Ion Beam Therapy Center) ... 16

^{12}C fragmentation measurements for hadrontherapy @ GANIL – B. BRAUNN (LPC Caen) ... 16

A benchmark of nuclear Monte Carlo models for carbon ion therapy and the FIRST experiment: high precision fragmentation cross-section measurements for hadron therapy and space applications – T. T. BOEHLEN (CERN/KI/SU) ... 17

Status of the Geant4-DNA project – A. IVANCHENKO (CNRS/IN2P3/CENBG) ... 17

The effect of cardiac dose received during radiotherapy of breast cancer on the nanostructure and mechanical properties of bovine pericardium tissue – E. WOODS (U. of Surrey) ... 18

Experimental and theoretical evaluation of the local effect model M. BEUVE (LIRIS/IPNL) ... 18

Application of the Microdosimetric Kinetic Model to evaluate the dose effect relation for head and neck squamous carcinoma cells exposed to high LET ions – D. DABLI (U. Clermont) ... 19

Assessment of the biological quality of a therapeutic proton beam by Monte Carlo simulations and comparison with microdosimetric measurements – M. LATOCHA (AIT GmbH) ... 19

Hadrontherapy: a Geant4 open-source application for proton/ion therapy studies – P. CIRRONE (LNS-INFN) ... 20

ENLIGHT++ "The European Network for Light Ion Therapy" and related projects: PARTNER, ULICE, ENVSION – M. DOSANJH (CERN) ... 20

Radioisotopes in diagnostics and therapy

Oral Communications

Production of innovative radionuclides at ARRONAX and ^{211}At RIT – F. HADDAD (GIP ARRONAX & SUBATECH) ... 22

^{149}Tb radio-immunotherapy - advances of short-range alpha radiation and 4.1 h half-life demonstrated in vitro and in vivo – M. MIEDERER (Universitätsmedizin Mainz) ... 22

Radiation Protection Aspects Related to Lutetium-177 Use in Hospitals – R. HENKELMANN (Isotope Technologies Garching) ... 23

Preclinical studies with non-standard and carrier-free radioisotopes from ISOLDE-CERN – G. BEYER (Isotope Technologies Dresden) ... 23

The Future for ^{99m}Tc and ^{99}Mo in nuclear medicine – D.M. LEWIS (General Electric Healthcare) ... 24

Feasibility study of an accelerator-driven production of ^{99}Mo for ^{99m}Tc generators using a high-power LINAC – L. MACIOCCO (AAA) ... 24

Gallium-68 – a candidate for use in clinical routine – M. HARFENSTELLER (ITG) ... 25

Posters

Bremsstrahlung dosimetry: a valid system to estimate OARs doses in ^{90}Y-Zevalin treatments – C. ARRICHIELLO (INT Fondazione "G. Pascale") ... 28

^{32}P-radioactive implants for low-dose-rate (LDR) brachytherapy of benign stenoses of the urethra and the common bile duct – W. ASSMANN (U. of Munich) ... 28

Positron Range Effects in High Resolution 3D PET Imaging – J. UDIAS (U. Complutense Madrid) ... 29

SWAN: a combined centre for radioisotope production, proton therapy and research in Bern – S. BRACCINI (LHEP Bern) ... 29

Radiopharmaceuticals Production and Research Centre at the University of Warsaw – J. JASTRZEBSKI (U. of Warsaw) ... 30

Many small versus a few big. A note on scale and numbers when physics is helping medicine – J. C CLARK (U. of Edinburgh) ... 30

Production of Radioisotopes for Medical Applications at the SINQ Spallation Neutron Source Using Protons and Fast Neutrons – L. ZANINI (PSI) ... 31

Production of radioisotopes with high specific activity at the high-flux reactor of ILL Grenoble – U. KÖSTER (ILL) ... 31

Production and application of the low energy electron emitter ^{161}Tb for endoradiotherapy as a better alternative to ^{177}Lu – K. ZHERNOSEKOV (PSI) ... 32

Receptor Targeted Lymphoscintigraphy Using Dextran-Mannose Derivatives – D. NICULAE (NIPNE) ... 32

Quantification of internalisation of EGFR-binding Affibody molecules. Methodological aspects – M.T. CHEW (U. of Surrey) ... 33

No Carrier Added radionuclides produced by accelerators for biomedical applications – F. GROPPI (U. Milano & INFN) ... 33

ROMOL-99 – The Rossendorf Fission Mo-99 Process – G. BEYER (Isotope Technologies Dresden) ... 34

Medical Isotopes Production at Multi Megawatt Proton Facilities – H. RAVN ... 34

^{188}Re-Radiolabelled Antibodies For Targeted Radiotherapy – D. NICULAE (NIPNE) ... 35

Targeted Radiotherapy of Cancer using Anti-Epidermal Growth Factor Monoclonal Antibody radiolabelled with ^{177}Lu – D. NICULAE (NIPNE) ... 35

PNPI Medicine Center on the Base of 1000 MeV Proton Cynchrocyclotron and Constructed 80 MeV Cyclotron for I=100 mkA – D. SELIVERSTOV (HEPD-PNPI) ... 36

A versatile automated apparatus to optimize the synthesis of PET radiotracers – L. CRACIUN (NIPNE) ... 36

Multi Ci $^{188}W/^{188}Re$-Generator and New Rhenium-188 Applications – T. NIKULA (Isotope Technologies Munich Ag)..... 37

Efficient production of carrier-free ^{86}Y and its application in nuclear medicine – D. LUKIC (U. Hospital, Geneva)..... 37

^{99}Mo production at FRM II - an essential contribution to a European supply problem – C. MÜLLER (FRM II)..... 38

Prospects in medical imaging

Oral Communications

Challenges towards simultaneous PET-MRI – S. VANDENBERGHE (Ugent)..... 40

Multimodality approach in the study of Tumor Angiogenesis: Magnetic Resonance Imaging (MRI), Synchrotron Radiation based micro-CT (SRμCT), Positron Emission Tomography (PET) and Histological Examination to follow the vessel formation – M. DOMINIETTO (ETH and U. Zurich)..... 40

ClearPEM-Sonic: the combined positron emission mammograph and ultrasound elastography scanner – B. FRISCH (CERN and Technische U. Wien)..... 41

$LaBr_3$ and LYSO monolithic crystals coupled to photosensor arrays for TOF-PET – P. DENDOOVEN (KVI U. of Groningen)..... 41

Optimization of a table-top synchrotron light source for radiological applications – M. GAMBACCINI (U. of Ferrara)..... 42

Clinical and Pre-clinical applications spectral x-ray detectors – A. BUTLER (U. Canterbury)..... 42

The MAGIC-5 lung CAD systems – R. BELLOTTI (U. Bari & INFN)..... 43

Posters

The Atomic Force Microscope images of the nanostructure of red blood cells membrane under the action of ionizing radiation and other physicochemical influence – E. KOZLOVA (Institute of General Reanimatology, Moscow)..... 46

AX-PET: Demonstration of an Axial PET Concept for Brain and Small Animal Imaging – C. JORAM (CERN)..... 46

The biological effectiveness of Intra-Operative RadioTherapy (IORT) beams – L. MANTI (U. Napoli & INFN)..... 47

Region based MRI analysis for the early assessment of the Alzheimer's disease – A. CHINCARINI (INFN Genova)..... 47

Production of monochromatic x-ray beams for medical imaging by using a table-top electron accelerator and parametric x-rays – A. LOBKO (INP Minsk)..... 48

Investigation of an Amorphous Silicon Detector for Ion Radiography – J. ENGELKE (Universitätsklinik Heidelberg)..... 48

Performance Evaluation of SiPM Photodetectors for PET Imaging in the Presence of Magnetic Fields – J. UDIAS (U. Complutense Madrid)..... 49

Real Time Imaging of Stopping Distributions in Biological Targets for Antiprotons – S. SELLNER (MPI)..... 49

Novel thin scintillating crystalline materials for high resolution imaging – P. HORODYSKY (Crytur Ltd, Czech Rep.)..... 50

Performance test of a compact gamma camera for nuclear and medical physics applications – N. GOEL (GSI, Darmstadt)..... 50

High Resolution X-ray Microradiography – J. TOUS (Crytur Ltd, Czech Rep.)..... 51

Gamma spectroscopy of inorganic scintillators and their potential imaging applications – J. MARES (AS CR)..... 51

Improving image quality in positron emission tomography – M. RAFECAS (IFIC Valencia/CSIC)..... 52

Silicon photomultipliers in PET and hadrontherapy applications – G. LLOSA (IFIC (CSIC-UVEG))..... 52

Advances in photodetection and read-out electronics for PET applications – M.G. BISOGNI (U. & INFN Pisa)..... 53

CERIMED : A European and Multidisciplinary Open Campus for Research on Medical Imaging – C. OLIVER (U. AIX – Marseille II)..... 53

Timing performance of a TOF-PET detector system developed at CERN using SiPMs – F. POWOLNY (CERN)..... 54

Position-sensitive detector for animal PET tomography – V. BELYAEV (MEPHI)..... 54

Progress in the domain of physics applications in life science with an invention for substantial reduction of premature cancer deaths: the need for a paradigm change in oncology research – D. CROSETTO (Crosetto Foundation)..... 55

Design and construction of the ClearPET/XPAD small animal PET/CT scanner – C. MOREL (CPPM AMU and CNRS/IN2P3)..... 55

Energy resolution analysis of SiPM-based Gamma locator – V. BELYAEV (MEPHI)..... 56

Dose monitoring in ion therapy by means of prompt radiation – E. TESTA (IPN Lyon)..... 56

Progress in the domain of physics applications in life science with an invention for substantial reduction of premature cancer deaths: the need for a paradigm change in oncology research – D. CROSETTO (Crosetto Foundation) ... 55

Design and construction of the ClearPET/XPAD small animal PET/CT scanner – C. MOREL (CPPM AMU and CNRS/IN2P3) ... 55

Energy resolution analysis of SiPM-based Gamma locator – V. BELYAEV (MEPHI) ... 56

Dose monitoring in ion therapy by means of prompt radiation – E. TESTA (IPN Lyon) ... 56

Progress in the domain of physics applications in life science with the 3D-CBS invention for substantial reduction of premature cancer deaths: an optimized PET for low cost low radiation dose high efficiency cancer screening – D. CROSETTO (Crosetto Foundation) ... 57

Early detection of diseases by detecting small lesions with MRI compatible amplifying PET/TOF or SPECT probes using SiPM photodetectors – F. GARIBALDI (INFN Roma and ISS) ... 57

Medical application of spin-polarized He-3 – S. KARPUK (U. of Mainz) ... 58

Extension and validation of an analytical model for in-vivo PET verification of proton therapy – a phantom and clinical study – F. ATTANASI (U. Pisa & INFN) ... 58

3 gamma medical imaging using liquid xenon and ^{44}Sc radio nuclide – J-P. CUSSONEAU (SUBATECH & IN2P3-CNRS) ... 59

High accuracy detectors for medical applications and synchrotron radiation research – I. TIKHONOV (BINP) ... 59

Polar Pixelization in High Resolution Small Animal PET – J. CABELLO (U. of Valencia/CSIC) ... 60

Imaging a proton beam for eye cancer therapy with LHCb VELO microstrip detectors – G. CASSE (U. of Liverpool) ... 60

Design guidelines for a Compton camera for prompt-gamma imaging during ion beam therapy: a Monte Carlo simulation study – M-H. RICHARD (IPN Lyon) ... 61

Charged Particle Imaging for real-time control during ion therapy – P. HENRIQUET (IPN Lyon) ... 61

Prompt-gamma-ray monitoring during carbon ion therapy: comparison between measurements and Geant4 simulations – F. LE FOULHER (IPN Lyon) ... 62

Sinogram-based time offset correction method for time-of-flight PET – E. CLEMENTEL (U. Ghent – Medisip IBBT) ... 62

Real time monitoring of the Bragg-Peak position in ion therapy by means of single photon detection – M. TESTA (IPN Lyon) ... 63

The future role of CZT detectors in nuclear medicine – D.m. LEWIS (U. of Liverpool) ... 63

Investigations on novel imaging techniques for ion beam therapy – I. RINALDI (DFKZ Heidelberg) ... 64

Novel technologies in radiation therapy

Oral Communications

A study on repainting strategies for treating moving targets with proton pencil beam scanning for the new Gantry 2 at PSI – S. ZENKLUSEN (PSI, ETH Zurich) ... 66

Mitigation of target motion in scanned ion beam therapy – C. BERT (GSI) ... 66

The TOM'5 System for Multibeam Tomotherapy – N. ACHTERBERG (Strahlenklinik-Universitätsklinikum Erlangen) ... 67

Electron cooling application for cancer therapy accelerator facility – V. VOSTRIKOV (BINP, Novosibirsk, Russia) ... 67

A cyclotron-linac complex for carbon ion therapy – A. DEGIOVANNI (TERA) ... 68

A proposal for a low-cost size superconducting multi-use accelerating facility for protons or light ions (LOCMAF) – E. GAZIS (NTUA) ... 68

Posters

A multi-port, high dose rate, fixed field synchrotron based protontherapy installation – F. MÉOT (CEA & IN2P3) ... 70

Innovative Isocentric gantry for the Cancer Therapy by Non Scaling FFAG – D. Trbojevic (Brookhaven National Laboratory) ... 70

Metal microdetectors for measuring and imaging beams of particles – V. PUGATCH (NASU) ... 71

Facility for Hadron Radiotherapy of the Joint Institute for Nuclear Research – G.V. MYTSIN (JINR) ... 71

Phosphenes in Carbon Ion Tumor Therapy – D. SCHARDT (GSI Darmstadt) ... 72

Magnetic measurements for medical accelerators – M. BUZIO (CERN) ... 72

Evaluation of different detectors for homogeneity measurements in scanned ion beams – B. HARTMANN (German Cancer Research Center) ... 73

A plastic scintillating optical fiber dosimeter with photodiode readout – L. PERALTA (LIP) ... 73

A Proton Range Telescope for Quality Assurance in Hadrontherapy – D. WATTS (TERA) ... 74

Performance of a pixelized amorphous silicon detector in medical ion beams – M. MARTIŠÍKOVÁ (DKFZ, Heidelberg) ... 74

Implementation and test of the Dose Delivery system of Centro Nazionale di Adroterapia Oncologica (CNAO) – S. GIORDANENGO (INFN) ... 75

R&D of ion sources and cyclotrons for hadron therapy facilities – S. GAMMINO (INFN-LNS) ... 75

Superconducting Magnet Technologies as basis for Design of Medical Carbon and Proton Synchrotron at Dubna – A. KOVALENKO (JINR) ... 76

Hybrid optical tracking techniques for organ motion estimation – G. BARONI (Politecnico di Milano & CNAO Foundation) ... 76

Ion therapy dosimetry by fiber-coupled thin-film-luminescence detectors – F. KLEIN (German Cancer Research Center) ... 77

Beam Angle Optimisation in Particle Therapy – S. SPEER (Strahlenklinik Erlangen) ... 77

Gantry 2 - the next generation of a proton scanning gantry at PSI – D. MEER (PSI) ... 78

Open issues and need of experimental data for proton therapy applications – M.G. PIA (INFN Genova) ... 78

New projects of cyclotrons C235 and C400 for proton and ion therapy – E. SYRESIN (JINR) ... 79

Formation of primary radioactive carbon ion beams applied for cancer treatment and PET – E. SYRESIN (JINR) ... 79

Progress and perspectives of INR radiological center in Troitsk – S. AKULINICHEV (INR of RAS) ... 80

A Gantry-less Delivery of Radiation Therapy – D. DIMITROYANNIS (Kansas City Cancer Center, USOncology) ... 80

Design and performance of an ionization chamber monitor for IBA proton treatment lines – M. LABALME (LPC Caen) ... 81

New equipment and new technology for the mass treatment of the oncological diseases by the proton beam – V. BALAKIN (Protom) ... 81

Range validation for electrons, protons and alpha particles in Geant4 – C. ZACHARATOU (Niels Bohr Institute) ... 82

The Port Homogeneity Index: a density based index for the selection of optimal beam configurations for robust heavy ion radiotherapy planning – F. AMMAZZALORSO (U. Hospital Giessen and Marburg) ... 82

MedAustron – Austrian Hadron Therapy Centre – A. FABICH (EBG MedAustron) ... 83

Gantry Work Package of PARTNER and ULICE Projects – M.M. NECCHI (CNAO) ... 83

Special Magnets for medical accelerators – J. BORBURGH (CERN) ... 84

Future Information Sharing In Hadron Therapy – D. ABLER (CERN – U. Oxford) ... 84

Simulating the beam polarisation for Microbeam Radiation Therapy (MRT) using the Geant4 toolkit – J. SPIGA (U. Cagliari & INFN) ... 85

Radiobiology in therapy and space science

Oral Communications

Early events in the formation of genetic damage by heavy ions

Abstract ID: 58

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Double-strand breaks (DBSs) are critical lesions and their spatial distribution is crucial regarding repair capability and biological effects. Ion irradiation leads to streaks of spatially localized damaged chromatin domains across cell nuclei revealed by repair protein immunostaining. Efficient repair after carbon ion irradiation is indicated by loss of the DSB marker H2AX, but repair is less pronounced with increasing ionizing density. Repair impairment after exposure to stopping carbon ions is the basis of the enhanced biological efficiency of heavy ion therapy.

To study the effect of localized dose deposition on the early damage response, the recruitment of GFP-tagged repair proteins to ion-induced DSBs was monitored by live cell microscopy at the beam end. Recruitment times from seconds up to minutes were observed depending on the protein. The motional activity of DSBs was also analyzed in living cells up to 12 hours post irradiation. Superimposed to the fast Brownian motion, a slow mobility of damaged domains (mean square displacement about 0.6 $\mu m^2/h$), most likely driven by normal chromatin diffusion, was observed independent of the radiation type. A (transient) formation of repair clusters could occasionally be observed, but long range displacements of DSBs did not generally occur. In conclusion, damaged chromatin shows a restricted mobility independent of lesion density and irradiation, supporting the notion that the spatial proximity of DNA breaks is required for the formation of radiation-induced chromosomal exchanges. Importantly, the processing of ion-induced DSBs is not coupled to an increased mobility enhancing the probability of translocations or cancer risk. These results offer important clues toward understanding the repair of multiple damage sites.

The Space Radiation Environment - Constituents, Characteristics, and Models

Abstract ID: 39

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The space radiation environment is a highly variable and dynamic one, with a number of constituent particle sources that need to be individually considered depending on the type of space mission planned. The Galactic Cosmic Rays form a slowly varying higher-energy background over the 11-year solar cycle, on top of which the sporadic, lower-energy, but essentially unpredictable Solar Particle Events with their proton emissions feature especially during the Solar Maximum periods.

In the case of operations in Earth orbit, or for transits from the Earth to deep space, a degree of protection from these external charged particle sources is offered by the Earth's magnetic field, but on the other hand the Earth's trapped electron and proton radiation belts need to be considered. For large-scale space structures, such as the International Space Station or possible future Exploration missions, or for eventual lunar or planetary surface operations, the secondary particle background from Cosmic Ray fragmentation and neutron production is significant enough for it be taken into account in mission design as well as in operational planning.

This presentation gives a summary overview of these various space radiation environment sources, together with a brief description of the different models available for their prediction. Some current ESA projects, observational activities and experimental results in this domain are also outlined.

A proposal for an experimental facility at CERN for research in hadron-therapy

Abstract ID: 42

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The feasibility is presented of setting-up an experimental facility at CERN, to be made available to European institutes, for research in radiobiology and dosimetry with light-ion beams, with minimum impact on CERN main activities. The possibility is first discussed of injecting and decelerating protons rather than antiprotons in the AD, providing beams with kinetic energies in the range 5–300 MeV. Proton beams were never decelerated in the AD in this energy range and this will require machine studies.

The acceleration and extraction of 12C6+ ions is also in principle possible, but it will need a detailed study. A study of the production of carbon ions requiring a new ion source or development work on the present source is needed. A study will then be needed on the accelerator chain, Linac3, LEIR, PS and AD, to accelerate the carbon beam to the required energy range. Other possibilities involve providing carbon ions from LEIR or from the PS to an experimental facility in the East Area.

A CERN involvement with hadron-therapy could be based on a three-stage scenario, short, medium and long term: 1) in a first phase (3 years) provide 100–300 MeV protons from the AD, offering beam time for the experiments in the range one to two months per year; 2) at the same time, carry out a detailed feasibility study for providing 100–400 MeV/u 12C6+ beams from either the PS or the AD, from the fourth year onwards; 3) assess the feasibility to set-up a dedicated experimental facility served by the AD – once the antiproton program has been terminated – to provide light ion beams (alpha particles to carbon or oxygen) from a few MeV/u to about 400 MeV/u.

The intent of this talk is to stimulate discussion on the potential interest of setting up a European collaboration to fund the project.

The Monte Carlo Code FLUKA in Ion Therapy: Status and Outlook

Abstract ID: 56

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Biological calculations in tumour therapy with ions depend on a precise description of the radiation field. In carbon ion irradiation, nuclear reactions cause a significant alteration of the radiation field. Therefore, the contribution of secondary fragments needs to be taken into account for accurate planning of the physical and biological dose delivery in the scheduled treatment.

Treatment Planning Systems (TPS) for ion beam therapy essentially use analytical algorithms with input databases for the description of the ion interaction with matter. On the other hand, Monte Carlo (MC) codes with sophisticated nuclear models are more efficient (though slower) computational tools for handling the mixed radiation field. Therefore, MC codes can be very valuable tools to support ion therapy TPS.

This contribution will address the application of the FLUKA MC code to ion beam therapy. Specific developments will be summarized. Comparisons with available experimental data and an overview of applications performed at several institutions (HIT, INFN, MGH etc.) will be given. These include calculations of physical and biological dose deposition in water as well as in tissue in comparison to analytical TPS, applications to Positron-Emission-Tomography, production of databases for new TPS and characterization of therapeutic beams. The results support the reliability of the FLUKA code for manifold treatment-planning related activities in ion therapy. However it is necessary to extend the collection of nucleus-nucleus cross-section data to better validate and eventually improve the models for specific and quite sensitive applications, like PET imaging, but also to provide a better description of mixed radiation fields for radiobiological calculations.

Treatment plans in particle therapy

Abstract ID: 55

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A major issue of modern radiotherapy is the delivery of sufficiently high dose to the target, whereas the exposure of healthy tissue should be minimized. Swift light ions offer significant physical and radiobiological advantages compared to photon radiation.

So far the technologically most advanced project to apply charged particles in radiotherapy was the GSI pilot project, now followed by the dedicated HIT facility. Ion beam radiotherapy requires sophisticated and efficient dose calculation and optimization procedures to obtain acceptable treatment plans.

These aspects are integrated within our treatment planning system (TPS) TRiP98, clinically used in the pilot project, and further used as a research prototype. Since ab-initio calculations of radiobiological effects

are neither reliable nor computationally feasible for years to come, we use the versatile Local Effect model (LEM) for the planning of all irradiations. Suitable approximations allow reasonably fast calculations of RBE-weighted dose even in complex configurations.

Recent improvements for low-LET radiation, such as protons, will allow to compare plans with different ion-beam modalities under realistic conditions. Optimization of biological dose distributions is an important aspect of treatment planning. Simultaneous optimization of multiple fields under constraints results in enhanced target conformation and sparing of organs at risk.

Future developments aim at "adaptive" treatment planning, i.e. dose painting and irradiation of hypoxic tumours. Considerable experimental efforts are necessary to validate the biological dose distributions predicted by the TPS. Unique devices like the Bio-phantom developed at GSI provide the means to measure one- and two-dimensional distributions of cell survival.

The INFN Treatment Planning System Project

Abstract ID: 59

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Several technologies developed by the Italian institute of nuclear physics (INFN) for fundamental physics have been applied to medical imaging and particle therapy techniques. The partnership with leading industries has always been crucial for successful applications. Within this framework is the implementation of a Treatment Planning System (TPS) for hadrontherapy with C-ion beams, but not exclusively, in partnership with the IBA Group, with the contribution of the TPS manufacturer Elekta.

Several INFN research groups that have developed competencies in different scientific areas are cooperating to the task: experimental and phenomenological nuclear physics, Monte Carlo (MC) and techniques for numerical analysis, radiobiology and hardware development for monitoring purposes.

A TPS prototype is currently being studied. In order to achieve a fast plan optimization, the dose distribution is computed using look-up tables obtained from MC simulations. These are performed using Fluka and an implementation of the Local Effect Model (developed by the GSI Biophysics group).

Nuclear fragmentation experiments for C-ion are now performed at the INFN's Laboratori Nazionali del Sud (LNS) (30-80 MeV/n). Further experiments are scheduled at SIS (GSI) in the framework of the FIRST experiment (200-400 MeV/n), in collaboration with other European Institutes (GSI, ESA, CEA). Radiobiological experiments are underway at LNS and Laboratori Nazionali di Legnaro, on rodent and human cells (C-ion @ 8-80 MeV/n). Lighter ions (A=6-12) will also be used, to reproduce the effects of fragments (up to 20 MeV/u).

These experiments will provide reliable data for the validation of the simulations and for further improvements of the physical and radiobiological models to be used in the TPS.

Syncrotron Radiation Therapy: a promising alternative to treat brain tumors

Abstract ID: 12

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Synchrotron radiation (SR) therapy is a promising alternative to treat brain tumors, whose management is limited due to the high morbidity of the surrouding healthy tissues. Several approaches are being explored by using SR. The European Synchrotron Radiation Facility (ESRF) in Grenoble (France) has devoted one of its lines to biomedical research, highly focused nowadays to the development of new radiotherapy techniques. At the ESRF three techniques are under development: Stereotactic Synchrotron Radiation Therapy (SSRT), Microbeam Radiation Therapy (MRT) and, more recently, Minibeam Radiation Therapy (MBRT). Those radiation therapy programs are progressing rapidly towards the clinical trials with promising results for the treatment of high grade brain tumors.

