HADRONTHERAPY, KNOWLEDGE AND EVIDENCES

The Second International Workshop of
The Romanian Society of Hadrontherapy

ABSTRACT BOOK

THE ROMANIAN SOCIETY OF HADRONTHERAPY
November 12-14, 2010, Cindrel Hotel, Paltinis, Sibiu
ROMANIA

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SUMMARY

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NOVEMBER 12 (Friday)

Workshop program: 09:00-10:30 AM

WORKSHOP OPENING

Acad. Prof. Dr. Nicolae Victor Zamfir, President of the Workshop Scientific Committee

General Director of NIPNE-HH, Bucuresti / Magurele, Romania, email: dirgen@nipne.ro

DESCRIPTION OF THE ETOILE PROJECT

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Light ion hadrontherapy, especially with carbon beams, are now used in clinical condition for cancer therapy in Japan (Chiba and Hyogo) and Germany (Heidelberg), and following the pioneering work initially carried out at Berkeley and Darmstadt. This method, which requires heavy-duty equipment, has demonstrated the advantages of carbon ions for the very accurate treatment of deep-seated tumours which are inoperable and radioresistant. In France, the ETOILE project (*Espace de Traitement Oncologique par Ions Légers dans le Cadre Européen*) is the future national facility for hadrontherapy that will be operational in Lyon for treatment in few years (2014-2015). ETOILE will be able to cure more than 500 of the 1000 patients treated each year (for whom existing treatments would have little effect). The specificity of this project will be presented as well as the research program using a joined research platform included in the ETOILE center. A large community of doctors, biologists, computer scientists and physicists, all belonging to higher education units in the Rhône-Alpes Region or great research institutes are already involved in this R&D program towards the goal to optimize, secure and open up the application domains of tumor treatment by light ions.

PROTON RADIOTHERAPY FACILITIES AT THE IFJ PAN IN KRAKOW

Urszula Sowa, Paweł Olko, Jan Swakoń, Dominika Adamczyk, Teresa Cywicka-Jakiel, Joanna Dąbrowska, Barbara Dulny, Leszek Grzanka, Tomasz Horwacik, Tomasz Kajdrowicz, Barbara Michalec, Tomasz Nowak, Marta Ptaszkiewicz, Liliana Stolarczyk

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In the Henryk Niewodniczański Institute of Nuclear Physics of the Polish Academy of Science (polish acronym IFJ PAN) in Krakow, Poland, in cooperation with the Department of Ophthalmology and Ophthalmic Oncology of the Collegium Medicum, Jagiellonian University and the Centre of Oncology of the Maria Skłodowska-Curie Memorial Institute Krakow Branch, is running the project of designing and operating a proton ocular radiotherapy facility in which the 60 MeV proton beam accelerated in the AIC-144 isochronous cyclotron of IFJ PAN is applied. The facility will be able to satisfy national needs of ocular melanoma therapy in Poland (about 100 cases per year).

The facility has been completed and is ready for operation. In the cyclotron building the therapeutic room and the control room have been fully equipped with beam steering and control elements [2]. The beam-line and beam modification system are ready for eye tumor proton radiotherapy applications. The parameters of the proton beam at the isocentre are sufficient to irradiate eyeball tumors at all locations. Our measurements of the Bragg peak show that its range (90% at the distal edge) in water is 28.2 mm. The beam intensity is sufficiently high to assure

a 0.4 Gy/s dose rate from the proton beam and could be increased to 1 Gy/s, if required. It means that the time of tumor irradiation during one session will be shorter than 1 min, typically about 40 s [1].
At present the medical procedures using solid state phantom dosimetry instead of water phantom dosimetry is tested. The research also concentrates on developing better computer treatment planning software. The documentation with results of control measurements is prepared for commissioning. In August 2010 a contract with IBA was signed for the supply of the PROTEUS C-235 cyclotron with a building and the essential technological infrastructure. Within 3 years the research and proton radiotherapy center will be constructed, thus being the first stage of development of the Polish National Centre for Hadron Radiotherapy (NCRH). The additional application for the rotating gantry was submitted to the Ministry of Science in Poland. The project is financed by the structural funds of the European Union within the Innovative Economy Operational Programme (POIG).