The preclinical studies on SSRT and MRT have shown promising results on healthy tissue sparing capability and ablation of highly agressive tumor models, paving the way to clinical trials currently in preparation at the ESRF. With this aim, different dosimetric aspects from both theoretical and experimental points of view have been assessed in SSRT and MRT. In particular, the definition of safe irradiation protocols, the beam energy providing the best balance between tumor treatment and healthy tissue sparing in MRT and MBRT, the special dosimetric considerations for small field dosimetry, etc will be described. In addition, for the clinical trials, the definition of appropiate dosimetry protocols for patients according to the well established European Medical Physics recommendations will be discussed.

Finally, the state of art of MBRT developments at the ESRF will be presented. MBRT is the most recently radiotherapy technique implemented at the ESRF.

Radiobiology in therapy and space science

Posters

Solid-state detector and radiobiological response in clinical particle beams: numerical comparison of amorphous track models

Abstract ID: 2

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Amorphous track models (ATMs), also called 'track structure models', are used to predict the response of radiobiological systems (e.g. cell survival) in beams of heavy charged particles (HCPs) such as protons and ions. Currently, the best known ATMs are the Ion-Gamma-Kill (IGK) approach developed by R. Katz and co-workers and the Local Effect Model (LEM) by Scholz and Kraft. The latter is applied in radiotherapy for biological dose optimization in carbon ion treatment planning. ATMs also had reasonable success in modelling the behaviour of solid state radiation detectors under HCP radiation.

The wide-spread applicability of ATMs, however, is seriously hampered by numerous subtle assumptions, submodels and the lack of published, verifiable computational procedures. We are therefore developing a generic, open-source and publically available ATM code library (http://libamtrack.dkfz.org) that is supposed to faciliate the application and numerical comparability of ATMs as well as serve as a frame-work for the implementation of new models.

Here, we present the library project, its current status and implementation and examples of its application

Energy Transfer, DNA Normal Modes of Vibration, Bubbles and DNA Damage

Abstract ID: 3

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Neutron diffraction experiments on a deoxyribonucleic acid (DNA) film show the DNA normal modes of vibration (NMVs). They show that before DNA undergoes a first-order phase transition it nucleates in bubbles, and among these there are closed spaces whose size is characterized by NMVs, which was corroborated by differential scanning nanocalorimetry (DSNC) with which DNA hairpin–drug complexes are analyzed. The DNA molecule is an ordered, well-structured geometrical chain of atoms describing a charged polymer.

Biomolecules are fashion-moving objects: biological function is a consequence of movement, but keeping in mind that macro is the result/consequence of micro. In the DNA bubbles NMV the base pairs are opened and closed in an orderly way. The genetic transcription mechanism is affected by charged amino acids, Ca2+ and polymerase. The bubbles are nucleated by the effect of temperature T in a localized manner. Some bubbles can grow at the expense of some others and then DNA is denaturalized. What happens beyond affects what one is observing. The time between pulses is long enough in order that excitations do not become exhausted and form biphotonic excitations, which favour the oxidation of guanine (G) forming a polaron G+·, which evolution depends on the accessibility of the base and on the dissolvent, and can be measured and analyzed vs. time. This evolution is sensitive to digestion by 7,8-dihydro-8-oxo-2′-deoxyguanosine, which can be analyzed by gel and visualized with formamidopyrimidine-DNA glycosylase.

The objective is to design useful artificial sequences: –GCG-box–Probe A–Buffer region–Probe B–TATA-box–GCG-box– (C=cytosine, T=thymine, A=adenine). There is evidence of an intermediate induced state.

The calibrated electroporation for express-diagnostics of latent damages of red blood cells membranes under the action of ionizing radiation

Abstract ID: 6

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The effects of chemicals and ionizing radiation on the erythrocyte membrane are typically characterized by latent damages. The purpose of our investigation is to register the damages of erythrocyte membranes immediately after the action of ionizing radiation and different physical-chemical factors.

The method is based on electroporation of erythrocyte membranes in vitro by the calibrated pulse electric field with strength 1100 V/cm at once after the external factors action. The additional membrane defects due to external factors action will be the additional active centers of electroporation and the hemolysis rate will be increased. There was studied the ionizing radiation impact: accelerated electrons, gamma-radiation, accelerated charged heavy particles bor-ions.

Results: The kinetic of electric breakdown is alternated under the action of ionizing radiation. The degree of additional defects depends nonlinearly on their dose. It was numerically estimated the reduction or increase of radiation action on red blood cell membrane by farmchemicals.

The method of calibrated electroporation can be useful for pre-clinic testing of ionizing radiation and farm chemicals influence on erytrhocytes. Also this method can be used for the diagnostics of the state of the erythrocyte membranes during radiation therapy, during the work on accelerators and at the places with the raised radiation level. It may be useful for diagnostics of biological effect under low dose radiation.

Development of carbon therapy set up at LHEP JINR

Abstract ID: 10

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The goal of project is design of set up for carbon therapy based on “Nuclotron-M” carbon beam at LHEP JINR. The first stage includes design, test and choose base line option. The main issues are beam focusing system to produce beam size about FWHM=(4-6) mm, beam energy scan system in the range (85-430) MeV, beam X-Y scanning system for sensitive area 20x20 cm2, beam position monitors with resolution 0.5 mm and energy resolution about 10%, control and DAQ systems.

Precise dose distribution inside cancer will be done due to using patient beam X-Y scanning system and well beam energy control. X-Y scanning system based on precision magnet current shape control. Traditional ionization and proportional cambers will be used. Beam energy can be change by 2 ways: by filters and by control of accelerator magnetic field value. dE/dx will be measured by silicon detector or like LHC beam monitors based on thin scintillator. X-Y scanning system and beam monitors must be mount on the same mechanical platform.

DAQ and control system will be design, test and used for planning and measurement dose distribution during cancer expose by carbon ions.

The first experiments carried out in JINR have shown perspectivity of biophysical researches of processes on destruction of cancer cells with use nanosecond pulses of electromagnetic radiation of the high power.

Ion therapy with electromagnetic radiation of the high power is proposed to used for cancer efficiency study.

Experiments on application of high power microwave radiation to biomedicine using the JINR free electron maser

Abstract ID: 11

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High pulsed power microwave radiation gives new possibilities in the biomedicine, particularly to cancer cell damage study. Cooperative influence of microwaves and conducting micro- or nanoparticles provides local and selective action of microwaves on cancer cells. First results of JINR successful experiment are reported on cancer cells killing with the help of high power microwaves propagating through the thin gold layer.

The microwave source was the JINR free electron maser with the power of 20 MW and frequency of 30 GHz. The microwave fluence was about 1 J/cm2 during cell irradiation, number of pulses was 300 -1000. In the culture medium there are the cancer cells located on an object glass near the golden layer. The cell disruption was observed through 30-60 minutes after irradiation. The cells leaved the glass in the form of large conglomerates. Through 12 hours there were no irradiated cancer cells on the object glass.

The preliminary study of processes leading to cancer cell damages was performed to estimate the perspective of such technique.

The Legnaro SPES-BNCT project

Abstract ID: 14

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BNCT (Boron Neutron Capture Therapy) is a binary radiation therapy. First, a boronated substance is injected in the patient body, then the patient is irradiated with thermal or epithermal neutrons. Only those cells containing 10B will be damaged by 11B nuclear fragments, while the healthy surrounding ones remaining undamaged. Such a peculiar behaviour of energy releasing allows of conceiving a cellular radiation therapy.

The last 200 cases, reported in the international conference held in Florence on November 2008, have pointed out BNCT is a successful therapy for: head-neck recurrent tumours, recurrent glioblastoma tumours, malignant melanoma (MM) of skin and mucosas. MM has increased its morbidity exponentially during the past twenty years: 750 new patients per year only in the Veneto region (5,000 cases per year in Italy). The traditional radiotherapy is ineffective. On the contrary, high-LET tumour-targeted radiations have shown to be highly effective.

Legnaro laboratories, in collaboration with the Physics and Biological Departments of the University of Padova and with the Venetian Oncology Institute, have launched the SPES-BNCT project on the 1999. The project provides the platform of a multidisciplinary research on BNCT from medical, radiobiological, detector physics, radiation physics and accelerator technology prospective.

The project aims are: i) to construct a neutron source based on a RFQ proton accelerator (30 mA, 5 MeV); ii) to synthesize new boron carriers with high 10B tumour/tissue uptake ratio, which have also photo-dynamic therapeutic efficacy (PDT); iii) to construct new mini tissue-equivalent gas-proportional counters to properly measure the radiation field quality; iv) IT studies to implement microdosimetric data in new dedicated treatment planning.

Accelerator based epithermal neutron source for boron neutron capture therapy

Abstract ID: 19

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Presently, boron neutron capture therapy is considered to be a promising method for selective treatment of malignant tumors. The results of clinical tests with nuclear reactors showed the possibility of treating brain glioblastoma and metastasizing melanoma not subject to treatment by other methods. The broad implementation of the BNCT in clinics requires compact inexpensive sources of epithermal neutrons. A low-energy accelerator has the potential for meeting the requirements. It is world-recognized that the best reaction is the 7Li(p,n)7Be reaction. This report describes the "best" epithermal neutron source created.

The novel tandem-accelerator with vacuum insulation is used to produce a 2 MeV proton beam with the current up to 10 mA. While the 7Li(p,n) reaction is excellent from the neutronics point of view, the mechanical, chemical, and thermal properties of lithium metal prevented it from being a candidate for a target. By now all problems of a lithium target have been solved, namely i) the effective cooling was implemented to keep lithium layer solid in order to preclude the propagation of Be radioactive isotope, ii) the controlled evaporation of a thin lithium layer was used to reduce the accompanying gamma radiation, iii) substrate materials as resistant to blistering as possible were found.

Thus, a pilot accelerator-based source of epithermal neutrons, which is specially designed for a wide use in oncology clinics for BNCT, has begun to operate successfully in the neutron generation mode. The facility is ready to measure neutron spectra and can be used for in vitro and in vivo investigations. We believe there is no technical reason that a machine capable of generating the current needed to deliver therapy in reasonable times could not be built.

Antiproton Cancer Therapy - Current Status and Future Plans

Abstract ID: 24

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The ultimate goal of radiotherapy is to maximize the dose to the tumor while minimizing the effect on surrounding healthy tissue. Heavy charged particle show a clear physical advantage over x-rays due to the inverse depth dose profile where the maximum of energy is deposited at the Bragg peak. Additional therapeutic advantages are expected compared to protons when using heavier particles through enhancements of the relative biological efficiency (RBE) of densely ionizing particles.

In 1985 it was proposed by Kalogeropoulos et al. to use antiprotons. Due to the annihilation at the end of range the physical dose deposited in the Bragg peak is enhanced by a factor of two. Additionally it is expected that the RBE is enhanced as part of the additional energy deposited locally comes from ion recoils and nuclear fragments.

Since 2003 the AD-4 collaboration at CERN has been studying the biological effect of antiprotons on V-79 Chinese Hamster cells. We have collected clonogenic survival data and initial analyses show enhanced biological effects tightly confined to the Bragg peak area. Based on these results we have performed comparative dose planning studies between protons, carbon ions, and antiprotons. Dose volume histograms can be used to analyze different scenarios. Additional activities of the collaboration include studies on real time imaging of the dose distribution and R&D on liquid ionization chambers and there use as LET measuring device.

In this talk we will present an overview of the experiment, the current status of the measurements, and describe plans for future studies.

BNCT (Boron Neutron Capture Therapy)

Abstract ID: 44

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BNCT (Boron Neutron Capture Therapy) has been proposed as a promising form of therapy in 1936. It is a binary technique consisting in the administration of a 10B compound to the patient who is then irradiated with a thermal (<10keV) neutron beam: the 10B(n,alpha)7Li capture reaction produces high LET charged particles which stop in the cell with the boron causing its apoptosis. BNCT would combine the targeting principles of chemotherapy and the localization capability of radiotherapy, and could be fundamental for those types of tumours that have not witnessed an improvement of the survival curve in the last 20 years: extended tumours (stomach, liver, lung), tumours located near or in vital organs (brain), radioresistant tumours (melanoma).

BNCT is presently limited by the need of a high neutron flux available only at nuclear reactors and by the lack of specificity of the boron carriers; it is performed in USA, Japan, Argentina, Sweden, Finland, the Netherlands, with phase 1 (toxicity) and phase 2 (efficacy) trials.

The INFN PhoNeS (PhotoNeutron Source) project is addressing both the BNCT limits. The collaboration has developed a converter+moderator system to be installed in front of the head of a standard radiotherapic linac for the production of a thermal neutron beam which has been characterized in terms of intensity and energy spectrum, and is now using this beam for studies of the boron content in biological samples (urine, blood, tissue) to obtain kinetic curves (boron content as a function of the time from the patient uptake). The paper will describe the project status, and the use of the beam and the imaging systems for the study of the boron concentration in explanted lungs affected by mesothelioma in view of a possible application of BNCT.

Binary therapy using gold nano-particles to enhance photon deposited dose

Abstract ID: 60

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Recently, methodologies using monoclonal antibodies that target specific tumor cells have been used to bring active compounds in the vicinity of these cells. One approach uses radioactive compounds of alpha or beta–emitters. Alternatively, chemotherapeutic compounds have been attached to this delivery mechanism. The use of such approaches is interesting but limited due to the fact that the therapeutic compound is already active at time of delivery and during secretion by the body. More in particular with radioactive compounds an important whole body dose (red marrow dose) as well as renal toxicity are limiting factors for the efficacy of the treatment. It is the goal of this paper to investigate a delivery method that could potentially have most of the benefits associated with the previously listed therapeutic modalities ´and has almost none of the disadvantages. Which means:

(i) Differentiation between malignant and healthy cells.

(ii) Enhanced effectiveness.

(iii) Image guidance possibilities.

(iv) Activation methodology (i.e. Only active were it needs to be active).

(v) Large therapeutic window.

Dose enhancement due to the presence of gold nano–particles has been proposed already both by means of an injectable contrast agent as by the use of mono–clonal antibodies or other targeted delivery methods. In this presentation we will investigate the radiobiological ramifications of using nano-particle (NP) enhanced radiation treatment, taking into account contributions from Auger electrons and using a monte carlo based dose deposition code (Geant and MCNPX) combined with cell response code (MCDS) to yield single and double strand break densities. The endpoint of this investigation is to determine the optimal energy of the photon beam interacting with the NPs.

Relative biological effectiveness and inactivation cross section for CHO-K1 cells irradiated by different ions

Abstract ID: 73

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In this study the LET-dependence of cell survival for CHO-K1 cells irradiated by carbon and neon ions beams with various LET values were examined and compared to the data of other groups. The results for inactivation of CHO-K1 cells irradiated by 12C, 20Ne, 40Ar, 56Fe ions were collected and analyzed. These data show that relative biological effectiveness (RBE) as the function of linear energy transfer (LET) curve has two components:

•strongly depended on type of ion and track structure (LET<800 keV/micrometer)

•and without these dependences (LET> 800 keV/micrometer).

The inactivation cross section (sigma) as the function of LET and (Z/beta)*2 show lack of ions dependence suggesting that track structure is less important in the biological effectiveness of ions. The data were collected and analyzed in order to extend the comparison of biological effectiveness to ions with different atomic numbers.

Analysis of radiobiological mechanisms in cells exposed to light ion irradiation

Abstract ID: 75

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The final response of cells to ionizing radiation depends on the physical parameters of radiation (energy, type of ions) as well as on biological characteristics of the cells (cell line, repair capacities). Whether the cell dies or survives is an outcome of complex interplay between various inlay physical, chemical and biological processes.

To analyze various data sets, the Probabilistic two-stage model (Kundrát P: Detailed analysis of the cell-inactivation mechanism by accelerated protons and light ions. Physics in Medicine and Biology, 51, (2006)) has been used. In this model, the "first stage" involves physical and chemical phase of the radiobiological mechanism, i.e. energy deposition to the cell, and the "second stage" is characterized by the response of the irradiated cell to damage caused by radiation, i.e. biological phase.

The probabilistic two-stage model enables to recognize two types of DNA lesions caused by ionizing particles: lethal damage created by a single track and less severe lesions, where only a combination of at least two events may be lethal. The model also takes into account the result of cellular repair processes.

The analysis of several survival curves of cells irradiated by various ions will be presented.

Use of fission neutrons for medical therapy and radiobiological studies

Abstract ID: 84

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Biological and clinical use of fission neutrons is motivated by the high linear energy transfer (LET) of up to 100 keV/µm. The high LET leads to cellular effects different from photons of the same energy, e.g., a lower oxygen enhancement ratio, OER, compared to photons. Neutrons in the respective energy range of 2 MeV display a steep depth dose curve so that only tumours with close contact to the body surface can be treated. Suitable types of tumours are mainly "radio-resistant" adenoid cystic carcinoma of the salivary glands, lymph node or skin metastases from various cancer diseases, and chest wall metastases of breast cancer. Examples of the radiation effects will be shown.

At the fission neutron facility of the former reactor FRM, many biological studies were undertaken to assess RBE, OER, fractionation and other effects on cells and animals. 715 patients were irradiated until 2000, the majority with palliative intent. The irradiation facility MEDAPP at the new FRM II displays a comparable beam quality. Since 2007, 90 patients have received 425 irradiations. Biological research is continued, e.g., by use of newer systems like epithelial megacolonies generated from a human squamous tumour carcinoma line (J. Kummermehr et al., LMU).

Fast reactor neutrons can also be employed to study effects of, e.g., space radiation. The secondary radiation in a space-capsule gives rise to an important environmental hazard during long-term space exploration beyond the magnetic shield of the earth (C. Baumstark-Khan, C. Hellweg, DLR). The potential risk has to be quantified in ground-based experiments.

R&D in novel simulation methods

Abstract ID: 88

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Monte Carlo simulation plays a valuable role in support of bio-medical research in various domains, such as radiotherapy, medical imaging, radiation protection and radiobiology.

New experimental requirements have emerged in the recent years, which challenge general-purpose Monte Carlo transport codes in domains like nanodosimetry, nanotechnology-based detectors, radiation effects on components, plasma physics etc. They concern the capability of addressing complex multi-scale problems, which encompass both macroscopic aspects (e.g. conventional dosimetry) and the investigation of nano-scale phenomena (e.g. the biological effects of radiation).

While Monte Carlo simulation tools are currently available and have been widely used to address either scale of the problem, several open issues at the conceptual level of particle transport in matter still hinder a seamless approach to the simulation of multi-scale problems.

A R&D project has been launched in 2009 at INFN to address fundamental methods in radiation transport simulation specific to these new experimental requirements. It focuses on simulation at different scales in the same experimental environment: this set of problems requires new methods across the current boundaries of condensed-random-walk and discrete transport schemes. The project gathers an international, multi-disciplinary team.

An overview of this new R&D project is presented, together with the developments in progress and the first achievements. A wide discussion with the bio-medical community would be especially valuable to identify requirements and open issues

Voxel based pathomechanistic models for TCP (tumour control) and NTCP (normal tissue complication)

Abstract ID: 102

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Treatment planning for high LET radiation needs locally weighted RBE correction. But after getting Cobalt-equivalent-dose distributions, there is additional need for TCP and NTCP optimisation. It's the same problem as for usual kind of X-ray treatment planning. Conventional measure of NTCP is based on a phenomenological approach after Lyman and Kutcher, which takes an integrated parameterised Gaussian as effect probability - depending on dose and partial volume of specific organs. Beyond that the model is global, not able to use local or voxel based information. For TCP doesn't exist a similar model.

We have developed a TCP model on basis of total number of "clonogenic tumour stem cells" TSC and their local volume density [1/cm^3]. If there exists any measuring system identifying TSC-density this model will be helpful for dose painting. Mathematical basis for this model is Poisson's statistic. Radiobiological parameters can be drawn by the a and b values of the specific tumour entity. This generally voxel based model fits well to the scarce clinical data available.

Extending this model for the calculation of NTCP we use Poisson's statistic as well, but the parameter changed form TSC to minimal functional subunit (mindamv). As mentioned some years ago (e.g. by Brahme) critical organs may be modelled as parallel or serial in relation to the architecture of the organs - or anything combining both e.g. spinal cord -. With only one additional parameter, which may be called functional reserve (fures), all clinical date can be adopted and the phenomenological data by e.g. Burman can easily be fitted. The advantage: it's generally voxel based and may be adopted by a Voxel-TPS.

Malignant Induction Probability (MIP) Maps for X-ray and Particle Beams

Abstract ID: 103

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The risk of inducing secondary malignancies during radiotherapy must be considered when deciding upon appropriate cancer treatment. A new model based on Poisson statistics and the linear quadratic model can be used to predict malignant induction, taking into account the balance between malignant cell induction and cell killing caused by two classes of chromosomal damage. The main features of the model are that the peaks in malignant induction probability (MIP) can be shifted to lower dose regions with increase in RBE or by an increase in radio-sensitivity (e.g. leukaemia induction), but are moved to higher doses for lower radio-sensitivities (for tumours such as sarcomas) and with greater fractionation.

The model has been implemented using MATLAB software where physical doses can be displayed as well as MIP maps and also a MIP calculation over the entire volume at risk. Results show that the risk of a secondary malignancy is more than halved for a single field of protons with respect to single field x-rays. However, when using multiple opposed x-ray fields the only region in which malignant induction probability is significant is in the penumbra where as for protons there is also a risk in the low to intermediate dose entrance regions.

The general conclusion from this study is that particle therapy should employ as few beams as possible, with minimal normal tissue traversal, in order to reduce the risk of inducing secondary cancers. Use of rotating gantries would help in this respect. More work is necessary to develop the model further, with use of more complex field arrangements to assess the benefits of using MIP maps as part of the treatment planning process.

Ion Beams for Radiotherapy

Abstract ID: 107

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Carbon ions offer potential advantages for radiotherapy as compared to conventional radiation and protons. Most important is the increased energy loss in the Bragg peak, which gives rise to an enhanced biological effectiveness in the target vs. surrounding tissue. In vitro studies also demonstrated a reduced oxygen effect, which should allow increased efficiency in the treatment of hypoxic tumours. Moreover, heavy ions suffer less from lateral scattering than protons and induce an activation of irradiated tissues, which allows an in vivo monitoring of the applied dose in the patient by using positron emission tomography.

Radiotherapy with heavy ion beams was first investigated by the pioneering work at Berkeley in 1977. Since then, the interest in carbon ion therapy has increased enormously especially in Japan and Europe. There are currently 3 facilities treating patients with carbon ions: two in Japan and the Heidelberg facility (HIT), which started clinical operation in late 2009. Several new clinical facilities are scheduled to start operation within the next few years in Marburg and Kiel (Germany), Pavia (Italy), Gunma (Japan) and several more are in an advanced planning state in Austria, France and China.

HIT features three treatment rooms and a QA-area, all equipped with active beam scanning. One of the treatment rooms is equipped with the first isocentric gantry for ions. Beams of protons, helium, oxygen and carbon ions are offered and will be used to evaluate the clinical potential of high LET radiation as compared to low LET radiation. The implications for medical physics reserach in treatment planning, dosimetry and quality assurance, as well as medical research will be outlined.

^{12}C fragmentation measurements for hadrontherapy @ GANIL

Abstract ID: 108

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Hadrontherapy treatments require a very high precision on the location of the dose in order to keep the benefits of the precise ions' ballistic. The largest uncertainty on physical dose is due to ion fragmentation. Up to now, the simulation codes are not able to reproduce the fragmentation process with the required precision. The constraints on nuclear models and fragmentation cross sections between 30 and 100MeV/u are not sufficient.

To constraint the codes, we have performed an experiment on May 2008 at GANIL with a 95 MeV/u ^{12}C beam. The goals were the measurement of the fluence, energy and angular distributions of the fragments coming from the nuclear reaction between ^{12}C and water-like PMMA targets of different thicknesses : from 0.5 to 4cm. At 95MeV/u, the ^{12}C Bragg Peak depth in PMMA is 2cm.

To detect the charged particles, the experimental set-up included five three stages E/E telescopes with two Si detectors and one CsI scintillator. These telescopes were mounted on rotating arms in order to cover angles from 0° to 60°. The setup also included four DEMON detectors to measure the neutrons at four different angles.

A benchmark of nuclear Monte Carlo models for carbon ion therapy and the FIRST experiment: high precision fragmentation cross-section measurements for hadron therapy and space applications

Abstract ID: 114

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When human tissues are irradiated with ions nuclear physics processes have a notable impact on the resulting spatial dose distribution and its biological effect. Hadron therapy and space radiation research (e.g., for inter-planetary space flights) are two important application areas involving such ion irradiation. It is therefore of interest to acquire a precise knowledge about nuclear interactions and enhance the predictive capabilities of modelling approaches for projectile-target combinations and energies relevant for these applications. Monte Carlo (MC) codes are valuable tools to predict radiation fields of ions in tissues and are employed in hadron therapy and space applications for the simulation of nuclear interactions as they are able complement and bridge shortcomings of frequently used analytic codes. However, inherent nuclear reaction models are currently of a limited precision with room for improvement.

This work reports a benchmark of the current performance of nuclear MC models of FLUKA and GEANT4 with existing data of charge-changing cross-sections and double-differential fragmentation yields for C on water and polycarbonate. To allow for a more extensive and detailed comparison, further data is needed.

The FIRST experiment, presented in the second part of the poster, is a thin-target experiment which plans to enlarge the available measurement data-base by acquiring an extensive set of high precision cross-section measurements differential in energy and angle. Target-projectile combinations include C-C, O-C, Fe-C at an energy range of 0.2-1.0 GeV/n. These data will benefit the hadron therapy and space radiation community and are aimed to improve the accuracy of nuclear reaction models.

Status of the Geant4-DNA project

Abstract ID: 117

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The Geant4-DNA project develops open-source simulation software in the framework of general-purpose Geant4 Monte Carlo simulation toolkit. The main objective of this software is to simulate biological damages induced by ionizing radiation at the cellular and sub-cellular scale.

This project was originally initiated by the European Space Agency for the prediction of deleterious effects of radiation that may affect astronauts during future long duration space exploration missions.

In this poster, the Geant4-DNA collaboration presents an overview of the whole ongoing project, including its most recent developments already available in the new Geant4 public release (9.3, December 2009). Developments of relevant physics models and new Geant4 Physics Lists components are discussed.

The effect of cardiac dose received during radiotherapy of breast cancer on the nano-structure and mechanical properties of bovine pericardium tissue

Abstract ID: 121

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In radiotherapy of breast cancer, especially in treatment of the left breast, the heart is an organ at risk, with all parts susceptible to radiation-induced complications. The aim of this project was to investigate the effect of ionising radiation on the fibrous structure and associated mechanical properties of pericardium tissue, with respect to cardiac dose received during radiotherapy.

Fresh bovine pericardium samples were irradiated with 6MV photons using a linear accelerator to doses ranging from 5Gy to 40Gy. The dimensions of the topographical features of the control and irradiated fibrous pericardium tissue samples were measured using Atomic Force Microscopy (AFM) in imaging mode. The mechanical behaviour of the pericardium tissue was investigated by means of uniaxial tensile testing.

From AFM work, it was found that the ionising radiation caused an increase in the mean diameter of the collagen fibrils. This increase in diameter can be attributed to the induction of cross-links in the collagen fibrils by the radiation, resulting in aggregation of fibrils together. The stress-strain results demonstrated a trend in which the tissue modulus increased and the stress relaxation decreased slightly as the radiation dose increased. This result is consistent with the cross-link induction theory, however the changes were very small and results had poor reproducibility. Thus for the range of clinical doses, this damage was found not to affect the associated mechanical properties in a statistically significant manner, and so should not alter the mechanical functions of the pericardium on the whole.

Experimental and theoretical evaluation of the local effect model

Abstract ID: 126

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The Local Effect Model (LEM) is a track-structure model, which is to be used to plan tumour treatments by hadrontherapy with carbon ions. To this aim, the LEM [1] assumes that cell-killing is induced by the generation of local lethal events. Based on the concept of local dose, the LEM allows one to calculate cell survival to any ionizing radiation simply from the determination of the cell survival to X-ray irradiation and from the size of the cell nucleus.

By comparing the predictions of the LEM to experimental data [2], we observed however that not only measurements for X-ray irradiations but also measurements for a beam of high-LET ions were required to fit LEM parameters. On a theoretical point of view, we pointed out some confusions and a mixing in the use of microscopic and macroscopic quantities [3]. We also showed that any pure local effect theory should only predict a linear behaviour in cell-survival curves. We concluded that the quadratic terms predicted by the LEM are due to artefacts stemming from an improper use of expected quantities (the local dose). Considering stochastic effects and non-local (non-targeted?) effects may help to improve such models.

[1]: M. Scholz et al. "Computation of cell survival in heavy ion beams for therapy the model and its approximation." Radiat. Environ. Biophys., 36:59–66, 1997.

[2]: M. Beuve et al. "Parameters and Local Effect Model predictions for head and neck squamous carcinoma cells exposed to High Linear Energy Transfer ions"; International Journal of Radiation Oncology Biology Physics 71(2):635-642. 2008.

[3]: M. Beuve "Formalization and theoretical analysis of the Local Effect Model" Radiat. Res. 172(3) 394-402 July (2009)

Application of the Microdosimetric Kinetic Model to evaluate the dose effect relation for head and neck squamous carcinoma cells exposed to high LET ions

Abstract ID: 129

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Several models have been proposed to predict the biological effects of high LET particles, based on the microdosimetric concepts and quantities. One of the earliest models was proposed by Kellerer et al. This model provides a mathematical formulation of the "Dual Radiation Action Theory", proposed by LEA to explain the formulation of chromosome abberations in cells irradiated by charged particles. The evolution of knowledge about the radiobiological mechanisms involved in the cell inactivation led to the development of more detailed models.

One of the new microdosimetric models is the "Microdosimetric Kinetic Model" proposed by RW Hawkin. Recently Kase et al have published a comparative study of the MK model and the LEM in the calculation of the biological dose for treatment planning in Hadrontherapy. In their study, an amourphous track structure model was used to calculate the ernergy deposition for both models.

In this work we use the MK model to calculate the survival probabilities of head and neck squamous carcinoma cells (SC61 and SQ20B cells) exposed to high LET ions. Unlike Kase et al, we use the Monte Carlo method to simulate the energy deposition. Then the Geant4 simulation toolkit is used to generate the initail energy distribution in the cells. Previous analyses of the dose-effect relation of SCC61 and SQ20B cells with the Local Effect Model (LEM) and using the stochatic deposition method was reported by Beuve et al.

The first part will be devoted to the anlysis of the geant4 simulation toolkit. The microdosimetric concept of the proximity function is used to perform this anlysis. Finally, the results obhtained with the MK model will be analyzed and the model parameters of the two cell lines will be compared in term of radiosensitivity to high LET ions.

Assessment of the biological quality of a therapeutic proton beam by Monte Carlo simulations and comparison with microdosimetric measurements

Abstract ID: 135

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The knowledge of radiation quality in an irradiated human tissue or organ is essential to understand occurring radiation effects. To evaluate radiation quality, usually two supplementary approaches are taken: measurements and numerical simulations. Microdosimetric measurements allow for assessing energy distribution of the radiation field. This can be then used to obtain the biological effectiveness of a radiation. Numerical simulations provide cost effective prediction of radiation effects for example for space applications, and may also be useful in radiation therapy by supporting developments of treatment planning systems.

Using protons for the treatment of ocular melanoma (especially of posterior pole tumors) the radiation quality of the beam must be precisely assessed to preserve the vision and to minimize the damage to healthy tissue. The physical quality of a therapeutic proton beam at the Centre Antoine Lacassagne in Nice (France) was measured using microdosimetric techniques, i.e. a minituarized version of a Tissue Equivalent Proportional Counter (TEPC). Measurements were performed in a 1 µm site at different depths in a lucite phantom. Experimental data showed a significant increase of the beam quality at the distal edge of the Spread Out Bragg Peak (SOBP). In this paper, the numerical simulation of the experimental set-up is done with the FLUKA Monte Carlo radiation transport code. The calculated microdosimetric spectra are compared with the measured ones at different depths in tissue for a monoenergetic proton beam (E=62 MeV) and for a modulated SOBP. Numerically and experimentally determined RBE values are in good agreement. The calculated frequency-averaged and dose-averaged lineal-energy mean values are consistent with measured data.

Hadrontherapy: a Geant4 open-source application for proton/ion therapy studies

Abstract ID: 140

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As a consequence of the request of new advanced tools to evaluate the dose delivered to the patients in external radiotherapy with protons/ions, it appears of particular importance to develop and validate simulation programs able to facilitate the design of transport beam lines for therapy or/and to perform Treatments Planning (TP) calculations. The TP procedure exhibits additional complications, especially for ion beams, related to the complex nature of ion interactions with the matter.

In this context, and in the framework of an international collaboration between different Institutes, we recently started a research program with a twofold aim.

Firstly, we aim to provide the proton/ion hadrontherapy community with an open-source Monte Carlo-based application, entirely based on the Geant4 toolkit. The application, named Hadrontherapy, is developed and maintained by an international collaboration of medical physicists and researchers. Hadrontherapy can simulate dose, fluence and LET distributions of primary and secondary particles in a phantom and, moreover, it also provides a useful tool for the simulation of typical nuclear physics experiments. The implementation of the Relative Biological Effect (RBE) calculation is also in progress.

On the other side, we have recently started an experimental activity for a better knowledge of carbon ion interaction with materials of interest in hadrontherapy, in order to validate the physical models implemented in the Monte Carlo applications.

In this work the main characteristics and functionalities of the Hadrontherapy Geant4-based program will be presented and an extensive set of comparisons between simulation and experimental data will be reported.

ENLIGHT++ (European Network for Light Ion Therapy) and related projects: PARTNER, ULICE, ENVSION

Abstract ID: 200

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ENLIGHT was established in 2002 to co-ordinate European efforts in hadron therapy and is now composed of more than 300 participants, from 20 countries. A key success of ENLIGHT has been uniting traditionally separate communities so that clinicians, physicists, biologists and engineers with experience and interest in particle therapy work together and has been a successful in forming a common European platform and bringing together people from diverse disciplines and countries.

ENLIGHT demonstrates the advantages of regular and organised exchanges of data, information, best practices as well as determining and following strategies for future needs in research and technological development in hadron therapy. In 2006, the ENLIGHT community agreed the goals of the network could be best met by two complementary aspects: the research in areas needed for effective hadron therapy, and the networking needed for establishing and common standards and protocols for treating patients.

Presently there are now three EC funded projects: PARTNER, ULICE and ENVISION. PARTNER is a Marie-Curie training network of European Institutes, which provides high- level academic and technical training to researchers with the aim to prepare the future generation leaders in the field of hadron therapy. ULICE is a 4 year project to respond to the need for greater access to hadron-therapy facilities for particle therapy research. Both existing facilities in Heidelberg and Milan are amongst the partners and will provide 691 hours of beam-time to external researchers. ENVISION tackles the problems of on-line dose monitoring and quality assurance by developing novel imaging modalities related to dose deposition and allow assessing the treated volume and provide reliable indicators of the delivered dose.

Radioisotopes in diagnostic and therapy

Oral Communications

Production of innovative radionuclides at ARRONAX and ^{211}At RIT

Abstract ID: 29

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ARRONAX, acronym for "Accelerator for Research in Radiochemistry and Oncology at Nantes Atlantique", is a high energy and high intensity cyclotron. It will turn into operation in the beginning of 2010 in Nantes (France). It is mainly devoted to the production of radionuclides for medicine. A priority list based on the capability of the machine as well as on the need expressed by the European medical community through a questionnaire has been set.

It contains isotopes for imaging (^{82}Sr/^{82}Rb and ^{68}Ge/^{68}Ga generators and ^{64}Cu, ^{44}Sc) and for therapeutic use (^{67}Cu, ^{47}Sc and ^{211}At).

Astatine is the heaviest radiohalogen and ^{211}At is one of the most promising α-emitters for medical applications. The half-life of ^{211}At is relatively long compared with that of other radionuclides available for α-RIT ($T_{1/2}$ = 7,2 h).

A large collaboration effort has been done in Nantes for many years both on the production and extraction of 211At and its labelling.

The production will be done in ARRONAX using a 28 MeV alpha beam hitting a bismuth target evaporated under vaccum on AlN support. For recovery of astatine, two methods have been developped : liquid extraction and dry extraction. For labelling, a special attention has been focused on antibodies. Succinimidyl AstatoBenzoate (SAB) is used to bind ^{211}At on the antibody by esterification of lysin residue. In vitro as well as in vivo stability have been tested on a murine model. An overall labelling yield of around 50 % was obtained.

In the near future, ARRONAX will participate in a radioimmunotherapy collaborative project (Alpha-RIT) using ^{211}At coupled to a specific antibody to treat patients with disseminated residual disease of prostate cancer. ARRONAX will have to produce large activities of ^{211}At for phases I and II clinical studies.

^{149}Tb radio-immunotherapy - advances of short-range alpha radiation and 4.1 h half-life demonstrated in vitro and in vivo

Abstract ID: 101

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Radioimmunotherapy (RIT) of disseminated diseases in which individual cells or cell clusters are remaining requires a radionuclide that is capable of sterilizing individual cells with minimal radiotoxicity to surrounding healthy tissue. α particles exhibit high linear energy transfer and very short range in tissue, making them ideal for single-cell killing. ^{149}Tb is a radiolanthanide that emits α particles with only 28 µm range in tissue. Feasibility and potential advantages of ^{149}Tb over other radioisotopes in RIT have been studied in preclinical experiments using different monoclonal antibodies targeting leukemia, lymphoma and gastric cancer.

149Tb was produced at ISOLDE-CERN by on-line mass separation of spallation products released from a Ta target irradiated with 1 GeV protons. The monoclonal antibodies HuM195, Rituximab and d9ECad were conjugated with CHX-A-DTPA and labeled with ^{149}Tb with specific activities of 0.1-1.1 GBq/mg.

In vivo capability of treating disseminated cancer was investigated using a disseminated lymphoma mouse model. 149Tb RIT with 5.5 MBq labeled Rituximab 2 days after an intravenous graft of lymphoma cells resulted in tumor free survival for >120 days in 89% of treated animals. In contrast, all control mice developed lymphoma disease.

There are many unsolved clinical situations in oncology, where emitters are hoped to serve as therapeutic breakthrough to improve survival of cancer patients, e.g. disseminated single cell disease like leukemia, adjuvant treatment for circulating or loco-regionally remaining cells in solid tumors or treatment of minimal residual disease in lymphoma. Our experiments with ^{149}Tb produced at CERN demonstrate this emitter's potential to overcome limitations of other radioisotopes in selected clinical settings.

Radiation Protection Aspects Related to Lutetium-177 Use in Hospitals

Abstract ID: 82

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^{177}Lu is typically produced by direct irradiation with neutrons from enriched ^{176}Lu. During direct irradiation of ^{176}Lu a remarkable amount of ^{177m}Lu ($T_{1/2}$ = 160 d) is produced.

The ^{177m}Lu content in the labelling solution is mainly depending from the two factors: irradiation time and how much time has passed after end of the irradiation. Typically carrier added (c.a.) ^{177}Lu is produced in the irradiations positions, where the neutron flux is 1-3*10^{14} neutrons cm-2 s-1 and the irradiation time is 14 days. Reported values for the ^{177m}Lu/^{177}Lu ratio from several reactors vary between 0,01% and 0,02%. The hospitals are using their ^{177}Lu up to one week after end of the irradiation when the 177mLu/177Lu ratio has doubled.

^{177}Lu is mainly used to peptide labeling with typical doses of 7–9 GBq. If the ^{177m}Lu/^{177}Lu ratio is 0,02%, it means that a dose includes 1,4–1,8 MBq ^{177m}Lu.

To handle radioactive materials, which are above the free limit, it is required to have a radioactive material licence. For ^{177m}Lu the free limit is 1 MBq. If the free limit is exceeded the nuclide needs a specific licence or a licence as by-product. Hospitals which are using over 5 GBq c.a. ^{177}Lu should have a radioactive licence also for ^{177m}Lu.

During the labelling process and treatment the loss of radioactivity is typically 2 to 5% of activity which is equal to 90 kBq ^{177m}Lu. The release limit is 10 Bq/g waste. All waste should be collected and shipped to a radioactive deposit or let to be decayed.

A patient is going to extract approximately 80% of the activity (1,45 MBq) through urine relative fast. The highest allowed radioactive concentration in the sewage water canal is 50 kBq/m^3. It means that the patient urine needs to be diluted to 30 m3 after a cooling time, which is required to let ^{177}Lu decay.

Preclinical studies with non-standard and carrier-free radioisotopes from ISOLDE-CERN

Abstract ID: 92

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Systemic radionuclide therapy is a very challenging field of nuclear medicine. The search of new tracers that may become a radiopharmaceutical is driven mainly by disciplines as biochemistry, organic chemistry and coordination chemistry, while modern radiochemical or nuclear physics achievements are often not adequately included. Frequently the development of new radiopharmaceuticals is limited to the use of the rather small number of radionuclides that are commercially available.

We will review a series of experiments that have been performed from 1975 to 2005 in an interdisciplinary collaboration between nuclear medical institutions, radiochemistry and CERN-ISOLDE. We will illustrate how present-day technology developed partially at CERN (high energy proton induced reactions combined with high-tech physico-chemical separation techniques) improves the quality and choice of radioisotopes enormously.

These new high quality research radionuclides can significantly increase the efficiency in R&D towards improved systemic radionuclide therapies. The biological response as function of the individual radionuclide can be studied systematically with higher efficiency. The same concerns the relation between radiation energy and biological response for different lesion sizes.

We will present results from particularly efficient simultaneous multi-isotope measurements of biodistributions of several chelates and conjugates of rare earth elements. We also show examples of innovative PET and SPECT isotopes that, since they exhibit the same biodistribution as the respective therapy isotope, may serve for personalized in-vivo dosimetry.

In conclusion these experiments show the potential of introducing new commercially not available carrier-free radionuclides for diagnostics and therapy.

The Future for ^{99m}Tc and ^{99}Mo in nuclear medicine

Abstract ID: 54

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^{99m}Tc is an unusual radionuclide choice for imaging but has become the most frequently used radioisotope in nuclear medicine and has made single photon emission computed tomography (SPECT) an extremely powerful in-vivo diagnostic imaging tool. Recent advances in imaging camera technology offer a very promising future for this method of imaging but the supply of the radionuclide is now under threat.

^{99m}Tc is supplied to clinical users in the form of ^{99m}Tc/^{99}Mo generators loaded with the parent 3 day half-life radionuclide ^{99}Mo. ^{99}Mo is produced by a complicated supply chain that relies on nuclear fission of ^{235}U in nuclear research reactors. Most of these reactors are ageing and in 2010 there is just not enough of this specialised reactor capacity to meet all the world's demand for ^{99}Mo. There are existing reactors planning to start producing fission ^{99}Mo and several alternative methods are being proposed, some of which require accelerators not reactors. Unfortunately some nuclear medicine scans are already being diverted to different imaging methods that do not rely on the supply of ^{99m}Tc.

This paper will provide an industrial perspective on a situation which has been described as a 'crisis' for the nuclear medicine ^{99m}Tc. Reasons for selecting ^{99m}Tc and the latest instrumentation advances will be described, the clinical use of the different radionuclides will be summarised and current capacities of fission producers reviewed. The various alternative methods of producing ^{99}Mo will be examined with a commentary of the technical and economic challenges facing each of the options. Finally the latest news from the fission 'moly' supplier industry will be made available.

Feasibility study of an accelerator-driven production of ^{99}Mo for ^{99m}Tc generators using a high-power LINAC

Abstract ID: 47

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A compact accelerator-driven neutron activator based on a modified version of the Adiabatic Resonance Crossing (ARC) concept, proposed by C. Rubbia and experimentally demonstrated at CERN in 1997, has been developed with the aim of efficiently exploiting ion-beam generated neutrons for the production of radioactive nanoparticles for brachytherapy using small/medium-size cyclotrons for medical applications. A prototype of the activator is currently operational in JRC-Ispra, coupled with a 40 MeV – 50 μA cyclotron, and a higher scale version, to be coupled with the 70 MeV-350 μA cyclotron of the Arronax centre in Nantes, is under design (THERANEAN project). The experimental results obtained with the JRC neutron activator prototype indicate the feasibility of a cyclotron-driven production of -emitting radioisotopes for brachytherapy.

The possibility to produce ^{99}Mo through the ^{98}Mo(n,γ)^{99}Mo reaction induced by the neutrons generated using a high-energy (1 GeV)/high current (~1 mA) LINAC, and moderated/confined with an ARC-type activator has been also explored.

Two Monte Carlo codes (FLUKA, MCNPX) have been used to simulate the system and carry out a preliminary optimization of the system parameters. Activation results and system potential productivity in different configurations were compared with available results on ^{99}Mo production through ^{235}U fission in nuclear reactor. The possibility of an accelerator-driven fission-based production in the activator ^{99}Mo also examined.

Results show that the total world demand could be potentially covered with the ^{98}Mo(n,γ)^{99}Mo production using a 1GeV-4 mA LINAC-driven neutron activator.

Gallium-68 – a candidate for use in clinical routine

Abstract ID: 86

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The $^{68}Ge/^{68}Ga$ radionuclide generator (^{68}Ge, $T_{1/2}$ = 270.95 d) is an excellent cyclotron-independent source for the positron emitter ^{68}Ga which is successfully used in clinical PET. Nevertheless there remain open problems in the routine use related to the applicability of the technique in clinical environment and legal aspects.

An effective application of the generator produced ^{68}Ga can be limited by poor chemical and pharmaceutical quality of the generator eluate. Thus traces of metals, as a consequence of the use of metal oxide based matrixes; rather large volume and high acidity lead to suboptimal conditions of the radiolabelling reaction and can decrease the reproducibility in the routine preparation of ^{68}Ga-radiopharmaceuticals. In order to extend the shelf-life of the generator systems, high initial activities of the ^{68}Ge are used. A long-term utilization of the generator systems in non-gmp environment can cause, however, decreasing of pharmaceutical quality and conflict with legal aspects of in-house radiopharmaceutical production. Finally, users face the problem of the generator utilization, since long-lived ^{68}Ge can not be declared as decay waste.

In this context we propose a novel "metal free" $^{68}Ge/^{68}Ga$ radionuclide generator system dedicated for production of high quality gmp grade ^{68}Ga preparations. The concept includes an effective ^{68}Ge management and improved logistic for the routine utilization of the radionuclide generator system in clinical environment.

Radioisotopes in diagnostic and therapy

Posters

Bremsstrahlung dosimetry: a valid system to estimate OARs doses in ^{90}Y-Zevalin treatments

Abstract ID: 15

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Dosimetry for Organs at Risk (OARs) in patients undergoing Radioimmunotherapy (RIT) by ^{90}Y–Zevalin is currently performed by ^{111}In-Zevalin (pre-RIT) dosimetry, used to predict ^{90}Y–Zevalin biodistribution. Although this approach is considered the gold standard, it does not allow direct evaluation of OARs during treatment.

Aim of this work was the assessment of a method to estimate doses by Bremsstrahlung radiation from ^{90}Y-Zevalin (post-RIT dosimetry). 27 patients underwent ^{90}Y–Zevalin treatment: 17 patients performed both pre- and post-RIT dosimetry at one week intervals; 10 patients underwent only post-RIT dosimetry. Serial-Whole-Body Scans were acquired following ^{111}In-Zevalin or ^{90}Y-Zevalin administration. Red marrow residence times were obtained by counting blood samples (Sgouros., 1993), while residence times for remaining OARs were evaluated by image analysis (Wiseman, 2000). OLINDA/EXM software was employed to define S-values. Organ doses (Gy/GBq) estimated by pre- and post-RIT dosimetry resulted linearly correlated (R2=0,76). Percentage activity in organs showed equivalent kinetic trend in both studies. A further correction was performed for residual ^{111}In-Zevalin activity in the ^{90}Y images.

An image in 50-300 keV energy window was acquired for 10 patients immediately prior to ^{90}Y-Zevalin administration; the relative ^{111}In count contribution to each organ was subtracted to each ^{90}Y image. A linear correlation between pre- and post-RIT dosimetry was still observed (R2=0,51). No significant difference was found between pre- and post-RIT dosimetry, even comparing different group of patients. These results show post-RIT dosimetry is a valid method to quantify doses during RIT.

^{32}P-radioactive implants for low-dose-rate (LDR) brachytherapy of benign stenoses of the urethra and the common bile duct

Abstract ID: 16

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Objective: LDR brachytherapy can modulate wound healing avoiding hyperproliferation and benign stenosis of endogenous tubular structures such as bile duct or urethra.

Material and methods: The studies were conducted in a randomized double-blinded fashion. In 36 rabbits and 30 swine a scarred benign stenosis was induced endoscopically by laser or heat in the urethra and the common bile duct, respectively. Usual implants (stent, catheter) were equipped with activated ^{31}P-filled foils and inserted after balloon dilatation to locally irradiate the wounded stenosis tissue. The therapeutic range of the pure electron emitter ^{32}P of a few millimeter only causes minimal dose in the healthy surrounding tissue. Dose distribution is calculated by GEANT4 simulation. The animals were killed at 3 or 4 weeks after brachytherapy, and the target tissues were examined by histology.

Results: A dose range of 0, 15 and 30 Gy within 7 days showed no adverse dose effects in the surrounding tissue. No local or systemic side effects of brachytherapy occurred, and no radioactivity was lost by urine or bile, respectively. LDR brachytherapy significantly influenced the development of stenoses.

Conclusion: The ^{32}P-foil offers a simple and safe way to irradiate very precisely tissue with a dose up to some 60 Gy. The radiation safety can be assured with 10 mm thick plexiglass devices.

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Positron Range Effects in High Resolution 3D PET Imaging

Abstract ID: 34

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Positron range limits the spatial resolution of PET images and thus difficults the use of several radioisotopes, in particular in high resolution studies, like the ones employed in preclinnical research. Positron range has a different effect for different isotopes and propagation materials, therefore it is important to consider it during image reconstruction.

In this work we have considered positron range effects by means of Monte Carlo simulations with PeneloPET, a simulation package for PET developed in our group. The simulation models positron trajectories and computes the spatial distribution of the annihilation coordinates for the most common isotopes used in PET: ^{18}F, ^{11}C, ^{13}N, ^{15}O, ^{68}Ga and ^{82}Rb. Range profiles are computed for different positron propagation materials, obtaining one kernel profile for each isotope-material combination.

These positron range kernels were introduced in FIRST, the high performance 3D-OSEM PET image reconstruction software also developed in our group. FIRST uses these kernles taking into account the material in which the positron is annihilated, obtained for instance from CT images. In this way, different positron range corrections for each material in the object are considered. We compare resolution and noise properties of the images reconstructed with and without positron range modelling. For this purpose, acquisitions of different phantoms filled with different isotopes have been simulated for the ARGUS small animal PET scanner.

We conclude that positron range effects can be well accounted for during reconstructions, making it possible the use of ^{68}Ga, which does not require a cyclotron, in high resolution studies.

SWAN: a combined centre for radioisotope production, proton therapy and research in Bern

Abstract ID: 36

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Switzerland is strongly committed to high-end medicine and innovative technology in health care. In proton therapy (PT), breakthrough technology is developed at the Paul Scherrer Institute. The constantly improving treatment options in oncology and radiation oncology are now mature to integrate PT in the context of an academic hospital based clinical setting.

To exploit at best the high potential of PT, advanced diagnostics is essential. In particular, PET is nowadays becoming a fundamental tool in cancer therapy and, in the near future, will allow improving treatment planning by means of new radiotracers.

In order to engage appropriately in this highly complex field, the Bern University Hospital (Inselspital) together with the University of Bern has undertaken diligent work to identify the fundamental steps towards the implementation of PT together with radioisotope production and research. The outcome of this detailed scientific and technical study, together with a solid business plan, led to the foundation of the SWAN group. SWANtec AG is a holding with two subsidiary companies: SWAN Isotopen AG engages in the commercial production of radiopharmaceuticals for molecular imaging and SWAN Hadron AG is dedicated to plan, implement and run a PT center. A partnership model has been elaborated to integrate clinical and scientific partners into a national center with an innovative organizational approach. A foundation is foreseen to support patients and to foster research.