- Workshop program: 11:00-12:30 AM

HADRONTHERAPY: PRESENT STATUS AND FUTURE PERSPECTIVES - *(ED)*

Dan Mihailescu[1], Roberto Cirio[2], Irina Butuc[1], Roxana Panait[1]
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Any form of radiotherapy of malignant tumours that uses beams of hadronic particles (protons, heavy ions, pions, etc.) instead of photon or electron beams is known as hadrontherapy. Due to the particular characteristics of dose deposition mechanism of the heavy charged particles, hadrontherapy has many advantages over the conventional treatment techniques with photons and electron beams. However, hadrontherapy has a major disadvantage: is an expensive technique. Therefore, only 13 countries in the world (among which USA, Japan, Germany and Italy) have developed functionally hadrontherapy centres.

The purpose of this work, organized like a short review, is to describe the hadrontherapy technique as well as to analyze its present status and future perspectives in Romania and abroad. According to the last patient statistics more than 75000 patients where treated using hadrontherapy, most of them using proton beams. About 6000 patients have been treated only in 2009 (an increase of ~ 9%, compared to 2008). More hadrontherapy centres are planned for or are already under construction: 5 in Germany, 2 in Italy, Austria (1), France (1), USA (1), and South Africa (1). Only 5 of them will be equipped with synchrotrons to accelerate the carbon ions, mainly due to their higher cost. Hadontherapy does not (and should not) replace the conventional radiotherapy but this radiotherapy technique seems to be ideally suited to treat certain tumours that are deep-seated, located close to critical organs and respond poorly to conventional radiotherapy techniques.

CANCER EPIDEMIOLOGY IN ROMANIA AND WESTERN COUNTRIES, THE RATIONALE FOR ENRICHMENT THE METHODS AND FACILITIES FOR CANCER DIAGNOSTIC AND TREATMENT

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Worldwide, among the top 15 leading causes of cancer death, mortality decreased during the most recent period for the following sites: CRC, stomach, kidney, brain,leukemia, NHL, and myeloma in both men and women; lung, prostate, and oral cavity in men; and breast, ovary, and bladder in women. Cancers with increasing mortality during the most recent period include melanoma and esophageal cancer in men, pancreatic cancer in women, and liver cancer in both men and women.

Simple analysis of the number of cancers cases from Romania in the period 1968-2008 points out the approximately three times growth of these numbers.

The authors try to evaluate a number of the cancer cases through the view of the medical system efficiency and warn about efficiency of Romanian medical system in therapeutically controlling the neoplastic phenomenon now and in the immediate future.

The implementation of hadrontherapy in Romania increases the tumoral response for the cancers for which classic radiotherapy has proved helplessly.

In this sense they propose an improvement of the radiotherapy status in Romania and the enrichment of therapeutical facilities through the addition of the hadronterapy and other conformal, targeted and minimum invasive methods of treatments

E-REFERRAL AND E-SCIENCE PROTOTYPE INFRASTRUCTURE FOR HADRON THERAPY

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Advanced cancer treatment techniques, like hadron therapy, should benefit from state-of-the-art information technology to maximize their impact. Within PARTNER FP7 ITN project [1] we develop a prototype infrastructure to be used as:

1. eReferral allowing doctors to transfer patient information from local hospitals to hadron therapy facilities across European Union
2. eScience gateway allowing researchers to gather relevant information while preserving individual centres conditions.

The dual role of the platform will allow exploring the legal, ethical and technological challenges specific to these environments [2]. We present first steps towards a prototype based on a Rich Internet Application environment which is connected to grid resources for storing and procesing data. Specific services for hadron therapy community will integrate data semantically in a secure environment. The top to bottom layered architecture consists of a:

- presentation layer based on Liferay portal[3] and VINE Toolkit [4], offering users an easy to use customized experience.
- logical layer will provide modular functions to import, curate and analyze and data. These functions will be exposed through web services interface.
- resource layer running core services like VOMS for secure access, AMGA for metadata storage and cgMDR [5] for metadata annotation.