The first phase of SWAN has been approved and financed. A cyclotron laboratory for radioisotope production and research is now under construction. This centre features an external beam line located in a separate bunker, multi-disciplinary laboratories and GMP radiopharmaceutical production facilities.

Radiopharmaceuticals Production and Research Centre at the University of Warsaw

Abstract ID: 69

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Radiopharmaceuticals Production and Research Centre (RPRC) is a part of Heavy Ion Laboratory (HIL), the Polish largest nuclear physics facility, operating a Kmax = 160 cyclotron, which accelerates heavy ions up to mass 40 with energies up to 10 MeV/nucleon.

For the radiopharmaceuticals production a second proton/deuteron cyclotron (K = 16.5) is in the installation phase. The RPRC will be also equipped with adequate synthesis and dispensing units as well as the quality control equipment. The production and distribution of the basic radiopharmaceutical FDG for the Polish diagnostic centers will begin in 2011.

Other radiopharmaceuticals based on ^{18}F (as ^{18}F - Choline or ^{18}F - Dopa) will be also produced with already available equipment. After the subsequent European funding (already requested) a fully equipped ^{11}C radio-pharmaceuticals synthesis line should be also available (for e.g. ^{11}C - Choline, ^{11}C - acetate or ^{11}C - methionine production).

The research program will be pursued by the members of the Warsaw Consortium for PET Collaboration. It includes, among others, the new, innovative radiopharmaceuticals as well as the application of Positron Emission Tomography in biological and medical investigations.

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Many small versus a few big. A note on scale and numbers when physics is helping medicine

Abstract ID: 83

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In 1935 Lawrence writes to Bohr that it is much easier to get funds for physics through medical research. Still true, now. Lowering our gaze from high-flying proposals to everyday PET practice, we find the opposite situation: physicists at hard work for patients and medical science.

PET practice today offers employment opportunities for nuclear physicists. The clinical application of PET drives >10E6 procedures/y. There is an urgent need to improve and simplify the accelerators and for training more "hard-core" physicists to drive the technology, in a time where nuclear physics is going out of many University curricula. Most therapy or imaging applications use from (p,n), (p,2n) and (n,γ). For this we need not bigger but better machines. The need and pressure of scale is growing. New radiochemistries give room for smaller cyclotrons. Present research reactors are aging, compromising access to medical isotopes. More sources of high flux thermal neutrons are needed, for radionuclide therapy with high specific activity transition metals and rare earths. Most research PET labs have a research program in diagnostic agents. The close connection with imaging makes the search for good bio-vectors for systemic radionuclide cancer therapy feasible in many PET labs. A possibility is the use of bio-vectored "pure" Auger emitters (from (p,n) reactions!) for disseminated disease control, sparing non-targeted tissue.

All this needs help from big physics. Please open your minds to the humble needs of the large number of general practioners of PET.

Production of Radioisotopes for Medical Applications at the SINQ Spallation Neutron Source Using Protons and Fast Neutrons

Abstract ID: 94

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A high-power spallation source may offer important applications in nuclear medicine thanks to the high fluxes available and to the flexibility of proton and neutron irradiation. We consider an irradiation station in the SINQ spallation target at PSI. Calculations have been performed using MCNPX 2.5.0. Using the same concepts adopted for the solid target presently operating in SINQ, this station would have a fast neutron flux of about 2×1014 n/cm^2/s.

Two types of programs could be implemented. First, one could irradiate samples for the entire SINQ target life (typically 2 years). Samples could be placed in a position with pure neutron irradiation, or at the center of the target, in case a mixed neutron/proton spectrum is advantageous to give a higher production. One first example for this application is ^{44}Ti production (generator of ^{44}Sc used in PET). Our calculations show that the minimum target activity of 200 MBq could be reached irradiating 800 g of vanadium. Higher production can be achieved by placing the sample inside the target by proton and neutron irradiation. Production of ^{44}Ti is foreseen for the next target (starting irradiation in 2011).

The second program would require a more complex design of the station, in order to allow for sample insertion, irradiation for short time (typically one week) and extraction. The range of applications would increase tremendously. Several cases have been studied and we calculated the yields for reactions such as ^{64}Zn(n,p)^{64}Cu, ^{67}Zn(n,p)^{67}Cu, ^{32}S(n,p)^{32}P, ^{89}Y(n,p)^{89}Sr, showing that the production rate could be competitive with cyclotrons, and in some cases advantageous. Production of ^{99}Mo could be achieved via ^{100}Mo(n,2n)^{99}Mo, giving an alternative way to the production in reactors using enriched uranium.

Production of radioisotopes with high specific activity at the high-flux reactor of ILL Grenoble

Abstract ID: 96

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Institut Laue Langevin (ILL) in Grenoble operates a 58 MW high flux reactor. This powerful neutron source supplies intense extracted neutron beams for a great variety of experiments performed at 40 different instruments.

However, the ILL reactor has also in-pile irradiation positions with a neutron flux reaching 1.5E15 n/cm^2/s, unrivalled in Western Europe. Previously these beam tubes served mainly for specific cross-section measurements and for production of small quantities of special radioisotopes for scientific purposes. Recently ILL started the production of radioisotopes for medical applications. The high neutron flux guarantees highest specific activity in single-neutron-capture reactions and is particularly useful for double-neutron-capture reactions with short-lived intermediate radioisotopes.

Irradiation of enriched ^{186}W produces by double-neutron-capture ^{188}W. At ILL specific activities above 0.1 TBq ^{188}W per g of tungsten are reached after 50 days of irradiation. With four irradiation cycles per year, ILL has the capacity to provide a quasi-continuous supply of up to 5 TBq ^{188}W per year. In combination with the high quality ITG ^{188}W/^{188}Re generators this assures the required isotope supply for a large-scale application of endovascular brachytherapy with 188Re and of therapy with ^{188}Re labelled radiopharmaceuticals.

99Mo was produced by ^{98}Mo(n,γ) reactions with specific activities of 1 TBq/g and a chromatographic ^{99}Mo/^{99m}Tc generator was successfully operated with this material. ^{177g}Lu in non-carrier-added form and practically free of the usual contamination with long-lived ^{177m}Lu was produced via ^{176}Yb(n,γ)^{177}Yb(β-)^{177g}Lu followed by chemical Lu/Yb separation at ITG. This high-quality ^{177}Lu already entered clinical use for peptide receptor therapy.

Production and application of the low energy electron emitter ^{161}Tb for endoradiotherapy as a better alternative to ^{177}Lu

Abstract ID: 97

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Currently ^{177}Lu-labeled radiopharmaceuticals are successfully used in clinical nuclear oncology for therapeutic treatments. However, in spite of the promising clinical studies a further optimization of the therapeutic efficiency is absolutely necessary. Here primarily evaluation of alternative radionuclides is needed to intensify therapeutic effect of the radiopharmaceuticals.

Because of its physical and chemical characteristics, ^{161}Tb is an attractive candidate for therapeutic treatments in nuclear oncology. With 6.90 days half-life the low energy β-emitter ^{161}Tb is very similar to ^{177}Lu. It emits only a few photons useful for visualization by means of gamma camera. Additionally ^{161}Tb emits a significant amount of conversion and auger electrons and greater therapeutic effect can be expected.

^{161}Tb was produced as no-carrier-added by neutron irradiation of massive ^{160}Gd targets via indirect nuclear reaction ^{160}Gd(n,γ)^{161}Gd(β$^-$) ^{161}Tb. The separation by means of cation-exchange chromatography was developed and applied for production of up to 15 GBq of ^{161}Tb with an estimated specific activity of about 85 Ci/mg. The activity produced was successfully used for preparation of ^{161}Tb-labelled chCE7 antibodies and DOTA-peptides. The radiolabeling could be performed with the efficiency similar to the reaction performed using commercially available n.c.a. ^{177}Lu.

In addition, production aspects and application of non-pure positron emitter ^{152}Tb ($T_{½}$ = 17.5 h, 17 % positron branching) are discussed. The ^{152}Tb-labelled compounds might be useful for quantitative PET imaging and pre-therapeutic dosimetry as an analogue to the ^{161}Tb therapeutic agents.

Receptor Targeted Lymphoscintigraphy Using Dextran-Mannose Derivatives

Abstract ID: 110

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^{99m}Tc-sulfur colloid, filtered ^{99m}Tc-sulfur colloid and different microcolloids of ^{99m}Tc-labelled albumin are presently utilized for sentinel node detection, but none of these agents have ideal properties regarding selective accumulation in sentinel node, they are uptaked also by distal lymph node. The lymphoscintigraphy agent requires a high density of receptor substrate sites to achieve a receptor affinity required for proper sentinel node detection. The solution could be given by receptor-binding radiopharmaceuticals which can be synthesized with high specific activities, compatible with typical target tissue receptor densities.

The radiolabelling of the mannosyl-cysteine-dextran macromolecules with 99mTc resulting in a high purity and stability radiolabelled conjugate, suitable for sentinel node detection with low distal lymph accumulation, as well as their in vivo biological evaluation were the proposed aims of this study.

Different radiolabelling strategies, including novel ^{99m}Tc cores, were evaluated in order to select and optimize the most efficient and specific one. The quality control of radiolabeled conjugates using TLC and HPLC was performed; the RCPs of the probes were ranged between 93-99%. The biological evaluation (ex-vivo biodistribution and specific uptake) was performed in Wistar rats at 15, 30 and 60 min post injection. The biological data shows a rapid and highly specific sentinel node accumulation, up to 11% ID, and a very good sentinel node extraction in respect with the second node in the chain, up to 94% at 1h p.i.

The ^{99m}Tc labelled dextran-mannose derivatives show specific accumulation in the sentinel lymph node and could be further evaluated as potential agents for targeted lymphoscintigraphy.

Quantification of internalisation of EGFR-binding Affibody molecules. Methodological aspects

Abstract ID: 111

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The ability to measure quantitatively the amount of radionuclide or targeting agent internalised by tumour cell is important in nuclear medicine. Internalisation influences the local retention time, imaging quality of PET and SPECT and also the therapeutic effects of radionuclide therapy.

Here, we describe two fluorescence-based methods that used the fluorescence microscopy and flow cytometry. The CypHer method measures fluorescence of the internalised molecule pool. The Alexa488-quenching method is based on the difference between total cell bound and internalised fluorescence. We perform two slightly different methods using the Alexa488 quenching method.

^{111}In-labelled Z1907 was used for 'acid wash', the classic method to study internalisation as a comparison. The dimer (Z1907)2 could not be removed by acid and thus was not studied.

Two epidermal growth factor receptor (EGFR)-binding Affibody® molecules, monomer Z1907 and dimer (Z1907)2 were analysed in A431 cells. Epidermal growth factor (EGF), Cetuximab and a non-specific Affibody® molecule were used as controls.

The Alexa488-quenching method resulted in about 45% of EGF, 19-24% of the bound Affibody® molecules and Cetuximab being internalised by the tumour cells within one hour at 37 °C. Acid wash yielded a similar result for Z1907.

The Alexa488-quenching method is a suitable choice for internalisation screening of targeting agent and also works well with molecules that resist acid wash. The internalised fraction of Affibody® molecules indicates good uptake and retention of metallic radionuclide which will render good tumour to background values.

No Carrier Added radionuclides produced by accelerators for biomedical applications

Abstract ID: 116

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The applications of the radionuclides play a fundamental role in nuclear medicine, which, nowadays, has become an indispensable branch of medical science and, as the production of radionuclides and labeled compounds for medical applications, is becoming more and more a relevant branch of nuclear and radiochemistry.

At the Radiochemistry Laboratory of LASA – INFN Sez. Milano Italy, a wide range of high specific activity accelerator-produced radionuclides have been produced for a long time in No Carrier Added (NCA) form, for both basic research and application purposes and in particular for uses in metabolic radiotherapy and in related PET and SPET diagnoses.

In particular in the more recent years our studies have been devoted to optimize the production of the following RNs:

1. NCA ^{64}Cu, produced by ^{nat}Zn(d,αxn) and ^{nat}Zn(d,2pxn) reactions for simultaneous β+/β- metabolic radiotherapy with intrinsic PET imaging, including the short-lived radionuclide ^{61}Cu, and also ^{66,67}Ga as highly relevant radionuclides by-products;

2. NCA ^{211}At/^{211g}Po, produced by ^{209}Bi(alpha,2n) reaction, with internal spike of gamma emitter ^{210}At from ^{209}Bi(alpha,3n) reaction (and small amount of ^{210}Po as radiotoxic long-lived impurity), for high-LET radio- and immuno-radiotherapy;

3. ^{186g}Re, produced by ^{186}W(p,n) and ^{186}W(d,2n) reactions for bone metastases pain palliation by negatron (1.1 MeV) metabolic radiotherapy including SPET imaging;

4. NCA ^{177g}Lu, produced by the alternative indirect ^{176}Yb(d,p) and direct ^{176}Yb(d,n) reaction route for radiotherapy and for SPET.

In particular in this communication the detailed results obtained for ^{186g}Re and ^{177g}Lu production together with the QC tests for radionuclidic, chemical and radiochemical purities will be presented.

ROMOL-99 – The Rossendorf Fission Mo-99 Process

Abstract ID: 119

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The ROMOL-99 Process (Rossendorf Molybdenum-99 production) has been developed based on the >45 year experience in small to medium scale fission Mo-99 production at the ZfK Rossendorf (Germany).

The process is based on dissolution of Al-cladded UAl_x-Alloy targets in a mixture of NaOH and $NaNO_3$. After filtration and adsorption of the radioiodine at a silver coated absorber material and after acidification of the solution the ^{99}Mo is adsorbed in the classical way at an alumina column. The purification of the ^{99}Mo product is achieved by anion exchange followed by a high temperature refining process.

The advantages of this process are:

1. Safety: Digestion of the targets in a closed dissolver system under reduced pressure conditions without generation of process gases as H_2 for instance (as in other protocols).

2. After dissolving the filtrate contains practically only Mo and its daughter products, iodine, the alkaline elements and about 60-80% of the Pt-elements.

3. During the digestion process the U is transferred directly into the sodium di-uranate ($Na_2U_2O_7$) configuration, which does not adsorb Mo.

4. Nitrite, that is formed in the digestion process with a fraction of 12-15 % is destroyed during the acidification by Urea forming harmless nitrogen gas.

The first facility for this process is designed for up to 100 g of Aluminum in the target material and has been commissioned 2009. The practical production yield of high purity ^{99}Mo suitable for $^{99}Mo/^{99m}Tc$ generator loading.is 65-70 %.

Medical Isotopes Production at Multi Megawatt Proton Facilities

Abstract ID: 120

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Spallation, fragmentation and fission reactions induced by >100 MeV protons can produce essentially all nuclides of the chart of nuclides. This has been exploited in ISOL facilities like CERN ISOLDE for the study of mainly the short-lived nuclei (half-lives from milliseconds to hours) produced only in low yields. Here a number of new techniques in accelerator physics and radiochemistry have successfully been taken into use for separation of the short-lived species from the far more abundantly produced long-lived ones (half-lives from hours to days) often considered as disturbing waste.

The carrier-free longer-lived radioisotopes from ISOLDE that were hitherto not available elsewhere have shown in pilot biomedical experiments great potential for diagnostics and therapy. Presently they are produced in amounts sufficient to allow preclinical and in some cases also clinical studies.

It is proposed to make these new high quality research radio nuclides more readily available for a larger scale R&D not only towards improved systemic radionuclide therapies, but also to adapt the ISOLDE high-tech physical-chemical separation techniques for their future large-scale production.

Multi megawatt proton beams are being planned for a number of facilities: EURISOL, spallation neutron sources (e.g. ESSS at Lund), muon and neutrino factories as well as accelerator-driven sub-critical reactor systems.

We will discuss how medical isotopes could be produced in a parasitic way at such facilities.

^{188}Re-Radiolabelled Antibodies For Targeted Radiotherapy

Abstract ID: 123

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Radiolabelled antibodies with beta emitters offer a promising alternative for the management of different malignancies (radioimmunotherapy). The aim of the present work was the radiolabelling of CEA, VEGF and MUC1 monoclonal antibodies with ^{188}Re and the evaluation of the saturation binding of ^{188}Re-VEGF and ^{188}Re-MUC1 to HeLa tumour cells, as well as the induced cytotoxicity of radiolabelled antibodies in tumour cells by inhibition of the specific receptors functions and delivery of β-radiation doses.

For the synthesis of the ^{188}Re-anti-CEA-Mab, ^{188}Re-anti-VEGF-Mab and ^{188}Re-anti-MUC1, using 2-mercaptoethanol as reducing agent of –S-S- cysteine bounds a direct labelling method was employed. Optimization studies of radiolabelling processes lead to a 90 min. incubation time at 90 °C, with ^{188}Re-labeling yields higher than 95%.

The tumour cell lines (HeLa, MCF-7 and MDA-MB-231) were characterized as heterogenous tumour cells with high expression of the VEGF/ MUC1 receptors. 4 x 105 HeLa cell samples were used in evaluation of the saturation binding of ^{188}Re-anti-VEGF respectively ^{188}Re-anti-MUC1. The induced radiotoxicity of ^{188}Re-VEGF and of ^{188}Re-anti-MUC1 was evaluated by the MTT method using MDA-MB-231 and MCF-7 cell lines, respectively. The citotoxicity of these two radiolabelled antibodies was also tested by MTT using HeLa cell lines after 24 and 48 h incubation time.

The maximum binding of ^{188}Re-MUC1 to the expressive tumor cell receptors was reached for 0.3 μg antibody. The induced radiotoxicity of ^{188}Re-MUC1 is high, as the MCF-7 cells viability decreases fast to zero at 100 μCi. The ^{188}Re-MUC1 induces a cytotoxicity which decreases the HeLa cells viability up to 62.34%. The radiotoxicity and cytotoxic effect of the ^{188}Re-anti-VEGF on HeLa cells was high.

Targeted Radiotherapy of Cancer using Anti-Epidermal Growth Factor Monoclonal Antibody radiolabelled with ^{177}Lu

Abstract ID: 125

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Alterations in the EGFR (Epidermal Growth Factor Receptor) family are involved in the development of cancer leading to the stimulation of tumor growth, protection from apoptosis, angiogenesis, and the formation of metastases. Increased EGFR expression is an adverse prognostic feature of many cancers and in recent years the EGFR family has been a target for anti-cancer drug development. The epidermal growth factor monoclonal antiboby (anti-EGF-Mab) is an attractive targeting agent due to its low molecular weight (6 kDa) and high affinity for EGFR. ^{177}Lu is a promising short-range β-emitter for targeted radiotherapy, its mean range in tissue being 670 μm, properties that make this radionuclide suitable for micro metastatic disease.

This study aims to evaluate the synthesis parameters of the ^{177}Lu-antiEGF-Mab using a macrocyclic ligand (DOTAM) and its in vivo biodistribution in normal and HRS1 tumor bearing animal models.

The DOTAM-EGF complex was synthesized in high yield at room temperature in 0.1 M $NaHCO_3$ pH 8.2 using a mixture of DOTAM / anti-EGF-Mab in nonstoichiometric ratio. The complex was then labelled with ^{177}Lu with 95 % labeling efficiency. After i.v. injection, the animals were sacrificed, the expressive tissues were removed and their radioactivity was measured. A fast blood clearance was observed. Biodistribution evaluation revealed a major accumulation in peripheral tumor tissues (up to 12.49 % ID/g) at 24 h after i.v. injection while the tumor mass uptaked 7 times less activity. The liver, kidneys, and small intestine showed a moderate uptake (3.4 ID/g) in the first two hours post injection following a decreasing curve, up to 0.5 % ID/g at 72 h post injection. In conclusion, 177Lu-(DOTAM)anti-EGF-Mab is a promising radiopharmaceutical for TRT.

PNPI Medicine Center on the Base of 1000 MeV Proton Cynchrocyclotron and Constructed 80 MeV Cyclotron for I=100 mkA

Abstract ID: 127

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The PNPI proton therapy facility at the 1000 MeV synchrocyclotron is specialized on the treatment of head brain diseases and irradiated 1352 patients since 1975.

The next stage is the construction of a 80 MeV proton cyclotron with I=100 μA for eye's tumors treatment and the radiactive isotopes production, especially for Sr-Rb generators for PET. The cyclotron will be used as injector for a 150-250 MeV proton synchrotron.

A versatile automated apparatus to optimize the synthesis of PET Radiotracers

Abstract ID: 128

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An apparatus for automated synthesis of radiopharmaceuticals labeled with ^{18}F constructed at IFIN-HH for PET investigation is described. [^{18}F] fluoride was produced at the IFIN-HH cyclotron by irradiation of H_2O enriched 97 % in ^{18}O, with deuterons of 13 MeV or protons of 8 MeV.

The irradiated H_2O was transferred (injected) into the radiochemistry full automated processing systems which ensure the separation of ^{18}F- from H_2O, the labeling with 18F of a precursor compound by an acid or basic hydrolysis; then it is transformed in the radiopharmaceutical with 18F and finally purified a selective absorbants.

The system is easy to operate and contain a programmable logical controller which manages the entire operation program stored in its internal memory. The computer is used to assist the operator during the different steps of synthesis and to allow visualization of the process and printing the report.

The device served for the production of [^{18}F] FDG at the IFIN-HH cyclotron, one of the most used radiopharmaceutical in PET investigations. The synthesis module has configurated so that it is enough flexible to accomplish and other nucleophile reactions of labeling with short lived radioisotopes.

Multi Ci $^{188}W/^{188}Re$-Generator and New Rhenium-188 Applications

Abstract ID: 136

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Most rhenium-188 applications require high activity concentration. Typically $^{188}W/^{188}Re$-generators have an activity of 0.5 to 1 Ci and relative large elution volumes. Thus a concentration unit is required, which causes loss of time and activity and increases the finger doses remarkably.

We have developed a $^{188}W/^{188}Re$-generator from which can be eluted up to 3 Ci rhenium-188 depending on the specific activity of the tungsten-188 and the age of the generator. The elution volume is less than 10 ml isotonic saline solution and the elution time is less than one and half minute. Tungsten-188 breakthrough is of the order of 10-5 to 10-4. Other radiochemical impurities are negligible.

Stenoses in the cardio- and peripheral vascular area are remarkable health problems. In the peripheral vascular area re-stenoses occur in over 80% of all patients. When the re-stenosis area has been irradiated with a balloon catheter, which was filled with high volumetric specific activity ^{188}Re-solution, the re-stenosis rate was decreased below 20%.

Skin cancer (basal and epithelia) is the most common cancer with increasing rate. We have developed a new rhenium-188 based treatment. A rhenium-188 compound is immobilised into a polymeric matrix and is applied with a protective layer over skin cancer. Meanwhile over 1500 lesions have been treated with over 90% success rate with a single treatment.

Efficient production of carrier-free ^{86}Y and its application in nuclear medicine

Abstract ID: 196

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Due to its physical properties ^{90}Y is one of the most widely used radionuclide for targeted tumor therapy. However as a pure - emitter it can not be applied for accurate therapy optimization. For that purpose, an intermediate long-lived isotope ^{86}Y has been advanced. It can be produced by small-sized cyclotrons via the $^{86}Sr(p,n)^{86}Y$ nuclear reaction and then efficiently isolated. ^{86}Y was produced by irradiation of 60 mg of enriched $^{86}SrCO_3$ or ^{86}SrO. After bombardment the target material was dissolved and conditioned with NH_4OH. The isolation of ^{86}Y was performed by two electrolytical steps.

The first step was carried out with 2 A for 40 min while the second electrolysis was performed with 0.25 A for 15 min. Activity on Pt wire was recovered by immersing the wire into capillary syringe with 70 µl of 0.2 M of buffer (pH 4.75). 86Y was then directly applied for labeling of biomolecules. We demonstrated that ^{86}SrO is superior target material over $^{86}SrCO_3$ due to its higher thermal stability and higher content of Sr/mass unit.

The max beam acceptance was determined to be 9 µA for 2h providing thus 3 GBq of ^{86}Y. The production cycle was simplified and automated in order to prevent radiation exposure. ^{86}Y was recovered in acetate buffer (overall yield of 92.8%) and SA (0.2 Ci/µmol) was found to be comparable with highly pure ^{90}Y. Enhanced production of ^{86}Y was performed by irradiation of enriched ^{86}SrO using 14.2 MeV p-beam and 9 µA resulting in yields of 167 MBq/µA•h.

Improved work-up was successfully applied for isolation of ^{86}Y in a small volume of convenient buffer solution. The product was of high chemical purity which is essential for labelling of compounds relevant for nuclear medical application. This purity was demonstrated by labelling of DOTA-Biotin in excellent yields.

^{99}Mo production at FRM II - an essential contribution to a European supply problem

Abstract ID: 199

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^{99}Mo and its daughter isotope ^{99m}Tc represent 75 – 80 % of the need of radioisotopes for nuclear medicine. It is mainly used for scintigraphic examinations ranging approximately 8 million medical diagnoses per year in Europe.

World wide ^{99}Mo is produced by five research reactors, three of them located in Europe. The research reactors have an age of 43 - 52 years. The two most powerful of them, NRU at Chalk River, Canada, and HFR at Petten, Netherlands, need urgent and long-lasting repair within their primary nuclear circuits. Due to the relatively short half-life of ^{99}Mo (66 hours) it can not be produced on stock and the transfer between continents causes additional losses. Since 2008 and also for the upcoming years there is a drastic shortage in the supply of 99Mo worldwide. Beyond the actual shortage new sources for a sustainable production have to be established now.

The neutron source Heinz Maier-Leibnitz (FRM II) of the Technische Universität München, taken into operation in 2004, disposes of several high flux irradiation positions in its D2O moderator tank. A feasibility study shows that assuming 144 hours of irradiation about 17 kCi ^{99}Mo can be produced weekly at FRM II. The processing of the irradiated targets will be done by the pharmaceutical industry outside FRM II. Taking into account the considerable decay which takes place during the time needed for the production of the medically applicable specimen – ^{99m}Tc kids – about ½ of the European need could be served by FRM II.

Neutronics calculations and technical details of the necessary upgrade of the FRM II irradiation channels will be presented.

Prospects in medical imaging

Oral Communications

Challenges towards simultaneous PET-MRI

Abstract ID: 40

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PET-MRI will combine the excellent sensitivity of PET with the variety of contrast mechanisms for anatomical and functional imaging capabilities of MRI. Another reason to shift from CT to MRI is the relatively high dose associated with CT. There are however two major challenges before a fully integrated simultaneous whole body PET-MRI scanner with quantitative PET data can be built. The first limitation is the need for compact MR compatible PET systems.

To enable Time Of Flight PET inside an MR system the photomultiplier tubes have to be replaced with new compact MR compatible readout technology based on Silicon Photomultipliers. Within the Hyperimage collaboration compact PET detector stacks have been developed: LYSO crystals are positioned on top of a SiPM layer, an ASIC layer and an interface layer. The first tests show an energy and timing resolution of 18 percent and < 530 ps. These will be used to construct a complete small animal system and a human system is planned. The other major challenge in PET-MRI is the derivation of a density map to correct the PET image for attenuation to enable quantitative PET-MRI. Specific to PET-MRI is the attenuation caused by the MR accessories.

We developed MR ultrashort echo time (UTE) based attenuation correction. This method does not make any assumptions on patient anatomy. Based on a dual UTE measurement we derive a patient specific R2 map and classify the different tissue types using treshold R2 values. The method has been tested on 5 brain studies and results showed quantification errors below 10 percent. Coil attenuation was measured : quantification errors up to 30 % were found due to this effect. The potential of using the MR for motion correction of the PET data is also explored within the Hyperimage collaboration.

Multimodality approach in the study of Tumor Angiogenesis: Magnetic Resonance Imaging (MRI), Synchrotron Radiation based micro-CT (SRμCT), Positron Emission Tomography (PET) and Histological Examination to follow the vessel formation

Abstract ID: 52

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Several imaging techniques are available to study the neovasculature during tumor angiogenesis. MRI provides information on morphology,blood volume (TBV),blood flow (TBF) and on the average vessel diameter (vessel size index,VSI),PET enables studies of metabolic activity. To visualize the 3D vessel architecture at a capillary level (5-10μm) SRμCT is needed.Validation of in vivo imaging data is achieved by comparison with histology.

The aim of this work was to characterize vessel formation in tumors using multimodal imaging strategies in order to elucidate multiple aspects of the angiogenic process.

Twelve balb/c nude mice were injected s.c. with 106 C51 cells (colon carcinoma). For a first validation study, anatomical images,TBV,TBF,VSI maps of 6 mice were recorded using MRI.The animals were sacrificed and the tumors explanted for SRμCT in phase-contrast and absorption modes.

Thereafter a longitudinal MRI-PET study has been carried out using 6 mice. Measurements were performed every 3 days.PET protocol consists of the injection of 18F-MISO to visualize the hypoxic regions. Histological examination was performed on every tumor using the endothelial marker CD31,hypoxic marker pimonidazole and perfusion reporter Hoechst. The data were analyzed using the standard medical images approach and a novel method based on fractal analysis.

The results display significant tissue heterogeneity in the growing tumor. Differences have been found with regard to morphological appearance, physiological behavior and degree of hypoxia. Images from SRμCT showed a chaotic structure of the vessel architecture.

By using complementary imaging modalities it is possible to analyze various aspects of the vessel network formation in tumor tissue yielding interesting mechanistic insight.

ClearPEM-Sonic: the combined positron emission mammograph and ultrasound elastography scanner

Abstract ID: 30

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Breast cancer is among the most frequent cancer types for women. The average life-time risk is about one eighth. As early detection leads to high cure rates, breast cancer screening is a priority in healthcare policies. However, conventional methods like X-ray mammography and echography show lesions but lack specificity. Additionally, those techniques are based on tissue density differences that complicate diagnosis in the case of dense breasts. It is thus important to provide additional means for early detection.

The Crystal Clear Collaboration developed a positron emission tomograph for mammography, the ClearPEM. It is based on LYSO:Ce crystals read out on both sides with avalanche photodiodes. This allows measuring the depth of interaction in the crystals with a precision of 2 mm and contributes to good spatial resolution and high sensitivity. Trials on the prototype confirm a spatial resolution of 1.3 mm.

For ClearPEM-Sonic, this performance is expected to improve as the light yield of the crystals has been increased by 20% whilst keeping the same depth of interaction and energy resolution.

Yet, the main objective is to improve diagnosis by combining metabolic information from ClearPEM with morphological and anatomical information from a new-generation ultrasonic transducer that objectively quantifies tissue elasticity, developed by SuperSonic Imagine.

The main challenge of combining both modalities is, aside from the mechanical integration, the fusion of both images to guarantee excellent mapping precision. This has been solved by immobilizing the breast and providing information about the position of both images in space via a combination of fiducial markers and high-precision positioning devices.

ClearPEM-Sonic is a CERIMED project with CERN as a partner.

$LaBr_3$ and LYSO monolithic crystals coupled to photosensor arrays for TOF-PET

Abstract ID: 66

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Positron emission tomography (PET) detectors based on a monolithic scintillation crystal coupled to a photosensor array can maximize scanner sensitivity and allow excellent intrinsic spatial resolution as well as depth-of-interaction (DOI) correction. Investigating the suitability of such detectors for time-of-flight (TOF) PET, we are focusing on the promising combination of fast and bright $LaBr_3$ and LYSO scintillation crystals with silicon photomultiplier (SiPM) light sensors that provide low noise, high gain and small transit-time jitter.

In order to correct for the time walk as function of the 3D annihilation photon interaction location in the crystal, a maximum likelihood estimation algorithm to determine this location was developed. It was applied to a 20×20×12 mm3 LYSO:Ce crystal coupled to a fast 4×4 multianode photomultiplier (Hamamatsu H8711-03) and a bare 18.2×16×10 mm3 $LaBr_3$:Ce(5%) crystal coupled to a Hamamatsu S11064-050P(X) 4×4 SiPM array. Throughout the LYSO crystal, the time walk spans a range of ~100 ps. Time walk calibration allows an event-by-event correction, resulting in an almost complete time walk cancellation. For the $LaBr_3$ detector, time walk vs. DOI spanned only ~15 ps. For 511 keV photons, a single detector timing resolution for the LYSO and $LaBr_3$ detectors of 305 ps and 225 ps FWHM, respectively, was achieved.

The intrinsic timing resolution of bare $LaBr_3$:Ce(5%) crystals coupled to SiPMs was studied using small (3×3×5 mm3) crystals coupled to single Hamamatsu MPPC S10362-33-050C SiPMs. For 511 keV photon pairs, a coincidence resolving time (CRT) of 101 ps FWHM was obtained.

The setup and analysis of the experiments will be presented and favourable conclusions for TOF-PET using sensor arrays on monolithic crystals will be drawn.

Optimization Of A Table-Top Synchrotron Light Source For Radiological Applications

Abstract ID: 95

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Within the Seventh Framework Programme (FP7) of the European Commission, a three-year project named LABSYNC has been recently funded with the aim of designing a complete small facility around the MIRRORCLE light source, a laboratory sized commercial synchrotron developed in Japan [1]. The Medical Physics group of Ferrara University is one of the seven partners of the LABSYNC consortium. Within the project, we will be responsible for the design of an X-ray imaging beamline for diagnostic and therapy applications owing to the broad experience in the physics of diagnostic radiology acquired through the years, in particular for the application of synchrotron radiation to mammography and the development of tunable quasi-monochromatic x-ray beams.

Preliminary investigations have confirmed the potential of small-scale synchrotron light sources for medical imaging applications. Indeed, Monte Carlo simulations have demonstrated that x-ray beams generated by the interaction of MeV electrons with target materials of diagnostic interest are far more intense than those generated by conventional x-ray tubes [2]. Furthermore, significant improvement in x-ray beam monochromaticity can be achieved by viewing the x-ray emission from a direction orthogonal or antiparallel to that of the incident electron beam. Since the energy range involved is significantly beyond the diagnostic range an optimization of x-ray detector characteristics is also desirable.

Finally, if electron beams with energies of about 20 MeV will be available then also monochromatic X-rays produced by Parametric X-ray Radiation might be tested.

[1] http://www.kuleuven.be/labsync/

[2] M. Marziani et al "Optimization of radiography applications using x-ray beams emitted by compact accelerators.", Med. Phys. 36, 2009.

Clinical and Pre-clinical applications spectral X-ray detectors

Abstract ID: 63

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Photon counting detectors are of growing importance in medical imaging since they enable routine measurement of photon energy within x-ray beams. Detectors such as Medipix2 and its successor Medipix3 record the energy of incident photons with minimal loss of spatial resolution. This is being investigated for both pre-clinical and clinical applications.

Early investigations and clinical guidance have suggested that computed tomography (CT) is an appropriate modality for incorporating these detectors. For CT, detectors need only cover an arc, typically 3cm wide and 100cm long. This can be achieved using a 2 X n array of Medipix detectors. In addition, CT can be performed with dead spaces and inhomogeneity across the active area. This is important because many sensor materials with high quantum efficiency, such as CdTe or GaAs, are difficult to produce and bond. Medipix detectors can achieve the necessary count rates for full body CT as they have very small pixels where each pixel counts at near megahertz rates. Clinical experience with dual energy systems (using kV switching) have shown that CT provides the most clinically relevant data because overlapping structures can be removed.

Applications currently under investigation by the Medipix3 consortium and its partners include:

K-edge imaging: Using spectral information to measure heavy elements (eg. pharmaceutical preparations of iodine, barium, and gadolinium).

Atomic substitution: This involves replacing potassium or calcium with chemical analogues such as strontium or rubidium.

Nano-particles: Nano-particles are being developed which are tailored to specific disease states. Medipix3 collaboration members are currently manufacturing nano-particles.

The MAGIC-5 lung CAD systems

Abstract ID: 23

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Lung cancer accounts for the most common cause of cancer-related deaths in the United States with some 160000 deaths, i.e. around 28% of all cancer deaths, expected in 2009. Low-dose X-ray Computed Tomography (CT) is a reliable tool in terms of lung cancer early diagnosis: the radiation dose for a screening session is smaller than that of clinical CT scans and lung nodules smaller in diameter are more likely to be diagnosed.

As a matter of fact, large scale screening programs based on lung CT scans are time consuming: each case report takes from 30 minutes to 1 hour. However, when assisted by Computer Aided Detection (CAD) systems, radiologists have been shown to perform with a better efficiency in terms of both sensitivity and time saving.

We present the CAD systems for lung nodule detection in chest CT scans developed in the framework of the Medical Applications on a Grid Infrastructure Connection (MAGIC-5) Project, granted by the Italian National Institute of Nuclear Physics (INFN). The project started as a spin-off of high energy physics software development and involves a community of researchers in constant contact with - some of them also involved in - Astroparticle and High Energy Physics experiments.

The MAGIC-5 CAD systems consist of several pattern recognition modules, based on statistical and adaptive algorithms:

i) lung parenchyma segmentation;

ii) detection of nodule candidates;

iii) feature extraction;

vi) false positive reduction;

v) classification of nodule candidates.

The systems were tested on CT scans from three different databases:

Italung CT, Trial database (20 CTs); ANODE09 competition (5 CTs); LIDC database (83 CTs).

The most relevant results, as well as the prospects, will be presented and discussed.

Prospects in medical imaging

Posters

The Atomic Force Microscope images of the nanostructure of red blood cells membrane under the action of ionizing radiation and other physicochemical influence

Abstract ID: 5

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After the influence of ionizing radiation and other different actions on the blood the erythrocytes can change their macrostructure and microstructure. This study provides the results of comparison of red blood cells membrane nanostructure after they have been affected by ionizing radiation and some farmchemicals.

Materials and method. The native blood was acted by external factors in vitro. The smears of erythrocyte monolayers were prepared. The images and spatial profiles of the cell surface were obtained by atomic force microscope. There was used spatial Fourier transform to decompose the initial complex profile into series of simple ones. This made it possible to compare surface parameters after exposure of red blood cells to different external actions.

Quantitative differences between membrane profile harmonic composition parameters (amplitude and spatial period) after physical impact (ionizing radiation, impulse electrical field) and after chemical impact (glutaraldehyde, perfluorocarbon) were experimentally confirmed. For ultraviolet radiation the height of nanostructures was 1,5 – 2 times greater than for normal erythrocytes. Such experimental and theoretical approach may lay down to analyze of mechanisms of different factors effect on red blood cells both in research and in clinics, in particular for the control of cell membrane structure after the working in zones with raised radiation level, in accelerators, after the radiation therapy.

AX-PET: Demonstration of an Axial PET Concept for Brain and Small Animal Imaging

Abstract ID: 13

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The AX-PET collaboration is developing a novel concept for high resolution PET imaging to overcome some of the performance limitations of classical PET cameras.

Our detector consists of a matrix of long LYSO scintillation crystals, axially arranged around the field of view, and Wave Length Shifter (WLS) plastic strips, orthogonal to the crystals. The energy measurement and the transverse coordinates (x, y) are provided by the crystals, while the axial coordinate (z) is obtained from the strips. Crystals and WLSs are individually read out by (B-field insensitive) G-APDs. The AX-PET concept allows for a true 3D and parallax free reconstruction of the photon's interaction point(s) in the crystal matrix with a spatial resolution which is in first approximation determined by the width of crystals and strips.

The sensitivity of the detector can be increased by adding (radially) crystal layers, without compromising the spatial resolution. The photon tracking capability allows identifying Compton interactions in the matrix (Inter Crystal Scatter). Simulations indicate that approximately 70% of those events can be fully reconstructed; the others can be discarded in order to maintain the full spatial resolution.

Two AX-PET modules – each with 48 crystals and 156 WLS strips – have been built. Dedicated front-end electronics and specific simulation and reconstruction software have been developed. The results of characterization measurements in the lab indicate a position resolution of better than 2mm in each of the three coordinates, excellent energy resolution (~12%) and a coincidence time resolution of 1.8 ns (all values are FWHM at 511 keV). Coincidence measurements with point-like sources and with with with PET phantoms are in preparation.

The biological effectiveness of Intra-Operative RadioTherapy (IORT) beams

Abstract ID: 18

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Intra Operative Radiation Therapy (IORT) is a combined treatment modality in which a large single dose of radiation is delivered concomitantly with tumor resection. IORT electron beams achieve dose rates that can be 100-fold greater than those used in conventional radiation therapy.

The biological effects of chronic dose-rate irradiations have been traditionally well studied in radiation biology. However, the actual effectiveness of the extremely high dose per pulse and dose rates delivered by IORT is presently not taken into account in treatment planning. Early breast carcinoma represents one of the tumors of choice for undergoing IORT.

We here report on the in vitro clonogenic survival for the breast cancer carcinoma MCF-7 cell line using an IORT beam as a function of dose rate and dose per pulse.

Region based MRI analysis for the early assessment of the Alzheimer's disease

Abstract ID: 20

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Neuroanatomical structures are affected by the interplay of genetic and environmental factors, age, and disease. Such effects are particularly true in healthy ageing individuals and in those who have neurodegenerative diseases. The ability to use imaging to identify structural brain changes associated with different neurodegenerative disease states would be useful for diagnosis and treatment. However, early in the progression of such diseases, neuroanatomical changes may be too mild, diffuse, or topologically complex to be detected by simple visual inspection or manually traced measurements of regions of interest. Computerized methods are being developed that can capture the extraordinary morphological variability of the human brain.

Neuroanatomical features can be compared within and between groups of individuals, taking into account age, sex, and disease state, to assess the structural basis of normality and disease. In this talk we will show our advances on structural MRI analysis taken on subjects affected by the Alzheimer's disease.

Hippocampal atrophy is characteristic of this disease but, since its assessment is often an error-prone and labour-intensive manual measurement, we provide a robust automatic analysis of a small brain region centered in the hippocampal area. As these images come from a variety of scanners and sites, we will show the strengths and limitations of our algorithms for the evaluation of a useful biomarker, and underline their potential as clinical and research tools. A brief note on the computational infrastructure, and a short comparison to other computer-assisted tools will also be given.

This work is funded by INFN within the MAGIC-5 project framework. Images and clinical data come from the ADNI database and the EADC group.

Production of monochromatic x-ray beams for medical imaging by using a table-top electron accelerator and parametric x-rays

Abstract ID: 22

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Monochromatic x-rays are very promising tool for low-dose high-quality medical imaging as well as for micro-beam and indirect radiotherapy. Besides, tunable monochromatic x-rays can broaden the diagnostic potential by producing dual-energy images. However, monochromatic x-ray beams with intensity needed for wide medical applications at present can be retrieved only from synchrotron light sources. Thus, progress in applications of monochromatic x-rays in life sciences depends on the availability of dedicated sources.

It was shown [1], that combination of a compact electron accelerator (energy some tens MeV, beam current ~ Ampere) and parametric x-rays generated by relativistic electrons in a crystal target can provide bright monochromatic x-rays with tunable energy (PXR source). Physics of the parametric x-rays is well studied by many research teams around the world [2], some examples of accelerators also exist, and thus feasible monochromatic x-ray source can be developed. For instance, LABSYNC project [3] has been recently funded by the EC with the aim to develop a complete light facility around the laboratory synchrotron [4].

The report proposes evaluations of achievable parameters for medical PXR source, describes problems such as target heating and damage, discuss challenges such as an accelerator beam properties and x-ray optics for x-ray beam conditioning and control.

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3. Di Domenico G. et al // Proc. 51st Workshop of INFN Eloisatron, in press

4. Yamada H. // NIM B199 (2003) 509

Investigation of an Amorphous Silicon Detector for Ion Radiography

Abstract ID: 25

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Ion beam radiation therapy is a highly precise form of cancer therapy, which requires accurate knowledge of the dose delivered to the patient. Dose calculations are performed based on x-ray computed tomography (CT). However, since CT uses photon attenuation for the acquisition of images, the stopping power for heavy ions can only be determined with an increased uncertainty. Ideally would be to image the patient directly with the ion beam by measuring the energy loss of high-energy ions traversing through the patient.

Amorphous silicon detectors widely-used for portal imaging on linear accelerators show excellent response uniformity and reproducibility. Therefore it stands to reason to investigate amorphous silicon detectors for ion radiography.

Our straight forward approach to show the feasibility of the a-Si:H detector is to image a frozen knuckle of pork with proton and carbon ions of different energies. Radiographic measurements have been carried out at the Heidelberger Ion-Beam Therapy Center (HIT). The object has been irradiated with a constant ion beam energy in a homogeneous field. The response behind the object has been measured with an amorphous silicon detector RID256L, a commercially available flat-panel supplied by Perkin Elmer, Inc. (D-65199 Wiesbaden, Germany). The signal of the detector has been corrected for dead pixels and the homogeneity of the detector response.

The corrected radiographies show a clearly visible knuckle of a pork. The image information is energy and particle species dependent.

The RID256L a-Si:H detector was shown to be a promising candidate for ion radiography. Proton and carbon ion radiographies with biological samples are viable. Further studies are needed to improve the quality of the acquired images.

Performance Evaluation of SiPM Photodetectors for PET Imaging in the Presence of Magnetic Fields

Abstract ID: 33

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PET detector modules able of work in the pressence of strong magenitc fields would provide extremely useful for in-beam PET studies as wellas in combined MRI and PET detectors, and thus they are being actively seeked by many groups. To overcome the effect of intense magnetic field in photomultiplier tubes, alternate photon detecting devices are being tested, such as the multi-pixel photon counter (MPPC) or silicon photo-multiplier (SiPM), recently introduced as a solid-state photodetector, which consists of an array of Geiger-mode photodiodes (microcells). It is a promising device for PET due to its potential for high photon detection efficiency (PDE) and its foreseeable immunity to magnetic fields. It is also easy to use with simple read-outs, has a high gain and a small size.

In this work we evaluate the in field performance of three 1×1 mm2 (with 100, 400 and 1600 microcells, respectively) and one 6×6 mm2 (arranged as a 2×2 array) Hamamatsu MPPCs for their use in PET imaging. We examine the dependence of the energy resolution and the gain of these devices on the temperature and reverse bias voltage, when coupled to LYSO scintillator crystals under conditions that one would find in a PET system. We find that the 400 and 1600 microcells models and the 2×2 array are suitable for small-size crystals, like those employed in high resolution small animal scanners. We have confirmed the good performance of these devices up to magnetic fields of 7 Tesla as well as their suitability for performing PET acquisitions in the presence of fast switching gradients and high duty radiofrequency MRI sequences.

Real Time Imaging of Stopping Distributions in Biological Targets for Antiprotons

Abstract ID: 43

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Antiprotons are interesting particles that have special properties when used in possible cancer particle therapy. They behave almost the same as protons in the entrance channel but deposit additional annihilation energy when they come to rest in the Bragg peak region. Thus, the number of antiprotons can be reduced while still delivering the same target dose to the tumor. Healthy tissue in the entrance channel is harmed less compared to protons which is a ultimate goal for cancer treatment.

Additionally, annihilation energy partially goes into the creation of new particles, especially pions. They exit the body mostly non-interacting and can be detected with an external detector, enabling a real time supervision of the irradiation process. This is currently not possible in any particle treatment method.

In our contribution we will present first results of the recent experiment carried out with the Antiproton Cell Experiment (ACE) at CERN's Antiproton Decelerator (AD) using a low-cost real time detector setup. Furthermore, we will compare them to simulations and develop improved set-ups for future experiments.

Novel thin scintillating crystalline materials for high resolution imaging

Abstract ID: 45

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Ce^{3+}-doped YAG or LuAG garnet crystals belong to fast, high light yield, mechanically and chemically stable scintillators that can be used in high-resolution 2D-imaging applications [1] (down to mum range). Ce^{3+}-doped YAG or LuAG thin plates coupled to CCD detector were used for high resolution imaging [1]. Besides Ce^{3+} dopant we also looked for novel scintillators, namely (Y-Lu)AG garnets doped with other rare earth ions as Eu^{3+} or Pr^{3+}. These new dopants or previously mentioned Ce^{3+} influence and change (Y-Lu)AG emission (peaking from the UV to the red visible ranges), their scintillation efficiency and decay time. Different properties of these scintillators allow us to select the most suitable ones to be used with various detectors as CCD's, PMT,s or Si-diodes. E.g. LuAG:Pr in the UV emitting scintillator is the promising one for high resolution imaging with in the UV sensitive CCD or PMT due to shorter emission wavelength while in the red emitting LuAG:Eu one can spectrally match better to CCD or Si-diode photodetectors. Recently, except the Cz-grown bulk (Y-Lu)AG crystal scintillators also thin film systems manufactured by Liquid Phase Epitaxy (LPE) method became of interest [2].

The main goal of this presentation is to summarize scintillation and spectroscopic properties of thin Cz-grown plates or LPE layers of the doped by selected rare earth ions (Y-Lu)AG scintillators including measurements of their scintillation responses [2] and 2D-imaging with different CCD's, PMT's or diode photodetectors.

[1] J. Tous, M. Horvath, L. Pina, K. Blazek and B. Sopko, NIM Phys. Res. A 591 (2008), 264-267.

[2] P. Prusa, M. Nikl, J.A. Mares, M. Kucera, K. Nitsch and A. Beitlerova, Phys. Stat. Sol. A 206 (2009), 1494-1500

Performance test of a compact gamma camera for nuclear and medical physics applications

Abstract ID: 46

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The gamma camera consists of a 76 mm diameter and 3 mm thickness cylindrical continuous LYSO (Lutetium Yttrium OxyorthoSilicate) crystal optically glued to the surface of a crossed-wire multianode position sensitive photomultiplier tube (PSPMT) R2486 from Hamamatsu photonics.

We implemented a novel individual multianode readout approach (IMAR) in combination with a sophisticated position reconstruction algorithm [1]. The method allows exploiting better the intrinsic characteristics of the PSPMT, thus yielding excellent position linearity and improved spatial resolution of 1 mm (FWHM) over the complete photocathode surface.

We achieved a useful circular field of view of 20 cm^2 substantially larger than the field of view of a conventional resistive network based system. Although the developed gamma camera is intended to be used for the pulse shape characterisation of HPGe detectors, it can also be used for medical physics applications because of its unprecedented performance.

[1] C. Domingo-Pardo, N. Goel, J. Gerl, T. Engert, I. Kojouharov, H. Schaffner, I. Masahiro, "A position sensitive - ray scintillator detector with enhanced spatial resolution, linearity and field of view", IEEE Transactions on Medical ImagingVolume 28, Issue 12, Dec.2009.

High Resolution X-ray Microradiography

Abstract ID: 50

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High resolution X-ray camera for micro-radiography based on CCD detector and precise thin YAG:Ce or LuAG:Ce single crystalline screens and its different applications will be described and presented.

YAG:Ce or LuAG:Ce inorganic crystal scintillators are characterized by good mechanical and chemical stability, non-hygroscopicity, high scintillation efficiency and fast decays [1]. Screens prepared from these crystals can be used in equipments for detection of different kinds of radiation and particles (UV, VUV, electrons or ions or their beams, X- or gamma rays).

The high resolution X-ray camera consisting of high sensitivity digital CCD detector and thin YAG:Ce or LuAG:Ce scintillator imaging screen can be used in the low-energy X-ray radiation monitoring (up to 40 keV) [2]. The X-ray CCD camera was tested either with several small biological objects (insect or small animals) or with special grids. The 2D-spatial resolution achieved in the images was about 1 micron [2].

The 2D-spatial resolution of an X-ray or other ionizing radiation imaging systems is one of the critical parameters in non-destructive micro-radiography and radiation beam inspection. The main goal of this presentation is to compare different 2D-imaging systems and their 2D-resolution which can be in the micrometer range. These imaging systems can use various 2D PSD detectors (position-sensitive detector). Specifically, we will compare thin YAG:Ce or LuAG:Ce single crystalline screens with those based on the phosphor scintillating powders [2]. Finally, we will demonstrate the usage of X-ray CCD camera in imaging of very small biological objects (with 2D-resolution in the sub-micron range).

[1] J.A. Mares, et al., Rad. Meas. 38 (2004), 353-357.

[2] J. Tous, et al, Rad. Meas. 42 (2007), 925-928.