We are using the Virtual Organization *vo.partner.eu* to share medical data between hadron therapy centres. Configurable virtual machines will be installed at each centre and further federated in a peer-to-peer network. We aim at having all the components interoperable and exchangeable with commercial solutions preferred by the medical sector.

HADRONTHERAPY AT JINR DUBNA, PROTONTHERAPY IN HEAD AND NECK TUMORS, DUBNA EXPERIENCE - *(ED. - presented by Nicolae Verga)*

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EXTREME LIGHT INFRASTRUCTURE (ELI) AND HADRONTHERAPY

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ELECTRON PARAMAGNETIC RESONANCE SPECTROSCOPY: NEW TOOL IN HADRONTHERAPY

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The electron paramagnetic resonance (EPR) spectroscopy is a physical method of observing resonance absorption of microwave power by unpaired electron spins in a magnetic field. The EPR spectroscopy has many applications; two of them could be used in hadrontherapy. The first one is related with the possibility of the EPR to obtain the irradiation dose. The radiation produces free (unpaired) electrons, and the EPR signal intensity is proportional to the spin concentration and so to the total dose. The second application is related to the capability of the EPR to measure the free radicals species, which for example in proton therapy this species are the key in DNA damage.

Workshop program: 2:30-4:00 PM

EXTERNAL NEUTRON THERAPY IN SALIVARY GLAND TUMOURS, ADVANCED BREAST CANCER, UTERINE SARCOMA, IRRESECTABLE NECK NODES & MAXILLARY SINUS TUMOURS, RESULTS - *ED. (presented by Nicolae Verga)*

Fred Vernimmen 1**, Clare Stannard** 2 **& collab.**
1- Stellenbosch University and Tygerberg Hospital, Cape Town, South Africa
2- iThemba LABS, South Africa

SALIVARY GLAND TUMOURS TREATED WITH FAST NEUTRON THERAPY AT ITHEMBA LABS, FAURE, SOUTH AFRICA

Clare Stannard[1], Frederick Vernimmen[2], Dan Jones *4*, Evan de Kock[4], Elwin Mills[2], Victor Levin[1], Shaheeda Fredericks[4], Jos Hille[3], Alistair Hunter[1].
[1]Department of Radiation Oncology, Groote Schuur Hospital & University of Cape Town, Department of [2]Radiation Oncology and [3]Pathology, Tygerberg Hospital & University of Stellenbosch, [4]iThemba Labs, Faure

PURPOSE: To evaluate the results of patients with salivary gland tumours treated with fast neutron therapy at the cyclotron at iThemba LABS.
MATERIALS AND METHODS: Neutrons are produced at the cyclotron by the reaction of 66 MeV protons on a beryllium target. The beam was collimated and further shaped, initially by tungsten blocks and subsequently by a multiblade trimmer. The beam characteristics are similar to an 8 MV x-ray beam.
From 1989 to 2004, 446 patients with tumours of major and minor salivary gland were treated, 350 with radical intent. Of these 107 had macroscopic residual disease left after surgery, 60 tumours were not resected because of anticipated surgical morbidity and 179 tumours were irresectable. 197 (56%) were T4 tumours. They received 20.4 neutron Gy in 12 or 15 fractions over 4 or 5 weeks.
RESULTS: The 5 and 10 year overall local control probability was 54% and 43% and 5 and 10 year survival rates were 70% and 60% respectively. Local control and survival probability at 10 years was 71% and 79% for those with macroscopic residual disease after surgery; 37% and 72% for unresected tumours and 15% and 34% for irresectable tumours. Local control at 10 years was 100% for T1, 60% for T2, 39% for T3 and 30% for T4 tumours. Local control probability at 5 years was 72% for low grade malignancies and 46% for high grade malignancies and the 10 year survival rates were 80% and 57% respectively. There was no difference whether an initial or recurrent tumour was treated.
CONCLUSION: Neutron therapy appears to be the treatment of choice for salivary gland tumours with macroscopic residual disease after surgery and for irresectable tumours. The improved local control is associated with improved survival rates for these advanced tumours.