Gamma Spectroscopy of inorganic scintillators and their potential imaging applications

Abstract ID: 51

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Hybrid Photon Detectors (HPD) or Hybrid Photomultipliers (HPMT) are new kinds of photon detectors consisting of only a photocathode and Si-PIN diode used as an anode [1,2]. HPMT tubes are used at CERN for characterization of scintillating crystals, especially $PbWO_4$ (PWO) ones because they are used in CMS electromagnetic calorimeter or ALICE photon spectrometer PHOS. Recently developed HPD are used in Ring Imaging Cherenkov (RICH) detector of LHCb experiment.

The main goals of this presentation are: (i) to present properties of HPMT alone, (ii) to describe HPMT based gamma spectroscopy experimental set-up and its options and (iii) to present and summarize scintillation characteristics (photoelectron or light yields, energy resolution, proportionality etc.) of various inorganic scintillators the response and properties of which are between those of PWO (L.Y. of several ph/MeV) and CsI(Tl) (L.Y. ~ 60×103 ph/MeV). We will survey the scintillation characteristics of the Ce^{3+} or Pr^{3+}-doped aluminum garnets and perovskites. All measurements were carried out using HPMT set-up [1,2] under excitation of various gamma-ray lines (in the range 8 keV – 2.5 MeV) on either thin crystal samples (1 mm thickness) or on larger ones of ~ 1 cm3 volume.

Finally, we mention possibilities of applications of these scintillators in optoelectronic imaging accessories [3], especially in the systems for medical imaging.

[1] C. D'Ambrosio and H. Leutz, NIM Phys. Res. A 501 (2003), 463-498.

[2] J.A. Mares and C. D'Ambrosio, Opt. Mat. 30 (2007) 22-25.

[3] C. D' Ambrosio, H. Leutz, D. Piedigrossi, E. Rosso, V. Cencelli, F. De Notaristefani, G. L. Masini, D. Puertolas, F. Cindolo, J.A. Mares, M. NikI, M.

Improving Image Quality In Positron Emission Tomography

Abstract ID: 53

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The research activities of our group are aimed at improving image quality in PET by developing dedicated models and algorithms for image reconstruction and compensation of degradation phenomena.

Given a PET scanner, sensitivity can be increased by broadening the energy window. In small animal PET, where sensitivity is a crucial aspect, this approach allows more true coincidences to be registered, at the cost of an increase of scatter events. While in small animal PET object scatter is often neglected, inter-crystal scatter (ICS) can be very relevant, especially in novel scanner configurations made of small crystals and several radial layers. For low thresholds under 255 keV, ICS results in more than 2 signals per coincidence (multiple coincidences). These coincidences contain potentially useful information, and could be therefore used to increase sensitivity. On the other hand, multiple coincidences also affect the detected randoms rate, which cannot be accurately estimated using conventional methods.

In our group, we focus on image formation and degradation in PET from the basis: the 1st step is using efficient selection methods to identify as many true coincidences as possible, while reducing randoms. For this aim, we revisited conventional techniques and developed a new approach based on neural networks. A 2nd step is compensating for random coincidences. We demonstrated the weakness of well-established methods and developed a new approach to improve the singles rate method. We have also implemented strategies to include ICS in the reconstruction, and developed a novel algorithm to compensate for patient motion during the reconstruction. In parallel, we work on accelerating the reconstruction using GPUs and alternative pixelation schemes (based on polar pixels).

Silicon Photomultipliers in PET and hadrontherapy applications

Abstract ID: 62

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Silicon photomultipliers (SiPMs) offer an advantageous alternative to conventional photomultipliers in different fields. Since their recent development, an increasing number of groups is testing their application to medical imaging. Their characteristics allow to improve the performance of conventional devices, and also to implement innovative solutions in different applications.

A small animal PET tomograph with continuous LYSO crystals and finely granulated SiPM matrices is expected to have a spatial resolution better than 1 mm FWHM. Continuous crystals provide a high intrinsic spatial resolution and higher efficiency than pixellated crystals. SiPMs allow to stack several detector layers to enhance the efficiency while reducing the parallax error. A detector head with monolithic SiPM matrices has been built and characterized.

In hadron therapy it is essential to verify precisely the amount of dose delivered to the patient. Nuclear fragmentation is followed by the production of secondary particles, including single photons up to about 15 MeV. A Compton camera detector makes it possible to detect and locate the origin of these photons, allowing to estimate the delivered dose. A Compton detector consisting of $LaBr_3$ crystals coupled to SiPMs is an interesting option to detect such photons, since it provides a high detection efficiency at high photon energies.

These novel applications will be presented and discussed, and progress results will be shown.

Advances in photodetection and Read-Out electronics for PET applications

Abstract ID: 64

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PET is acknowledged to be the best functional imaging technique in clinic and in preclinical research. Better image quality and shorter scanning times require an improvement of the detectors performances especially in terms of spatial and energy resolution and sensitivity. Time resolution is also important for the improvement of the signal to noise ratio.

The advent of multimodality imaging techniques has also motivated the research on PET/MRI integrated systems where the PET detectors must be compact, insensitive to magnetic fields and not affecting the MR signal.

Scintillating crystals read-out by solid-state photodetectors could represent the key solution to all these demands. Silicon Photo Multipliers (SiPMs) are nowadays a mature technology exploited for various applications in nuclear medicine. The DASIPM2_INFN experiment developed in collaboration with FBK-irst matrices of SiPMs on the same silicon substrate with the aim of preserving the spatial resolution capabilities of the SiPM but on a larger sensitive area.

The design and fabrication of monolithic SiPM matrices started from the first prototypes of 2 x 2 pixels, 1 mm^2 each, to the latest 8x8 pixels, 1.5 mm^2 each (1 cm^2 active area), the largest SiPM matrices on a single substrate produced so far. The reconstructed image of a point-like ^{22}Na source put in front of a 8x8 SiPM matrix coupled to a 12x12x5 mm LYSO crystal provided a spatial resolution of less than 1 mm FWHM, the world best performance ever achieved to our knowledge. An 8-channel ASIC, suitable for the read-out of SiPM arrays has also been designed and manufactured following the current-mode approach exploited in the analog first stage to fulfil the severe constraints imposed by the SiPMs in terms of of dynamic range and speed of operation.

CERIMED : A European and Multidisciplinary Open Campus for Research on Medical Imaging

Abstract ID: 72

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Medical Imaging is continuously challenged by steady progress in medicine and biology.

Research and Development in Medical Imaging requires a large pluridisciplinary effort and important infrastructures to efficiently bridge the technological developments to the health world. Contributions from the academic and industrial sectors are essential and must converge to a place where the assembly of large scale prototypes, integrating novel technologies and new concepts, will allow their assessment and full validation in a well organized preclinical and clinical environment.

CERIMED, the European Center for Research in Medical Imaging, is a European Open Campus aiming at this ambitious goal.

This large 30M€ infrastructure is presently in construction in the heart of the university hospital Timone in Marseilles, France, and will be fully operational at the end of 2011. It will run as a facility for research laboratories and industries but also liaise with large national imaging centers in Europe and as such, contribute federating the different actors working in the field of biomedical imaging.

This talk will give a status of this project and explain how it will welcome large international collaborations addressing some important challenges of the future healthcare mission. A description of the different sectors (technology, radiopharmaceutical, preclinical. clinical) will be given. A few examples from the ongoing technological and clinical projects already launched will be shown to illustrate the potential of this approach and the strong momentum it can provide to the different sectors.

Timing performance of a TOF-PET detector system developed at CERN using SiPMs

Abstract ID: 76

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In view of the numerous spin-offs from the technological developments at CERN's Large Hadron Collider and its experiments, we report on a R&D program to extend the application of these cutting-edge technologies to other domains, such as medical imaging. Not only for positron emission tomography (PET), this work will likewise respond to the need to develop new ultrafast photodetection for the future linear colliders with unprecedented beam intensities.

High time resolution has become a prerequisite for time of flight (TOF-) PET if improved signal-to-noise ratio images, lower exposure rates and faster image reconstruction are required. The majority of commercial PET installations does not use TOF and is therefore limited to a timing precision at the level of ~2ns FWHM. The only commercial systems using TOF developed so far are the Philips "TruFlight" with 650ps and a new Siemens facility with 550ps temporal resolution.

The possibility to achieve time resolutions of ≤200ps, requires a substantial improvement in light production, -transport and transfer from the scintillator to the photodetector. Other light emission mechanisms, like Cerenkov emission, have also been considered and measured. This work summarizes our measurements employing LSO-SiPM photodetectors together with ultrafast discriminators, originally developed for the ALICE experiment, in a 'time-based' readout architecture. In a PET-like arrangement such a system yielded a time resolution of ≤350ps. It is shown that time resolution is dominated by the scintillator geometry and the Poisson-like arrival of scintillation photons at the photo-detector. Special timing tests were run with un-doped LuAG crystals emitting only Cerenkov photons. In this scenario, a time resolutions of 250ps was achieved.

Position-sensitive detector for animal PET tomography

Abstract ID: 77

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The presented work was to show the possibility of creating position-sensitive detector for annihilation gamma-quanta with spatial resolution of 1-2 mm. Hodoscopic photomultipliers were used as position-sensitive photomultipliers.

Hodoscopic photomultipliers allow for point-to-point correspondence of stand-alone scintillation detector element and coordinate position on the surface of photomultiplier`s photocathode. 2x68 thin plastic scintillators with 1x1 mm^2 cross section were used in the detector. The acquired spatial resolution was about 1.2 mm with 80 % annihilation gamma-quanta registration efficiency.

Progress in the domain of physics applications in life science with an invention for substantial reduction of premature cancer deaths: the need for a paradigm change in oncology research

Abstract ID: 78

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Despite annual cancer costs of $741 billion/yr ($750/citizen), the 38 most industrialized nations had only 5% reduction in cancer deaths over the past 50 yrs (heart disease was reduced by 64%). This article provides links to source data (from Government Agencies and WHO), easily verifiable by laymen. It analyzes why cancer costs increased about 100 times over the past 50 yrs and why cancer death reduction is nearly the same in less industrialized countries with much lower costs. It analyzes past errors to help correct them and identify new ways for the future. One striking solution is Crosetto's innovation for improving particle detection (recognized by an int'l review panel at FERMIlab, 1993). When applied to medical imaging, it can drastically reduce cancer deaths. Together with his other inventions, Crosetto conceived the innovative 3D-CBS technology (www.crosettofoundation.org/uploads/335.pdf), 400+ times more efficient than current 5000+ PET. This results in greatly reducing radiation dose and costs, permits extensive screening for early cancer detection of high risk people (essential for cancer survivors), dramatically increasing their chance for survival, making it imperative to immediately fund Crosetto's innovative project. If not, other solutions claiming greater potential should be pointed out, a forum organized for reviewers and authors claiming higher impact. Each author needs to support claims, consistent with the law of nature and ultimately judged by experimental results. This article provides procedures to ensure funding only the best proposals. Because the goal of cancer research is to promote solutions to greatly reduce premature cancer deaths at lower cost/life saved, each proposal should clearly state estimated death reduction, costs and duration.

Design and construction of the ClearPET/XPAD small animal PET/CT scanner

Abstract ID: 79

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The XPAD3 detector is a silicon photon counting detector developed at CPPM. It is made of 8 modules tiled to obtain a 12 x 7.5 cm^2 detection surface. Each module is composed of a silicon detector connected to 7 XPAD3 circuits using bump bonding and flip-chip technologies. Each chip is composed of 9'600 pixels of 130 µm.

The complete detector has more than 0.5 Mpixels. Every pixel includes a 12 bit counter with overflow. The scanning of the changes on the overflow bit allows to increase the image's dynamic range almost without limitations, but the depth of the software encoding. Important features of the detector are its programmable energy thresholds and the fast data with no dead-time during exposure. But the most interesting and exciting feature is the possibility to set the energy thresholds individually for every pixel dynamically. In biomedical imaging, this feature can be used to optimize detection of a contrast agent, while reducing the total dose of exposure.

We present a small animal hybrid PET/CBCT scanner for simultaneous X and gamma ray scans of the same field of view. It is based on the ClearPET phoswich detectors and on the XPAD3 detector. The complete hybrid system has been studied using the GATE Monte Carlo simulation platform. The final design includes the PET detectors appropriately shielded, the XPAD3 detector and a RTW X-ray tube with a Mo target. First measurements in presence of an X-ray beam scattered by a water phantom that hosts a positron emitting point source will be presented as well as images of mice and phantoms reconstructed from simultaneous PET/CT data acquisitions.

Energy resolution analysis of SiPM-based Gamma locator

Abstract ID: 80

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Gamma locator is a probe with diameter of 1 cm and length of 15 to 20 cm.

The probe consists of the radiation detecting part and the electronics part. The conducted energy resolution analysis has shown the possibility of creating SiPM-based Gamma locator in 70-700 keV energy area with LYSO and LSO crystals. Using the new scintillator $LaBr_3$:Ce we managed to increase signal/noise ratio by two orders.

The results presented show gamma locator energy resolution comparison for different SiPM and photomultiplier tubes. The best energy resolution was shown by MPPC Hamamatsu as photodetector and LYSO scintillator and was about 6%.

Dose monitoring in ion therapy by means of prompt radiation

Abstract ID: 85

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We present ongoing studies aiming at providing a real-time control of the dose distribution during ion therapy. Our goal is to implement combined modalities for real-time quality control of the deposited dose for future ion therapy centers. Several modalities are under development within this research program, including in-beam TOF-PET, in-beam prompt gamma and single particle imaging.

Prompt gamma imaging looks very promising in view of recent preliminary results, provided TOF is used to discriminate gamma from neutrons and scattered particles.

Preliminary studies have shown that, using a collimated gamma detector, the detected longitudinal photon profile is correlated to the ion range. Moreover, the count rate is compatible with a real time control of the Bragg peak position during a treatment.

Significant discrepancies are observed between our data and the yields calculated by Geant4, which stresses the need for the improvement of the nuclear models used in this code.

We are now developing a collimated detection setup, as well as a Compton camera, designed with the help of simulations.

In parallel, simulations and measurements are undertaken to study the possibility of using light charged particles for beam monitoring during carbon ion therapy, as well as TOF-PET acquisition between beam pulses.

Common electronics and DAQ are under development among CNRS labs for these imaging modalities.

These studies are carried out in the frame of the Rhône-Alpes Regional Research Program for Hadontherapy, and within the national project Nuclear Instruments and Methods against Cancer, driven by the CNRS-GDR MI2B.

Progress in the domain of physics applications in life science with the 3D-CBS invention for substantial reduction of premature cancer deaths: an optimized PET for low cost low radiation dose high efficiency cancer screening

Abstract ID: 87

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Experimental data demonstrate early detection obtainable through screening people at high risk saves lives. Signals most reliable for early detection show change in metabolism (up to 70 times higher in cancerous cells) at the molecular level. Early detection is achieved by accurate capture of all possible signals from tumor markers showing abnormal metabolism.

Current PET exams are costly and require a radiation dose over 10 times higher than ICRP recommends as safe for screening. Innovative 3D-CBS technology can capture simultaneously and accurately maximum signals from tumor markers from all organs to identify the smallest anomaly, at lower cost per signal captured, requiring minimum radiation. Increased efficiency and lower cost are obtained by the interrelation of inventions in physics, geometry, data-flow, system architecture, electronics, detector assembly, etc. This workshop, designed to stimulate discussion, provides an ideal opportunity to understand these complex interrelations and details of this invention through an oral presentation with answers to audience questions.

Innovations enable the construction of a cost-effective 3D-CBS device (www.crosettofoundation.org/uploads/336.pdf) with longer FOV, using economical crystals capable of accurate measurement of, a) total photon energy by weighting signals from 9 electronic channels, not current PET's 4; b) photon arrival time (TOF); c) spatial resolution of incident photons in the crystal: "x, y" coordinates and DOI; d) signal-to-noise ratio, possible because of capability to execute complex algorithms in real-time, sustaining high input data rate. Higher efficiency and more accurate measurements allow early diagnosis of cancer with reduction of false positives and false negatives at a lower examination cost.

Early detection of diseases by detecting small lesions with MRI compatible amplifying PET/TOF or SPECT probes using SiPM photodetectors

Abstract ID: 90

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Molecular imaging plays a crucial role in the modern medicine because of the capability of detecting early or hidden lesions. Radionuclides techniques allow imaging of the abnormal biological processes with very high sensitivity and resolution.

A way to improve these parameters is using small FOV probes close to the lesion together with larger FOV detectors thus enabling to focus small lesions while achieving the imaging of the entire organ. The detector placed next to the lesion determines the spatial resolution and sensitivity. Anatomical functional and molecular information so combined modalities improve the power of the system.

Examples will be presented of detectors for breast and prostate cancer diagnosis. A dual single photon detector for breast cancer has been built: a high resolution, high sensitivity small detector focusing the suspicious lesion and a larger one imaging the entire organ. The results of clinical trials show the advantages of this approach.

Our collaboration launched a project on a PET/TOF and SPECT MRI&MRS detectors for diagnosis of prostate cancer:a small endorectal probe coupled with a standard PET scanner. MRI has been chosen as anatomical modality because soft tissues are involved and for its MRS diagnostic capability. TOF provides advantages to the PET imager in terms SNR. It allows to get rid of the background of the bladder.The challenge is to design SiPM based detectors with proper scintillator and electronics. The role of a proper radiotracer will be examined. Measurements with LYSO scintillators coupled to SiPMs showed DOI resolution ~ 1mm. TOF measurements with SiPM compared to PMT and the compatibility up to 14 Tesla fields will be presented. Examples will be given of the extension of the technique to other applications, vascular diseases, breast

Medical application of spin-polarized He-3

Abstract ID: 91

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Polarization of He-3 by optical pumping techniques is well known since the early 1960ies with first applications in fundamental physics experiments. In 1994 it was discovered that one can use hyperpolarized He-3 as contrast agent for magnetic resonance lung imaging (MRI). Nowadays imaging with spin-polarized He-3 became more and more present in MRI diagnostics of the lung. MRI with hyperpolarized He-3 is an investigational technique to obtain high-resolution images of the airspaces following inhalation of spin-polarized He-3 gas. It is a sensitive method for the detection of ventilation defects and has been applied to a variety of lung diseases such as chronic obstructive pulmonary disease and asthma. The wide interest in this new method made it necessary to find ways of polarizing He-3 in large quantities with high polarization degrees.

The polarization apparatus in Mainz is based on the method of optical pumping of metastable He-3 atoms in a weak gas discharge at a gas pressure of about 1 mbar. Our concept of production of the hyperpolarized He-3 gas includes a remote type of operation, where the He-3 is spin-polarized in a central production facility from where it is transported to users. The hyperpolarized gas is stored and transported in relaxation-poor glass vessels, which are blown from iron free glass. Without internal coating, polarization decay times of up to 200h are observed, sufficient for shipping the hyperpolarized gas all around the world using specially designed transport units, which provide a homogeneously magnetic field to guide the spins. After usage the He-3 gas can be recovered, the transport vessels are refilled with freshly polarized gas and the cycle starts again.

Extension and validation of an analytical model for in-vivo PET verification of proton therapy – a phantom and clinical study

Abstract ID: 93

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The interest in Positron Emission Tomography (PET) as a tool for treatment plan verification in proton therapy has become widespread and its relevance continues to increase. The imaging-based strategy takes advantage of the nuclear inelastic reactions occurring between protons and nuclei in tissue during irradiation, leading to small amounts of β^+-emitting isotopes.

For successful implementation of the PET methodology for the clinical routine monitoring, a positron emission scanner and a reconstruction algorithm are nevertheless not sufficient to complete the quality assurance process. In fact, since the thresholds of inelastic nuclear reactions leading to tissue β^+-activation fall within the energy range of 15-20 MeV, the distal activity fall-off is correlated, but not directly matched to the distal fall-off of the dose distribution. Moreover, the physical interactions leading to β^+-activation and energy deposition are of different nature.

All these facts make it essential to further develop accurate and fast procedures capable to predict the expected PET images for comparison with the actual PET measurements in order to provide clinical feedback on the correctness of the dose delivery and of the irradiation field position.

The aim of this study has been to extend, with a view to an in- room PET application, an analytical filtering model and to implement and evaluate it in a fast and flexible framework to predict locally such activity distributions taking directly the reference planning CT and planned dose as inputs. The results achieved in this study for phantoms and clinical cases highlighted the potential of the implemented analytical model to substitute the sensitive and time-consuming Monte Carlo approach for the calculation of expected activity distributions.

3 gamma medical imaging using liquid xenon and ^{44}Sc radio nuclide

Abstract ID: 105

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The use of a liquid xenon Compton telescope to measure γ-rays for medical imaging applications is under study at Subatech. We report on a new nuclear medical imaging technique based on the direct 3D localization of each radio-nuclides disintegration with a spatial resolution of the order of 1 cm. Such measurement could be realized thanks to a new kind of radio-nuclides which emits a γ-ray quasi simultaneously with a positron.

The imaging principle is to reconstruct the intersection of the classical line of response associated to the positron annihilation with the direction cone defined by the third γ-ray. The most interesting radio-nuclide candidate, namely the ^{44}Sc, will be potentially produced at the Nantes cyclotron ARRONAX. To reach this objective, a R&D program and GEANT4 based simulations have been started in parallel.

The interest of the 3 γ technique was demonstrated in the case of small animal imaging, and the simulation of a liquid xenon camera for human body imaging based on the GATE toolkit is in development. A preliminary study of a liquid xenon Compton telescope used for proton therapy monitoring will also be presented. A small liquid xenon TPC prototype measuring both ionization with a micromegas structure and scintillation signal with a Gaseous PhotoMultiplier (GPM) is currently being tested at Subatech.

High accuracy detectors for medical applications and synchrotron radiation research

Abstract ID: 106

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In the present report, we summarize our experience in development of high resolution position sensitive gas detectors for medicine and synchrotron radiation experiments in Budker Institute of Nuclear Physics during last years.

We designed several modifications of Multistrip Ionisation Chamber with a pitch of channels from 0.4 down to 0.1 mm. Application of these detectors with high quantum efficiency (>65%) in a scanning system allowed to perform a high quality diagnostic imaging. The comparative parameters list of the detectors will be presented.

The detector with 0.1 mm strip pitch and 20 atm pressure of Xe demonstrates the best possible DQE and spatial resolution for gaseous detectors in wide range of X-ray energies. Additionally the results of feasibility study of the detector for beam position monitoring for Heavy Ion Therapy System will be presented.

Polar Pixelization in High Resolution Small Animal PET

Abstract ID: 113

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Reconstruction of PET data using iterative methods is a common approach in clinical and pre-clinical environments, given the increase in performance that computers have exhibited in the last few years. These methods are based on a system matrix that relates the probability of detecting an annihilation originated in a certain voxel in a specific detector element. The size of these system matrices is scalable to the number of voxels that comprise the field of view (FOV) and the number of lines of response, which makes the total size of these matrices intractable for regular computers. This matter has attracted the attention of some groups, proposing polar pixels and the like as an alternative to reduce significantly the size of the system matrix.

This work is focused on the prototype small animal scanner MADPET-II. MLEM is used as reconstruction method for all the pixelization schemes presented here. To improve image quality, we calculate the system matrix using Monte Carlo simulations (GATE). However, this approach is computationally expensive and therefore, the use of polar pixels to reduce the burden of generating and handling the system matrix is very attractive.

For this purpose only a small fraction of the FOV of the full scanner is simulated, reducing also the simulation time. Several alternatives for pixelization using polar pixels are presented, reducing the size of the system matrix down to 2% of the original size. Comparison of performance between pixelization approaches is studied aimed at finding an optimum alternative, compressing the system matrix without introducing any sort of extra artifacts due to the compression. For this purpose several phantoms have been simulated to assess the potential resulting artifacts in the reconstructed images.

Imaging a proton beam for eye cancer therapy with LHCb VELO microstrip detectors

Abstract ID: 115

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The silicon microstrip detectors for the LHCb Vertex Locator are arranged in double sided modules placed perpendicurarly to the beam to provide the radial and azimuthal hit point with high resolution.

The 300 micron thick half-circular detectors are designed to be sensitive to an inner radius of 8mm from the beam line. This particular geometry seems to be suitable for measuring the halo of a charged particle beam and therefore provide precise beam position and profile information (beam diagnostic) without interfering with the beam itself.

A first series of measurements to investigate this use of the VELO sensors has been performed with the therapeutical 62 MeV proton beam for eye cancer therapy of the Clatterbridge Centre for Onchology in the UK. The preliminary results of the beam profile and beam halo imaging are here presented.

Design guidelines for a Compton camera for prompt-gamma imaging during ion beam therapy: a Monte Carlo simulation study

Abstract ID: 124

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In order to take advantage of the assets of ion irradiation, the position of the Bragg peak has to be monitored accurately. It was recently shown that the detection of the prompt-γ emitted quasi-instantaneously during the nuclear fragmentation processes with a collimated scintillator detector makes it possible to locate the Bragg peak during proton or carbon ion irradiations. It was also shown that the TOF technique can be applied to discriminate γ-rays from the neutron background.

The use of a double scattering Compton camera with a beam tagging device is investigated to improve the detection efficiency. For the Compton camera, we propose to use two silicon strip detectors and one pixellated LYSO detector. The prompt-γ emission points are reconstructed by intersecting the ion trajectories given by the hodoscope and the cones reconstructed with the camera.

We studied the camera response to a photon point source by means of Geant4 simulations. More precisely, the nature of all the interactions which are likely to produce an energy deposit in the three detectors of the camera was analyzed. It was underlined that upper energy thresholds in both scatterers are required to select mainly Compton events (1 Compton scattering in each scatterer and one interaction in the absorber). We also studied the influence of various parameters such as the photon energy and the inter-detector distances on the camera response.

In the current configuration, for a photon source with a typical prompt-γ spectrum, the spatial resolution of the camera is about 6 mm (FWHM) and the detection efficiency 10^{-4} (Reconstructible photons/Emitted photons in the direction of the first detector). Finally, provided the detection efficiency is increased, the clinical applicability of our system is considered.