ADVANCED BREAST CANCER, UTERINE SARCOMA, IRRESECTABLE NECK NODES & MAXILLARY SINUS TUMOURS TREATED WITH NEUTRON THERAPY

Clare Stannard, Elizabeth Murray, Leon vanWijk, Marc Maurel, Peter Kraus, Frederick Vernimmen, Shaheeda Fredericks, Sandra de Canha
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Patients with locally advanced breast cancer were treated in a prospective randomised dose-seeking study in the early '90's comparing 17Gy neutrons with 19Gy, both in 12 fractions in 4 weeks. Local control rate, CR+PR, for the 74 patients was 68% for17Gy and 83% for the 19Gy arm. There was no difference in survival or acute toxicity but there were 3 grade 4 toxicities with the higher dose. The shorter course of 4 weeks was well tolerated with apparent improved quality of life.

From 1996-1999 a controlled trial of 18Gy neutron therapy in 4 weeks was compared with a 6 week course of 60Gy photon therapy. 22 of the 27 patients were evaluable and the local control, CR+PR, was 50% for the neutron arm and 60% for the photon arm. Median survival was 21% for neutrons and 13% for the photon arm. Again the shorter course of 4 weeks for neutron therapy was better tolerated than the photon arm with improved quality of life.
37 patients with uterine sarcoma were treated with neutron therapy, 18-20Gy in 5 weeks. Seven patients with completely resected tumours had an 83% 3 year local control and survival, 14 patients with incompletely resected tumours had a 45% 3 year local control and 33% 3 year survival and of the 15 patients with irresectable tumours there were 2 partial responses and a 19% 2 year survival. Four patients with incompletely resected tumours were locally clear when they died of metastases at 7-37 months.
There were 91 patients with maxillary antral tumours treated with neutron therapy, median dose of 20Gy in 12 /15 fractions in 4/5 weeks. 80 had T4 tumours and 11 were T3. Fifty were squamous carcinomas and the remainder were salivary gland malignancies. The local control rate at 2 years was 60% for salivary gland tumours, 30% for squamous carcinomas and 45% overall. Survival at 2 years was 80% for salivary gland tumours, 35% for squamous carcinomas and 57% overall. These results compare favourably with other neutron therapy series but chemoRT is showing promising results.
Several trials of neutron therapy for squamous carcinoma of the head and neck showed varying results but one showed improved local control for neck nodes. We treated 20 patients with irresectable neck nodes, from an unknown or small primary, with neutron therapy, 20Gy in 12/15 fractions in 4/5 weeks. The median diameter was 8.5cm.
There were 8 complete responses and 6 partial responses. The median survival was 25 months, range 3-91months, in the 8 patients achieving a complete response and 5.5 months, 3-16 months in the other12 patients.

FORTY YEARS FROM THE APPLICATIONS OF HIGH ENERGIES IN THE TREATMENT OF CANCER IN ROMANIA

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On October, the 20th, 2010, forty years were celebrated from the first application of high energy radiations in the treatment of the malign tumors in Romania. The high energy source of 30 MeV named Betatron was made by Atomic Physics Institute (IFA) in Bucharest, Romania. The experience gained by IFA due to a team of excellent experts including famous Romanian scientists (such as: Acad. Prof. Dr. Horia Hulubei, Acad. Prof. Dr. Serban Titeica, Prof. Dr. Florin Ciorascu, Corresponding Member of Romanian Academy and Prof. Dr. Ioan Ursu, Corresponding Member of Romanian Academy) who brought their contribution in the charged particle accelerator physics and technology and the application of radiation generated by such accelerators for the research of the structure of matter, the analysis by activation, industrial radiography and technological irradiations, had been permitting thus the extension of the high energy radiation applications in the domain of radiotherapy. The Romanian research activity turned to develop on a research contract basis starting with January, 1970, IFA concluded a contract No. 2/1970 - "Improvement of Romanian Existing Methods in the Radiotherapy of Cancer Tumors by Ultrapenetrant Radiotherapy Employing IFA 30 MeV Betatron". This contract had been managed by Prof. Dr. Florea Scarlat (at that time a scientific researcher within IFA Betatron Lab) on behalf of IFA and Prof. Dr. Ion Bîrzu, the initiator of high energy therapy in Romania, head of Radiology and Oncology Clinic of the "Dr. Ion

Cantacuzino" Hospital, on behalf Ministry of Health. Irradiations of the patients at IFA 30 MeV Betatron Accelerator based on the radiotherapy method finalized upon the above mentioned contract, started with October 20th, 1970 with the approval of Prof. Dr. Dan Enachescu, of the Ministry of Health.Considering the group of the patients treated by the high energy radiation method during that period, the results proved to be positive and satisfactory since some of the patients from that group extended their period of survival by 5 years.

NUCLEAR CROSS SECTIONS FOR THE RADIATION TRANSPORT CALCULATIONS IN HADRONOTHERAPY

Mihaela SIN*,Ana Maria POPOVICI, Gheorghe CATA-DANIL****
Bucharest University, Politehnica University of Bucharest***

PLANNING AND ONLINE MONITORING OF TREATMENTS WITH CARBON ION BEAMS

Andrea Attili
Istituto Nazionale di Fisica Nucleare (INFN)

Two important aspects in the field of advanced radiotherapy with ions beams are the implementation of a Treatment Planning System (TPS) and an online monitoring system for the verification of the correct delivery of the planned dose to the patient. Several INFN research groups that have developed competencies in different scientific areas of high energy physics (experimental and phenomenological nuclear physics, Monte Carlo (MC) and techniques for numerical analysis, radiobiology and hardware development for monitoring purposes) are cooperating to these implementations.

A TPS for hadrontherapy with protons and C-ion beams is currently being developed at INFN in partnership with the IBA Group, to deliver a certified software product. In order to achieve a fast biological optimization, the dose distribution is computed using look-up tables obtained from MC simulations. These are performed using Fluka toolkit and an implementation of the Local Effect Model (developed by the GSI Biophysics group).

In this framework, nuclear fragmentation experiments for C-ion are now performed at the INFN's Laboratori Nazionali del Sud (LNS) (30-80 MeV/n) and 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 also underway at LNS and Laboratori Nazionali di Legnaro, on rodent and human cells (C-ion @ 8-80 MeV/n). These experiments will provide reliable data for the validation of the simulations and for further improvements of the physical and radio-biological models to be used in the TPS.

An online beam monitoring system is also implemented at INFN and it is currently used in the beam line of the *Centro Nazionale di Adroterapia Oncologica* (CNAO) in Pavia. In the hospital-based facility, synchrotron accelerated beams of protons (from 60 to 250 MeV) and carbon ions (from 120 to 400 MeV/u) are steered actively during the treatment by means of two scanning magnets.

The implemented monitoring system is based on a set of parallel plate ionization chambers with the anodes segmented in pixels and strips, and it is placed close to the patient. The system has several important functions. It performs an online check of the instantaneous beam intensity and position, providing the necessary feedback to the accelerator and to the scanning magnets to steer properly the beam and to switch the energy when the slice of the tumor has received the correct planned dose. It also stops the irradiation if the measured values are outside the acceptable tolerances, in order to ensure a high degree of safety.

Workshop program: 4:30-6:00 PM

ABSOLUTE AND RELATIVE DOSIMETRY OF PROTON AND CARBON ION BEAMS USED IN HADRONTHERAPY

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In hadontherapy the dose determination, as accurate as possible, is required as an operative quantity to control beam delivery, to characterize the beam dosimetrically and to verify dose delivery. Many different types of detectors are available for dose measurements (calorimeters, ionizing chambers, films, solid state detectors, gels, etc.) but presently only the ionizing chambers (cylindrical and plan-parallel) can serve as reference instruments in ion beam dosimetry (IAEA TRS-398). The solid state detectors (including films, diodes, diamond detectors, TLDs, OSL detectors or fluorescence screens) have a dose response which is strongly LET dependent, their use being restricted to protons and mono-energetic beams of heavier ions. In the near future, ion beam dosimetry may be significantly improved by establishing calorimetric methods. Even if the calorimetry is the most direct way for measuring the absorbed dose to water, due to some practical difficulties, only few Primary Standard Dosimetry Laboratories are known to be developing primary standards based on water or graphite calorimeters. Having these perspectives, our work was focused on the calorimetry and ionizing chamber dosimetry. For all other detectors are presented only the advantages, disadvantages and their main applications. More information can be found in the recent review of Karger et al. For non-reference conditions, methods for calibrating the beam monitor depend on whether passive or active beam delivery techniques are used. QA measurements are comparable to conventional radiotherapy, but dose verification is usually single field rather than treatment plan based. Dose verification for active beam delivery techniques requires the use of multi-channel dosimetry, as the dose is delivered point-by-point.