Charged Particle Imaging for real-time control during ion therapy

Abstract ID: 131

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The aim of this study is to monitor efficiently the path of the beam inside the patient during a carbon ion therapy treatment session. We use the fact that, at an energy of 300 MeV/u, 55% of the incoming ions will undergo fragmentation processes, and half of these fragments will induce nuclear reactions too. Moreover, there is a strong correlation between the primary ion range and the production yield of secondary charged particles coming from these fragmentation processes.

Thus, the analysis of these particles offers a potential opportunity to determine the interaction points of the primary beam.

The principle, which resembles that of vertex identification in fixed target particle physics experiments, is to use a charged particle tracker to reconstruct the trajectories of the particles emerging from the patient and extrapolate them back to their production point.

Usually, the trajectory of those individual particles intercepts the line of flight of the incoming ion, which is known thanks to a precise charged particle hodoscope. However, the reconstruction of the corresponding vertex is limited by multiple scattering and the effect of secondary interactions.

The possibility to use multiple particle tracks produced at the same interaction points is under studies. It would open the way to a real vertex reconstruction, intrinsically able to give a three-dimensional measurement of the interaction point with accuracies of the order of 1 mm. A validation by a simulation program using data for the secondary proton yield and energy spectra and secondary proton tracking and vertexing is currently being carried out. First results from experiments provided at the GSI facility have validated our simulations (GEANT4).

Prompt-gamma-ray monitoring during carbon ion therapy: comparison between measurements and Geant4 simulations

Abstract ID: 132

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During a tumour therapy with light ions, the position of the Bragg peak must be known accurately. Indeed, a significant fraction of the incident projectiles undergo nuclear fragmentations during collisions with target nuclei. This leads to the emission of prompt particles which may carry information about the ion range. In our studies, we focus on prompt gamma-rays and we have shown that the depth profile of prompt gamma-ray emission is strongly correlated to the ion range and that the counting statistics makes it possible to foresee a realistic imaging system operating in real-time.

For this purpose, we have performed several experiments at GANIL (^{12}C ion beam at 95 MeV/nucleon) and at GSI (^{12}C ions at 300 MeV/nucleon), with PMMA or water phantom targets. A scintillator detector was placed behind a 20 cm thick lead collimator, perpendicular to the beam, and the TOF technique was used to separate prompt gamma-rays from a large background of neutrons and charged particles. Geant4 simulations have been undertaken to design the experimental setups and to interpret the data. In this communication, we present and discuss the comparison of Geant4 simulation results with experimental data. These simulations calculate the fragmentation yields, the production and transport of secondary particles.

Qualitative agreement between simulations and experiments is observed for the amount of energy deposited in the detector and for the time-of-flight spectrum shape. However some discrepancies appear both on the gamma production yield and depth profile. These discrepancies are discussed, mainly in terms of nuclear physics models which have to be improved.

Sinogram-based time offset correction method for time-of-flight PET

Abstract ID: 134

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Introduction: Before events are accepted in TOF-PET, the signal induced by the detected photon passes through a chain made by scintillation crystals, PMTs and boards for time/energy/coincidence windowing. Each of the different components of the chain induces a timing error resulting in a final delay between the time of detection and the time of acceptance of the signal. This time offset is a degrading factor in TOF PET imaging and must be accounted and corrected for. Commonly used calibration methods involve acquisition of sources in a known spatial position calculating an average time offset correction factor (CF) for each crystal.

We designed a time offset calibration method using a point source in multiple FOV positions without precise knowledge of the source location, calculating CFs for each LOR. The method exploits a geometrical equivalence between space sinograms (r, phi) and TOF sinograms (dx, phi).

Methods and Results: A point source was simulated in various FOV positions in a TOF PET scanner (650 ps time FWHM). A randomly chosen time offset (between 0-1200 ps) was applied to the response of each detection module, with a 10% inter-crystal variability. Our method was applied aligning the 2D TOF sinogram to the spatial one obtained by SSRB. For a 20 cm off-center point source with a time offset up to 300 ps, our correction method gives a 665 ps effective time resolution vs 790 ps for the uncorrected data. On a Gemini TF scanner, with expected 650 ps FWHM, for an off-center point source our method led to a 660 ps FWHM vs 690 ps with the standard offset correction and 720 ps for the uncorrected data.

Conclusion: Our method shows promising results in 2D, encouraging further work towards 3D extension which is 3D is non-trivial but possible and currently under study.

Real time monitoring of the Bragg-Peak position in ion therapy by means of single photon detection

Abstract ID: 137

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To monitor in real time the longitudinal position of the Bragg-Peak we are studying a novel non invasive technique that exploits the detection of prompt gamma-rays issued from nuclear fragmentation. Indeed, within less than a nanosecond following the ion beam impact with the target, photons and neutrons are emitted by the excited nuclei each time a nuclear fragmentation occurs. Since fragmentation occurs all along the ion path it is expected that the production of photons is tightly correlated with the ion range. This implies that, in principle, the measurements of prompt emitted photons could bring strong information both on dosimetry and the Bragg peak position. This was first verified with proton beams by Min et al.

We have recently performed two series of experiments at the GANIL and GSI facilities with 95 MeV/u and 310 MeV/u $^{12}C^{6+}$ ion beams, respectively. The carbon beam was stopped in a PMMA or water target. In both experiments, our collimated detectors were placed at 90 degrees from the beam direction and focusing on the target which was placed on a translating table, moving along the beam axis, to allow a full scan of the beam profile along the target. To discriminate the prompt photons from the background radiation, mainly due or induced by neutrons, we used the Time Of Flight (TOF) and the Pulse Shape Discrimination (PSD) techniques.

We show that TOF technique could make the real-time monitoring with prompt gamma rays feasible, since it avoids the use of bulky neutron shielding. On the contrary no correlation between the neutron production and the ion path was found.

We conclude that, detecting single photons by means of TOF measurements and with a collimated set-up, is also valid at high energies, typically used for ion therapy treatments.

The future role of CZT detectors in nuclear medicine

Abstract ID: 197

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The aim of this study is to monitor efficiently the path of the beam inside the patient during a carbon ion therapy treatment session. We use the fact that, at an energy of 300 MeV/u, 55% of the incoming ions will undergo fragmentation processes, and half of these fragments will induce nuclear reactions too. Moreover, there is a strong correlation between the primary ion range and the production yield of secondary charged particles coming from these fragmentation processes.

Thus, the analysis of these particles offers a potential opportunity to determine the interaction points of the primary beam.

The principle, which resembles that of vertex identification in fixed target particle physics experiments, is to use a charged particle tracker to reconstruct the trajectories of the particles emerging from the patient and extrapolate them back to their production point.

Usually, the trajectory of those individual particles intercepts the line of flight of the incoming ion, which is known thanks to a precise charged particle hodoscope. However, the reconstruction of the corresponding vertex is limited by multiple scattering and the effect of secondary interactions.

The possibility to use multiple particle tracks produced at the same interaction points is under studies. It would open the way to a real vertex reconstruction, intrinsically able to give a three-dimensional measurement of the interaction point with accuracies of the order of 1 mm. A validation by a simulation program using data for the secondary proton yield and energy spectra and secondary proton tracking and vertexing is currently being carried out. First results from experiments provided at the GSI facility have validated our simulations (GEANT4).

Investigations on novel imaging techniques for ion beam therapy

Abstract ID: 198

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Ion beams exhibit a finite range and an inverted depth-dose profile. These favourable physical properties enable superior tumour-dose conformality. However, they introduce sensitivity to range uncertainties. Thus, dedicated Quality Assurance procedures are desirable to enable in-vivo range verification before or during ion therapeutic irradiation.

Monte Carlo (MC) calculations based on the FLUKA code and experimental investigations are being carried out to address the feasibility and to compare the performances of particle-based radiographic or tomographic transmission and emission imaging techniques. The aim is to identify complementary methods to Positron-Emission-Tomography for future application at HIT.

These novel imaging techniques could use transmitted high energy primary particles for low dose 2D and 3D imaging to evaluate the correct patient positioning and verify the ion range before treatment, or emerging secondaries from the therapeutic beams to verify simultaneously and in-vivo the treatment delivery.

As a first step we study the clinical feasibility of heavy ion computed tomography (HICT) at HIT. MC results and experimental data taken with simple radiographic films and reconstructed using a backprojection algorithm support the feasibility of HICT. Further investigations are ongoing and the results will be reported. Following the so far promising results, MC calculations are being carried out to identify and optimize a more suitable detector system for particle radiography and tomography: a stack of ionization chambers.

Novel technologies in radiation therapy

Oral Communications

A study on repainting strategies for treating moving targets with proton pencil beam scanning for the new Gantry 2 at PSI

Abstract ID: 67

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Treating moving targets using a scanning gantry for proton therapy is a challenging, unexplored and unresolved problem. The interference of organ motion with the sequence of the beam delivery produces uncontrolled dose inhomogeneities within the target. One promising approach to overcome this difficulty is to increase the speed of scanning in order to apply the dose repeatedly (so called repainting). To obtain sufficiently high scanning speeds a new, technologically improved gantry - Gantry 2 - has been designed and is currently under construction at PSI. As there are many possible repainting strategies, the way repainting will be implemented on Gantry 2 will depend on the result of a careful analysis of the various treatment delivery strategies available. To this aim, and prior to the start of experimental work with Gantry 2, simulations of dose distribution errors due to organ motion under various beam delivery strategies were investigated.

In total over 200'000 dose distributions have been simulated and analyzed and selected results are discussed. From the obtained results we are confident to treat moderately moving targets on Gantry 2 using repainted pencil beam spot scanning. Continuous line scanning seems to be the most elegant solution, it provides higher repainting rates and produces superior results but is probably more difficult to realize. For larger motion amplitudes continuous line scanning still shows good results. To further reduce the dose inhomogeneity within the target volume and safety margins, gating or a breath hold technique is planned to be used for larger motion amplitudes.

Mitigation of target motion in scanned ion beam therapy

Abstract ID: 38

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Scanned ion beam therapy is an innovative technique for conformal treatment of tumors with high sparing of organs at risk in the vicinity of the target. Based on the positive experience of pilot studies in research centers several clinical facilities are currently constructed throughout Europe with the first patients already being treated at the Heidelberg Ion Beam Therapy Center.

Currently scanned ion beam therapy is limited to tumors that can be immobilized. In sites that move intra-fractionally such as the lung which is influenced by respiratory motion the interference of target motion and scanning process leads to inhomogeneous dose coverage of the clinical target volume even if margins are used. This interference is typically referred to as interplay.

The motion mitigation techniques rescanning, gating, and beam tracking have been proposed to allow treatment of intra-fractionally moving tumors. Rescanning breaks the interplay patterns by multiple irradiations of the planning target volume per fraction with proportionally less dose. Gating limits beam delivery to e.g. the end-exhale part of the breathing cycle resulting in reduced motion amplitudes at longer treatment times. Beam Tracking compensates target motion by adapting all beam parameters and thus does not require motion-related expansion of the clinical target volume.

At GSI, rescanning, gating, and beam tracking were implemented as experimental treatment delivery option. In addition, our treatment planning system TRiP was extended to 4D capability allowing dosimetric comparison between the different techniques. Within the contribution experimental results will be presented. In combination with data from treatment planning studies the pros and cons of the different motion will be discussed.

The TOM'5 System for Multibeam Tomotherapy

Abstract ID: 28

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Introduction:

The idea of tomotherapy is the most comprehensive IMRT concept for optimization of today tumour therapy with photons. It refers to a radiation treatment with a sequential exposure of body slices. For realization of this concept there are some technical developments to be found. Most of them are based on a multitude of beam angles set in place by a rotating gantry of the treatment device.

Materials and methods:

The apparatus for multibeam tomotherapy uses a ring-like gantry with a distinct set of five stationary treatment heads (Achterberg and Müller 2007). This proposed system patented by the authors is creating arbitrary dose distributions through intensity-modulation of fan beams by a combination of MLC operation and patient table movement.

We have made a simulation to evaluate the performance characteristics of our unit. By the means of the Monte-Carlo-programme BEAM we studied design and treatment geometry. The developed algorithm „Multifocal MLC-Positioning" for a synchronized driving of multileaf collimation and table movement allows us to perform radiation treatment planning. With BEAM and the treatment planning system Pinnnacle3 (Philips Medical Systems) dose distributions have been produced.

Results and discussion:

We present an optimized design of our static tomotherapy device and calculated treatment times and dose distributions of different patient cases. The examination of usual results of classic radiation therapy, conventional IMRT, other tomotherapy devices and the treatment with heavy particles (protons, carbon) shows the potential of the new system.

Achterberg, N. and Müller, R.G., Med. Phys. 34 (2007) 3926-3942.

Electron cooling application for cancer therapy accelerator facility

Abstract ID: 35

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Budker Institute of Nuclear Physics (BINP, Novosibirsk) is engaged in R&D of the new cancer therapy accelerator system based on the synchrotron with electron cooling.

The electron cooling is used for the ion beam accumulation in process of repeated multi turn injection into the main synchrotron from the fast cycling booster. After acceleration of ions the electron cooling is used for decreasing of beam emittance and momentum spread and for follow extraction of ion beam small fractions according to the irradiation process. Cold ion beam allows decreasing the apertures of synhrotron, high energy transfer lines and gantry.

The computer simulations results are in good agreement with experimental data obtained during the CSRe commissioning. Also, the electron cooling can be applied for accumulation of short lived radioactive nuclei which could be useful for cancer therapy.

Such technology opens the possibility to realize the irradiation with online PET visualization.

A cyclotron-linac complex for carbon ion therapy

Abstract ID: 65

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The machines used today for carbon therapy are 20-25 m diameter synchrotrons. For the ARCHADE project IBA is building a 400 MeV/u superconducting cyclotron weighting 700 tons and needing a 15 metres long Energy Selection System.

In the years 1993-1995 TERA designed a proton linac (LIBO = LInac BOoster) which runs at 3 GHz. A module was built with CERN and INFN and accelerated protons with the expected gradient: 16 MV/m. A 27 MV/m gradient was also obtained, which entails a peak surface field of 2.5 Kilpatrick.

TERA is now working on CABOTO (Carbon BOoster for Therapy in Oncology) which is placed downstream of a superconducting cyclotron. After a 3 GHz design, to reduce the overall length the frequency has been increased to 5.7 GHz. This paper describes such a fast-cycling cyclotron-linac complex which runs at 300 Hz for the multipainting of moving tumours.

In 23 metres the linac accelerates from 120 MeV/u to 400 MeV/u either C^{6+} ions or H^{2+} molecules. The 300 Hz source is the Electron Beam Ion Source EBIS-SC by DReEBIT (Dresden) which produces in 3 μs more that 108 C^{6+} ions. The K = 480 cyclotron weighs about 170 tons and the Cell Coupled Linac is made of eighteen 1.3 m long units (gradient = 40 MV/m, Kilpatrick = 2.9) powered by solid state modulators equipped with 12 MW klystrons.

By switching off the klystrons, the cyclotron-linac complex produces - in eighteen 15-16 MeV steps - beams of either C^{6+} ions or H^{2+} molecules with energies in the range 120 - 400 MeV/u. Smaller steps are obtained with a segmented 20 mm absorber and no Energy Selection System.

A proposal for a low-cost size superconducting multi-use accelerating facility for protons or light ions (LOCMAF)

Abstract ID: 57

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The growing incidence of cancer, its high mortality level and need for progress in the therapy of patients are still among the dominant problems in our days. As available statistics show, about 70% of cancer patients are treated by radiotherapy. According to estimates of the leading radiotherapy experts, hadron therapy (HT) will significantly complement the radiotherapy using traditional (x-ray, gamma, electron beam) sources, so that the creation of clinical HT centers represents the strategy of development in this field.

It is proposed the creation of a scientific consortium of the CERN-MS and NON-MS, in order to study a project for final design, construction and commissioning of, a ready for operation, a low-cost size superconducting multi-use accelerating facility for protons or light ions (LOCMAF) for use of: i) Hadron Therapy (HD), ii) Radio-isotopes Production (RiP) and iii) Tests Beam (TB) studies for the material science and medical physics research plus other applications.

The building, under the frame of the CERN Directorate for Accelerators and Technology, of a low-cost small size superconducting multi-use accelerating facility for protons or light ions and the training of the scientific personnel to its operation, materializes pragmatically the prospected Knowledge and Technology Transfer (KTT) from CERN to the involved countries, MS and non-MS, in an unique, solid and realistic way, coming exclusively from the research experience and results for a about 55 years of CERN operation.

Novel technologies in radiation therapy

Posters

A multi-port, high dose rate, fixed field synchrotron based protontherapy installation

Abstract ID: 1

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The RACCAM project (Recherche en Accelerateurs et Application Medicale http://lpsc.in2p3.fr/service_accelerateurs/raccam.htm), funded by the French National Research Agency over the 2006-2009 period, has studied a protontherapy accelerator installation based on a fixed field (FFAG) type of accelerator, injected by a 5-15 MeV range cyclotron.

This technology allows producing variable energy proton beams in the requested 70-230 MeV range for protontherapy use. It allows foreseeing the principle of providing dose delivery in excess of 10 Grays*liter/minute, to one or more extraction ports.

The contribution will report on this innovative, FFAG based approach, its technical aspects, its costing, and its implementation in an hospital environment.

Innovative Isocentric gantry for the Cancer Therapy by Non Scaling FFAG

Abstract ID: 8

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There is a dramatic increase in number of proton/carbon cancer therapy facilities in recent years due to their clear advantage over other radiation therapy treatments. The cost of ion cancer therapy is still prohibitive for most of the hospitals, and the dominant costs are beam delivery systems. First, reduction in the cost, size, weight, simplification in operation of the delivery systems - isocentric gantries is shown.

1. The original designs of carbon and proton isocentric gantries using non-scaling alternating gradient fixed field magnets (NS-FFAG)*, where weight of the transport elements of made of superconducting magnets without any iron, is 1.5 tons compared to 130 ton gantries recently constructed Heidelberg C facility at Heidelberg, while a proton Halbach permanent magnet gantry has an estimated weight of 500 kg. Improvements in the carbon design are reduction on maximum height and overall size - comparable to the new PSI proton gantry.

2. New idea and preliminary designs of fixed magnetic field acceleration with non-scaling FFAG will be shown. Advantage with respect to the cyclotrons is variable energy range and no need for the degraders (degraders introduce radiation and blow up the emittance of the beam). The 1 kHz rate and fixed magnetic field allows fast spot scanning and represents an advantage with respect to the synchrotrons.

Metal microdetectors for measuring and imaging beams of particles.

Abstract ID: 17

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Metal Microstrip as well as Micropixel sensors are discussed as detectors (MMD) of charged particles and X-ray beams. In comparison with other radiation sensors there are advantages of the MMD: high radiation tolerance (10-100 MGy); nearly transparent sensor – (~1 μm thickness); low operation voltage (20 V); perfect spatial resolution (5 – 25 μm); unique, well advanced production technology; commercially available readout hardware and software.

MMD applications:

- Micro-beam Profile Monitoring for Particles and Synchrotron Radiation
- Detectors at the focal plane of mass-spectrometers and electron microscopes
- Imaging sensors for X-ray and charged particle applications
- Precise dose distribution measurements for micro-biology, medicine (mammography, dental treatment, hadron-therapy) etc.

Currently available Metal Microstrip Detector (a row of 1024 nickel strips (2 μm thick, 40 μm width, 60 μm pitch) read-out via thin polyimide cable by 128-channel ASIC preamplifiers VA_SCM3 is characterized as a device for the beam diagnostics.

The results are presented of the first test of the micropixel readout chip, TimePix, as a metal detector of low energy ions in a focal plane of the laser mass-spectrometer. The TimePix detector provides two-dimensional imaging of ion beams and their charge/mass distribution allowing for tuning mass spectrometer 'on-line' (focusing, alignment etc.). 2-D mass-spectrometer data allow also to improve mass resolution by projecting mass-data from isotope's loci. The possibility to apply the obtained data for some deseases diagnostics is discussed.

Facility for Hadron Radiotherapy of the Joint Institute for Nuclear Research

Abstract ID: 21

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The research program on hadron radiotherapy at the proton Phasotron of the Joint Institute for Nuclear Research was started as far as in 1967. To the date a multiroom Medico-Technical Complex (MTC) for irradiation of cancer patients with protons, negative pions , and high energy neutrons was constructed and put into operation.

Various methods to treat oncological diseases have been developed and technically implemented at the MTC, such as application of a proton beam of different energies for a wide range of neoformations' locality (room # 1), the so-called "shoot-through" technique with a proton beam of maximum energy of 660 MeV (room # 3), treatment of onco-gynecological patients (room # 2), experiments to use such exotic particles in radiotherapy as negative pi-mesons which give some biological advantages to kill cancer cells in comparison to protons (room # 4), high energy neutron therapy (room # 5) and standard gamma therapy unite with radioactive cobalt source (room # 6).

Rapid progress of recent decades in medical diagnostics and computing has brought about the establishment of a new branch in radiology – the 3D computer scheduling and exposure sessions. Thereby, the method of 3D conformal irradiation of deep-seated tumours with a proton beam was implemented for the first time in Russia and is still applied today in one of the Complex treatment rooms.

Long-standing cooperation of MTC with the Medical Radiological Research Centre in Obninsk has made it possible to implement powerful programmes of proton therapy research. Today, about 100 patients annually take treatment at the Phasotron proton beam.

Phosphenes in Carbon Ion Tumor Therapy

Abstract ID: 26

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The phenomenon of particle-induced visual sensations ("phosphenes") like flashes or streaks is known from astronauts of the Apollo 11 mission in 1969 and later space flights and was ascribed to cosmic ray nuclei passing through the eyes [1]. The effect was further investigated in terrestrial experiments at accelerators with human volunteers. Light sensations were also reported from cancer patients undergoing radiation therapy. From various experimental studies it was found that Cerenkov radiation in the eye and direct stimulation of the retina were the predominant effects [2].

Many of the patients treated with carbon beams at the therapy facility at GSI reported bright visual effects during the irradiations. Most of these cases were tumors in the skull base, often located near the optic nerves and the eyes.

The present study, including a total of 39 patients, attempts to establish correlations of phosphene stimulation with local dose deposition near sensitive structures of the visual system, e.g. retina, optic pathways or visual cortex. In particular, the question whether phosphenes may result from interactions of beam particles (or secondary radiation) with the optic nerve alone without participation of the retina was subject of this study. The beam scanning system used at the GSI therapy unit delivers the dose dynamically voxel-by-voxel, and therefore offers unique conditions for such investigations. The beam energies in the range of 80 – 400 MeV/u used in patient irradiations were well below the threshold (≈480 MeV/u) for production of Cherenkov light in the vitreous body of the eye.

Magnetic measurements for medical accelerators

Abstract ID: 27

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Our group, which is responsible for the measurement of all of CERN's accelerator magnets, started in 2005 a collaboration with the Italian Centro Nazionale di Adroterapia Oncologica (CNAO). Hadron therapy magnets push the boundary in terms of required field quality when beam energy must change rapidly and precisely following complex powering cycles. Our contribution covered the following areas: development of specialized instruments, such as curved fluxmeters or large diameter rotating-coil probes; characterization of material samples; systematic testing of 25 main bending magnets and several prototypes; real-time field measurement systems for synchrotron control. We also measured field transients due to eddy currents, a topic of interest for different classes of fast-cycled machines such as linacs. We provided industrial partners with specialized instruments and know-how, which in turn will serve the community to obtain higher quality magnets in the future.

At present, a collaboration with MedAustron is being defined. As we work very closely with their magnet team, we expect that the experience gained with CNAO will provide a valuable early input.

We conclude this presentation with an overview of our capabilities in terms of design, manufacturing and calibration of instruments and components, which may be of interest in view of possible future collaborations. We summarize the range, accuracy and bandwidth of existing systems, and we highlight some of our specialties such as high-precision search coils and digital integrators.

Evaluation of different detectors for homogeneity measurements in scanned ion beams

Abstract ID: 31

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Increased accuracy in radiation delivery using scanning particle beams, leads to high demands on quality assurance (QA). At the Heidelberg ion beam therapy center HIT a daily control of the homogeneity over an irradiated area is performed with high-resolution radiographic films. As using this film type bears a lot of workload, considerations have been made to replace it by another device. Radiochromic films (Gafchromic® EBT2) and an amorphous silicon flat-panel detector (256L, Perkin Elmer, Germany) were tested regarding their suitability for homogeneity checks. Results were compared to radiographic film (Kodak X-Omat V).

All detectors were simultaneously irradiated by a homogeneous proton field (15x15cm², ESynchr=143 MeV) at HIT. Films were digitized with the VIDAR DosimetryPRO®Advantage(Red) scanner. The data acquired with the flat-panel were corrected for dead pixels and dark current. After converting pixel values into dose, the std. deviation σ of normalized dose values over 12x12cm² (middle of the irradiated field) was obtained. Relative doses were compared pixel wise to the tolerance level (±5%).

Radiographic film shows the best dose response homogeneity (σ = 0.8%). For EBT2 film a std. deviation of 4.6%, for the flat-panel of 2.0% were found. While for X-Omat film all relative doses lie within the tolerance levels, this is not true for EBT2 film. For the flat-panel 99.5% of the pixels show values within the tolerance range.

EBT2 films of Lot#F03110903 show high intra-sheet heterogeneities and thus are not suitable for field homogeneity checks. The flat-panel detector shows a good dose response homogeneity which could presumably be further improved using a pixel-map correction (currently investigated). The flat-panel is a promising candidate for use in daily QA.

A plastic scintillating optical fiber dosimeter with photodiode readout

Abstract ID: 32

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Inorganic scintillating crystals and plastics have been used as dosimeters for a long time [1]. A dosimeter made of scintillating plastic optical fiber have many advantages (the similarity to water is a big one) and some limitations. For instance, the production of Cherenkov light in the fiber by electrons in the hundred-keV range has been seen as a major drawback to this type of dosimeter, introducing a noise in the detected signal [2-3]. However this problem does not arise in radiology and brachytherapy applications because the beam energy is often below the Cherenkov production threshold.

The scintillating optical fiber dosimeter developed by our collaboration is a device capable of measuring doses delivered by X and gamma radiation in the tens of keV up to a few hundred of keV. The device consists of a blue-emitting, 5 mm-long plastic scintillating optical fiber (2 mm in diameter), coupled to a non-scintillating plastic optical fiber 300 mm-long. The scintillation light produced in the fiber is collected and conducted by the non-scintillating fiber to a photodiode with good spectral response to the produced light. The device has been tested for several X-rays beams in the 30 to 100 kVp and a small variation of 5% in the sensitivity has been measured for the full range. In-vitro clinical tests are under way.

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A Proton Range Telescope for Quality Assurance in Hadrontherapy

Abstract ID: 37

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A prototype 10x10cm active-area proton range telescope (PRT) has been built for use in quality assurance in hadrontherapy. The PRT uses two triple-GEM detectors for tracking and a stack of 3mm-thick plastic scintillators for the residual range determination of a diagnostic proton beam. The PRT has been tested at the Paul Scherrer Institut (PSI) in Villigen, Switzerland.

Presentation of the results will be followed by a discussion of plans to build a larger range telescope having a 30cmx30cm active area.

Performance of a pixelized amorphous silicon detector in medical ion beams

Abstract ID: 41

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Cancer treatment using ion beams is a highly conformal radiation therapy. The use of scanning beams further enhances the spatial accuracy of the dose deposition. It poses extensive demands on the quality assurance (QA) of the treatment. There is a need to improve the procedures by using a more efficient detector comprising good spatial resolution and online readout. It is desired to replace the time-demanding use of radiographic films for daily measurements of beam parameters, as well as the arrays of ionization chambers employed for patient dose verification, which provide limited spatial resolution. The flat-panel detector RID 256L (Perkin Elmer, Wiesbaden, Germany) was investigated for these purposes. It consists of an array of 256 x 256 amorphous silicon photodiodes with 800 µm pitch. Its irradiation by protons and carbon ions was performed at the Heidelberg Ion Beam Therapy center, Germany.

The acquired time-resolved beam profiles in two dimensions at different energies show that this detector is suitable for fast and convenient measurements of beam profiles as well as field homogeneity. It was also found to provide high signal to noise ratio. The observed afterglow effect and charge leak to neighbouring pixels were quantified and found to be of minor relevance for the foreseen measurements.

The strong energy dependence of the signal makes the RID 256L a promising detector for radiographic purposes. Therefore, imaging of biological samples with both, proton and carbon ion beams was investigated. The obtained results show clear structures corresponding to the photon radiography. A change of the contrast was observed with the beam energy and modality changes. A quenching of the signal at high ionization densities observed is currently being investigated.

Implementation and test of the Dose Delivery system of Centro Nazionale di Adroterapia Oncologica (CNAO)

Abstract ID: 48

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One of the most promising beam delivery techniques for particle therapy is the so called "active scanning" which uses scanning magnets to drive a pencil beam of particles through the target. The higher accuracy in the dose delivery requires a higher level of monitoring the position, width and intensity of the beam.

The Centro Nazionale di Adroterapia Oncologica (CNAO) in Pavia (Italy) is a synchrotron-based centre to treat many kinds of tumors with protons and carbon ions using active beam delivery. The CNAO Foundation, INFN and the University of Torino have developed and built the Dose Delivery system which includes the nozzle, several monitor chambers and the hardware and software interfaces to deliver and control the beam.

The CNAO monitor system features three kinds of parallel-plate ionization chambers: full integrating area to measure the total fluence, segmented in strips to measure the beam position, segmented in pixels to check the 2D dimension and position of the beam.

The electronic readout is based on TERA chips which allow a large dynamic range charge measurements at high converter frequency and without dead time.

To achieve the high scanning speed (more than 20m/s for both protons and carbon ions) and the accuracy required for the beam positioning (~0.1 mm), a fast and high-power power supply has been developed by OCEM S.p.A in collaboration with INFN and CNAO. A feedback on the scanning magnet currents is implemented to improve considerably the precision in the beam positioning.

The components involved in the beam delivering will be described, starting by the clinical requirements. Details will be given on the monitors design, tested characteristics, scanning system performances and interfaces with the the general CNAO control and interlock systems.

R&D of ion sources and cyclotrons for hadron therapy facilities

Abstract ID: 49

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Italy is present in the field of hadron therapy either with synchrotron-based and with cyclotron-based facilities. For both types of accelerators the availability of high brightness multiply charged ion beams is essential. At the Centro Nazionale di Adroterapia Oncologica (CNAO) of Pavia, proton and carbon ion beams will be accelerated up to 400 MeV/amu by a synchrotron and the beam injection is guaranteed by two ECR ion sources. A new design for a third, more powerful ECR ion source named MISHA, has been proposed and it will be described hereby. Other facilities, cyclotron-based, require high brightness fully stripped carbon beams and larger extraction voltages; for these facilities a MISHA source may be appealing.

At INFN the design of a superconducting cyclotron, able to accelerate light ions with charge to mass ratio q/A = 0.5 up to 300 MeV/n, has been developed in recent years. The main features of the accelerator design, developed within a collaboration agreement with the firm IBA, will be given. Some details will be also presented about a new partnership agreement between IBA and INFN for the implementation of the C400 cyclotron able to produce carbon beam at 400 MeV/n, according to the positive experience gained in these years of cooperation between scientific institution and private company.

Superconducting Magnet Technologies as basis for Design of Medical Carbon and Proton Synchrotron at Dubna

Abstract ID: 61

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The activity on the design and construction of a pilot proton-ion accelerator facility for medical applications based on the use of superconducting magnet technologies is briefly described.

The JINR Veksler-Baldin Laboratory of High Energy Physics (VBLHEP) has a long-term experience in the design and construction of different superconducting devices including synchrotron magnets. The Nuclotron, 6 A·GeV ion synchrotron manufactured at JINR during 1987-1992, was successfully put into operation in March 1993. The Nuclotron magnetic system makes it possible to provide a variety of operation modes from a fast cycled, one pulse per second, to a quasi-continuous one. The beams of protons and different ions up to iron have been accelerated and extracted from the Nuclotron.

Reliability and stability of the Nuclotron magnetic system were tested during 17 years operation and 40 real beam runs. Necessary development of some basic features of design the standardized proton-ion medical accelerator facility is discussed.

Hybrid optical tracking techniques for organ motion estimation

Abstract ID: 68

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In modern radiation therapy, the increased geometrical selectivity in radiation dose deposition obtained with photons IMRT and with the use of charged particle beams leads to a dramatically high sensitivity with respect to geometrical uncertainties in treatment set-up and/or uncompensated motion.

Appropriate image guidance strategies need to be applied on a routine basis for detecting short-term motion (physiological motion, respiration) and long-term modification (tumor shrinkage, edema, patient weight loss) of target volume and organs at risk position and configuration with respect to the CT-based treatment plan. When organ motion processes exhibit high temporal dynamics (typically respiration-driven), in-room imaging techniques benefit of the combined use of optical tracking technologies, aiming at providing a non-ionizing 4-D data flow of surface surrogates.

We describe a system capable of detecting hybrid configurations of control points (physical light reflecting markers, programmable laser light patterns) in variable combinations (number of physical control points, dimensions and features of the projected pattern), which is put forward to provide the required flexibility and reliability for facing the whole variety of clinical cases. Particularly for an application in particle therapy, where the real-time monitoring of beam entry surface position and beam path-length variations is essential in presence of organ motion, we investigated point-based, surface-based and combined registration methods in terms of accuracy in spatial localization. The ultimate goal is the safe applicability of adaptive correlation models for the estimation of target volume and organs at risk position in 4-D, in support of time resolved dose delivery techniques (gating, 4-D targeting).

Ion therapy dosimetry by fiber-coupled thin-film-luminescence detectors

Abstract ID: 70

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The use of particle beams in radiotherapy requires new approaches in dosimetry. As an in vivo and real-time tool for dose verification fiber-coupled carbon doped alumina (Al_2O_3:C), employing radioluminescence (RL) and optically stimulated luminescence (OSL), has been investigated and proven to be an option.

However, the luminescence efficiency of Al_2O_3:C changes for different energies of the proton or ion beam (Andersen et al. (2007), Edmund et al. (2007), Greilich et al. (2008)). This is due to high-LET and geometry effects, which both mainly contribute in the clinically interesting region of the Bragg peak. In order to quantify and study the high-LET efficiency effects independently, the geometry has to be deconvoluted.

Theoretical studies show that if we want to achieve a 5% maximum variation of the particle energy within the crystal for 10MeV protons, a Al_2O_3:C detector with a thickness of about 40 µm is required.

Therefore the objective of this project is to reduce the size of the Al2O3:C detectors by creating a thin film of Al_2O_3:C from crystal powder with light-transmitting epoxy glue directly on the fiber tip. In Al_2O_3 trials crystal powder layers of less than 100 µm were created. The luminescence light efficiency of these small layers was found to be sufficient to give a good RL and OSL signal.

Here, we present results for the new fiber detectors from measurements in a Cobalt-60 beam, a 6MV linac at Rigshospital in Copenhagen and Carbon ion beams at the HIT facility in Heidelberg.

Beam Angle Optimisation in Particle Therapy

Abstract ID: 71

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Within the last years particle therapy with protons and carbon ions has gained more attention due to the possibility of creating highly conformal dose distributions combined simultaneously with efficient sparing of organs at risk. Contrary to older treatment units, nowadays most of the recently built facilities are able to provide dose delivery with flexible gantries. The possibility to use more convenient angles will help to improve treatment quality. Because the optimal set of beams is often non-intuitive, a new algorithm for beam angle optimisation has been developed.

The algorithm is implemented in our in-house developed treatment planning system OptiC. It looks for a beam angle that will not affect any organ at risk. If this criteria cannot be fulfilled, OptiC will add a further beam and try to fill up the remaining part of the target volume. A total of three beams will not be exceeded. Finally, if every possible combination will harm one or more organs at risk, all combinations are optimized and evaluated using a penalty function. In order to avoid long computation times, special assumptions are made to speed up dose calculation and the optimisation loop. For example the time consuming calculation of the radiographic path length can be neglected by considering the depth dose curve being constant before and beyond the Bragg-peak.

The predicted dose approximation was compared with normally calculated dose distributions and it seems to be sufficient for beam angle optimisation. Errors introduced are compensated by fix correction factors. Finally, the beam angle optimisation algorithm was revised on a clinical prostate cancer treatment plan.

Gantry 2 - the next generation of a proton scanning gantry at PSI

Abstract ID: 81

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Since more than 10 years deep seated tumors are treated at the Paul Scherrer Institute with a scanned proton beam on Gantry 1. Based on this experience with spot scanning the medical facility was extended with a dedicated cyclotron and a new gantry which is now under construction. This new Gantry 2 will also be the framework to develop new scanning techniques with the aim to treat moving tumours. To achieve this, repainting of the target volume is one of the promising strategies. In order to avoid the accumulation of unwanted dead time especially in the case of repainting, a fast scanning system is required.

For the lateral proton beam displacement at the patient two fast sweeper magnets are used. Due to dedicated power supplies they have low setup time and allow scanning the beam continuously up to 2 cm/ms. Additionally the beam intensity can be modulated on a time scale of 50 µs using a deflector plate close to the proton source inside the cyclotron. Precise synchronisation of these fast actuators in the order of 10 µs requires a control system which is based on field programmable gate arrays (FPGAs).

To change the proton energy a mechanical degrader at the exit of the cyclotron is installed. Together with the beam line which is built up with laminated magnets this allows energy changes of typical steps within 80 ms. The nozzle of the gantry is optimized for a small proton spot of 3-4 mm sigma at the patient which offers also highest precision in the dose application.

The system will be completed with an in-room CT within reach of the patient table. The acquisition of 4d images in treatment position shortly before or after radiation will open new options for treating moving tumours.

Open issues and need of experimental data for proton therapy applications

Abstract ID: 89

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A wide survey of physics models and experimental data relevant to the simulation of radiotherapeutical proton beam lines has been performed. Several open issues have emerged, which affect the accuracy and reliability of Monte Carlo applications in this domain; they are especially relevant in the context where the application of Monte Carlo methods in treatment planning is envisaged.

An overview of the results of this project is presented, with particular emphasis on the clinical impact of the uncertainties in the existing Monte Carlo models. The requirements of new experimental data to strengthen the prediction capabilities of hadrontherapy simulations are discussed.

New projects of cyclotrons C235 and C400 for proton and ion therapy

Abstract ID: 98

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Proton therapy hospital centers have become wide spread in the world during the last decade. A medical cyclotron for these centers is developed by the IBA-JINR collaboration. This cyclotron design is a modified version of IBA C235 cyclotron. The goal is to modify the sectors spiral angle for improving of the cyclotron working diagram.

Carbon therapy is most effective method to treat the resistant tumors. A compact superconducting isochronous cyclotron C400 has been designed by IBA-JINR collaboration. This cyclotron will be used for radiotherapy with proton, helium and carbon ions. The $^{12}C^{6+}$ and $^{4}He^{2+}$ ions will be accelerated to the energy of 400 MeV/amu and will be extracted by electrostatic deflector, H^{2+} ions will be accelerated to the energy 265 MeV/amu and protons will be extracted by stripping.

Formation of primary radioactive carbon ion beams applied for cancer treatment and PET

Abstract ID: 99

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Accelerated 12C ion beams are effectively used for cancer treatment. The positron emission tomography is the most effective way of tumor diagnostics. The primary intensive radioactive ^{11}C ion beam could allow both these advantages to be combined. It could be used both for cancer treatment and for on-line PET. Formation of a primary radioactive ion beam at an intensity on the tumor target of 10^8 pps allows the cancer treatment by the scanning radiation method and on-line dose verification.

The 11C isotopes are produced in the nitrogen gas target irradiated by a proton beam. If the nitrogen target contains 5% of hydrogen, about $5{\cdot}10^{12}$ methane molecules can be produced each 20 minutes. The separated methane is loaded into the ion source.

The technique used for formation of radioactive carbon beams was developed and tested in the JINR electron string ion source (ESIS) Krion-2. The measured conversion efficiency of methane molecules to carbon ions is rather high; it corresponds to 17 % for C^{4+} ions. The experimentally obtained C^{4+} ion intensity in ESIS was about $2{\cdot}10^9$ ppp. The new ESIS-5T is under construction in JINR now at project ion intensity of $6{\cdot}10^9$ ppp.

The research was supported by the International Science and Technology Center, grant N°3454.

Progress and perspectives of INR radiological center in Troitsk

Abstract ID: 100

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We present the progress and perspectives of the new radiological center based on nuclear facilities of INR in Troitsk.

Its first stage, incorporating treatment rooms for distant radiotherapy with proton, photon and x-ray beams, is now going to receive first patients. The future second stage of the center will be mainly devoted to the development and application of nuclear medicine technologies. Among these technologies are high and low dose rate (HDR and LDR) brachytherapy, the therapy and diagnostics based on targeted delivery of isotopes, neutron-capture therapy (NCT) with new modificators of thermal neutrons etc.

The PET /CT and SPECT scanners will be present in the future center as well. We emphasize that the major part of necessary isotopes will be produced locally on the existing and future nuclear facilities of INR. We present and discuss last scientific results and technological progress in the domains of proton therapy, HDR brachytherapy and NCT.

A Gantry-less delivery of radiation therapy

Abstract ID: 104

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Modern radiotherapy is delivered, almost exclusively, to an immobilized patient who is placed supine/prone on a flat table top, with the radiation beam emanating from a gantry. A gantry mounted radiation source allows for clean, beam's-eye-view targeting, either from fixed angles or from an arc-like continuum. However, gantries present severe engineering constraints and thus cost burden the efficient implementation of new technologies.

We propose to treat the radiation therapy patient in an upright, gantry-less mode: a fixed, horizontal, intensity modulated beam is directed against the patient who is either seated or standing, in strict immobilization, affixed to a slowly rotating about a vertical axis, computer-controlled, turn-table.

As a first step to this novel modality, we will demonstrate a vertical CT scanner, the sine-qua-non equipment for modern radiotherapy treatment planning, along with a vertical clinical MR scanner.

The proposed gantry-less delivery can be strictly isocentric (as in Varian's RapidArc or Elekta's VMAT) or non-isocentric (as in TomoTherapy); it can be issued in continuous, intensity modulated arcs or from fixed angles. Such a techique is especially well suited for charged ion therapy, where magnetic rigidity demands monstrous gantries, accounting for one-third or more of the equipment costs.

In addition to favorable cost savings, there is an inherent engineering reliability to a radiation source mounted fixed, in a gantry less setup, be it a laser-driven or a resistive-wall accelerator, or even a traditional MLC equipped linac.

On the clinical side, we discuss how a vertical/standing patient positioning addresses well known issues for the most common radiotherapy indications: (a) lung , (b) breast and (c) prostate.

Design and performance of an ionization chamber monitor for IBA proton treatment lines

Abstract ID: 109

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The purpose of this study is the realization of an ionization chamber, called IC2/3, by the "Medical Applications" group of the LPC-Caen in collaboration with IBA. This detector has been developed to be used as an on-line monitor for protontherapy dedicated irradiation head for Pencil Beam Scanning.

This device measures the beam position, the beam spot size, dose and dose rate delivered to the patient. The position and the spatial distribution of the scanned beam are measured by using horizontal and vertical strips. A particular effort has been done on the transparency of the detector to reduce the angular straggling due to multiple scattering to avoid degrading the beam spot properties. For safety reason, the sensor is actually composed of two separate and redundant sensors called IC2 and IC3 in the IBA dedicated PBS Nozzle.

The first prototypes have been tested with proton beams at the "Westdeutsches Protontherapiezentrum Essen" (Essen, Germany). Proton beams of different energies were used to check the specifications requested by IBA. The dose rate can be measured with a relative uncertainty better than 1% for a beam current up to few nanoamperes. The spatial accuracy is better than 0.25mm. The low water equivalent thickness of the sensor leads to a scattering which does not exceed the tolerance of 1.25mrad at the beam energy of 230MeV. The collection efficiency is better than 99.5% for a polarization voltage of 1200V.

Once permanently set in the PBS dedicated nozzle, this monitor will enable users to control the position, the spot shape, accumulated dose and the dose rate for each irradiation. IC2/3 is found to be well suited for quality assurance of protontherapy beams.

New equipment and new technology for the mass treatment of the oncological diseases by the proton beam

Abstract ID: 112

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The proton radiation of the oncological diseases will be always more preferable in comparison with the Y-rays therapy on electron accelerators (even in the case of IMRT), if the proton radiation technology is similar to the IMRT technology. In other words, the proton radiation should be carried out from many directions and it intensity should be modulated (IMPT).

In order that the proton therapy becomes as mass applicabke as the Y-rays therapy on electron accelerators, it installation and operation cost should be comparable with the cost of the equipment based on the electron accelerators, which are basically using for the treatment of human cancer diseases now.

We have designed and create the proton therapy facility, which solves this problem.

It cost and operating expenses are lower than all worldwide operating centers have. The irradiation is carring out from many directions (multi-field irradiation) and the dose distribution and the beam energy can be fitted for each irradiation field, according to the algorithm, provided by the special optimization program.

In present time several samples of installation are creating.

One of them is installed in the municipal hospital of Protvino city for the clinical testing which is scheduled on 2010. Another one will be installed in Pushino (Moscow region) in 2010.

In 2009 the accelerator has been delivered to MIT (Boston, USA) for the testing and receiving of the FDA approval, and another one is assembling now in the hospital of Ruzomberok (Slovakia) for the medical certification according to the European Union rules.

Range validation for electrons, protons and alpha particles in Geant4

Abstract ID: 118

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Geant4 is a condensed history Monte Carlo program originally developed for applications in high-energy physics. The transparency and flexibility of the code has spread its use in other fields of research, e.g. radiotherapy and space science. The tailoring of a Geant4 application is the responsibility of the user, however, Geant4 physics models are implemented in ready-to-use physics lists which facilitate the development of specific applications being the best implementations in a given energy range.

In the 9.3 BETA public release of the code (June 2009), the "Low Energy" electromagnetic physics models were migrated to the design of the "Standard" electromagnetic physics package. A number of improvements were introduced in the code, followed by a thorough validation. It was the aim of the present study to validate the ranges of electrons, protons and helium ions against reference data from the United States National Institute of Standards and Technologies (NIST) ESTAR, PSTAR and ASTAR databases.

The general borderline for the overlap of Standard and Low Energy electromagnetic physics in Geant4 is 1 GeV. We thus concentrated on comparisons between alternative models below this energy value. The Low Energy models addressed were Livermore and Penelope. We compared Geant4 and NIST ranges of electrons in water, aluminium and lead. The best agreement was found for Penelope, except at very low energies in lead, where the Standard package gave better results. Geant4 proton ranges in water agreed with NIST within 1% for Standard physics lists. Alpha particle ranges calculated with the same package showed larger discrepancies from NIST data, which reduced to 5% for energies above 7 MeV.

The Port Homogeneity Index: a density based index for the selection of optimal beam configurations for robust heavy ion radiotherapy planning

Abstract ID: 122

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Background: Heavy ion therapy offers a dose conformity superior to any other external irradiation technique, thanks to its advantageous depth dose profile and increased biological effectiveness. However, the density patterns along the ray paths have a strong influence on the Bragg peak position, rendering the technique sensitive to positioning errors. A possible solution is to optimize robustness at planning time, e.g. by avoiding significant density interfaces in the field.

Material and Methods: A Port Homogeneity Index (PHI) was defined, to numerically quantify the influence of the density patterns along a beam. The PHI was used to choose irradiation directions for 10 patients with base of the skull tumors. For each patient two clinically plausible beam setups were chosen: one with low PHI and one with high PHI. For each patient and for each beam setup a carbon ion plan was calculated with the raster scanning technique (TRiP98) with single field optimization and a 2 mm safety margin. Subsequently, rigid positioning errors of 1-2 mm in AP, SI and LR directions were simulated and consequences on the dose conformity were assessed by means of dose distribution display, DVH analysis and calculation of some widely accepted dosimetric quality indexes.

Results: The initial plans showed comparable quality of target coverage for both beam setups. However, the plans prepared for beam configurations with low Port Homogeneity Index were often characterized by lack of robustness against mispositioning, as demonstrated by the effects of the simulated shifts on the dosimetry of such plans. The plans with high PHI were, instead, generally more stable.

Conclusion: The Port Homogeneity Index proved to be an effective, computationally light tool for the choice of beam setups.

MedAustron – Austrian Hadron Therapy Centre

Abstract ID: 130

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MedAustron is a synchrotron based accelerator facility for cancer treatment with proton and carbon ion beams.

In addition to the clinical application, the accelerator will also provide beams for non-clinical research, in the fields of medical radiation physics, radiation biology and experimental physics.

Gantry Work Package of PARTNER and ULICE Projects

Abstract ID: 133

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Up to now the most common technique in the radiation cancer treatment has consisted in the photon irradiation of the patient. In the last years a new field has been explored through the use of particle beams (protons and carbon ions). Whereas the proton technique is actually used and accepted from the medical community, the carbon technique is not yet commonly used. Treatment of tumors by hadrontherapy is greatly improved if the patient can be irradiated from different directions.

This task is performed by a gantry, a section of beam line that can be rotated around the patient. The technical challenges for the design of a carbon gantry are the high beam rigidity of the ion beam, requiring large and very heavy bending magnets, as well as the specified high precision of the whole system. Up to now, the Heidelberg Ion Therapy (HIT) facility is the first dedicated proton and carbon therapy facility in Europe and comprises the only carbon ion gantry worldwide. The main drawback of Heidelberg gantry is the high cost and huge size.

Due to the continuous growth and improvement of the light ion therapy in the world, several projects have born challenging this new task. In particular, two European projects, ULICE and PARTNER, dedicated a specific Work Package to the realization of a carbon gantry. The work will be performed under the supervision of CNAO and it will take three years The goal will be to conceive a device that is smaller or lighter or somehow "better" (cheaper, too) than the HIT one but with acceptable performances, in order to allow a wide(r) spreading and to increase the possibilities of having a gantry in the new carbon facilities. Such a design implies a critical and deep analysis of the gantries state of art and this is what is going to be presented here.

Special magnets for medical accelerators

Abstract ID: 138

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CERN collaborates with the CNAO (I) and MedAustron (A) facilities, to build special magnets for these medical accelerator facilities. Ten different types of bumpers, septa and kickers are developed for use in the low energy beam transfer line, the synchrotron and the high energy extraction lines.

Both 2D and 3D finite element simulations have been carried out to verify and optimize the field strength and homogeneity for each type of magnet and, where applicable, the transient field response. The detailed designs for the injection and dump bumpers, the magnetic septa and the fast chopper dipoles are presented. A conceptual design for the electrostatic septa and their high voltage circuits is outlined.

Future information sharing in Hadron Therapy

Abstract ID: 139

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Sharing information is a key aspect for the delivery of efficient health care and the gateway to new knowledge about disease and its treatment. At present there is no platform connecting people, information and research across the hadron therapy community in Europe.

Within the PARTNER FP7 project we will build a Hadron Therapy Information Sharing Platform (HISP) and a rare tumour database (RTDB) using collaborative grid technology.

The HISP conceptual architecture consists of a common access point to heterogeneous data sources using secure grid services. RTDB will access HISP to provide a view on rare tumours.

HISP will give researchers and clinicians a tool for medical data sharing, clinical analyses and epidemiological studies while RTDB will support modelling of cancer treatment outcome and indications for hadron therapy.

Our next steps are basic grid components' installation within the PartnerVO.eu virtual organization (VO) and defining the security policies, as well as tools for semantic data integration.

Simulating the beam polarisation for Microbeam Radiation Therapy (MRT) using the Geant4 toolkit

Abstract ID: 141

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Microbeam Radiation Therapy (MRT) is an innovative experimental technique potentially able to overcome the limitations of conventional radiotherapy for infantile brain tumors. Its effectiveness seems to be related to the ability of normal tissues to tolerate a very high radiation dose in small volumes, resulting in the preservation of the tissues architecture.

We present Geant4 Monte Carlo calculations of the dose distribution deposited by planar polarized microbeams at micrometric resolution. The simulation of the beam polarization, made possible by different libraries included in Geant4, is a crucial step in enhancing the comparability of experimental data and simulation results.