ESTIMATION OF HIGH ENERGY CARBON ION BEAM INTERACTION PRODUCTS ON LIVING SOFT TISSUE WITH COMPUTER CODE FLUKA

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Carbon ion is being used in treatment of cancer tumor in the form of high energy collimated beam. It is also among main heavy ions existing in cosmic ray. In the present work nuclear interactions between projectile carbon ion and the major elements existing in human soft tissue are studied. Computer code *ALICE* is used to estimate reaction products and relevant cross sections. The relative abundance of secondary nuclei due to interaction of high energy carbon ion with human tissue is obtained using FLUKA computer code. Carbon ion energy is considered varying between 70 MeV to 4.5 GeV. The interaction products of carbon ion beam with air, skin, muscle, bone and tumor is elaborated. For projectile energy of less than 100 MeV, the fragmentation reactions are not remarkable and mostly scattering reaction, elastic or inelastic, occurs. For projectile energy between 100 – 500 MeV, secondary particles with atomic number around Z=6 are produced. At higher energy, secondary particles with $8<Z<22$ are dominant.

DOSIMETRY IN CONTINUOUS AND PULSED HADRONTHERAPY BEAMS - METHODS FOR CALIBRATION AND MEASUREMENT

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Any kind of radiation therapy is subjected to a number of dosimetric checks, which traditionally include:
- reference dosimetry (direct measurement of absorbed dose in water per MU, under certain reference conditions, which must be the same for all centres using a certain type of treatment)
- non-reference dosimetry and QC procedures, including check-ups of the treatment plan

Each of the two dosimetry checks listed above involves a certain type of measurements and, of course, the adjacent instrumentation. A correct measurement also involves a correct calibration of the detectors and measuring systems involved in these procedures.

The paper present which methods are currently used for dosimetry in hadron beams (both continuous and pulsed), what instruments are currently available, how these dosemeters should be calibrated, and what are the current standards in place for the hadron therapy dosimetry.

ON LINE DOSE MONITORING IN ION THERAPY

N. Pauna, D. Dabli, P. Force, B. Joly, L. Lestand, G. Montarou, O. Bouhadida

Beams of heavy charged particles like protons or heavy ions, like carbon, represent the optimum tool for the treatment of deep seated, inoperable and radioresistant tumors growing in close vicinity to organs at risk. In-beam positron emission tomography (in-beam PET) is currently one of the available method for *in situ* monitoring highly tumor conformed charged hadron therapy by imaging the beta plus emitting isotopes produced during therapeutic exposures.

We present physical and radiobiological rationale for carbon ions as well as 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.

These studies are undertaken in the frame of the Rhône-Alpes Regional Research Programs for Hadrontherapy, and the National Project of Nuclear Instruments and Methods against Cancer, driven by the National Institute for Nuclear and Particle Physics of the CNRS.

Nicoleta M. PAUNA, MCF - Laboratoire de Physique Corpusculaire - Aubière cedex - FRANCE

DOSIMETRY IN 60 MeV PROTON RADIOTHERAPY BEAM AT THE INSTITUTE OF NUCLEAR PHYSICS IN KRAKOW

Urszula Sowa[1], Jan Swakoń[1], Paweł Olko[1], Marta Ptaszkiewicz[1], Roland Stark[2], Liliana Stolarczyk[1], Andreas Weber[2]

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The facility for proton radiotherapy of eye cancer at the Institute of Nuclear Physics Polish Academy of Science (Polish acronym IFJ PAN), Kraków, Poland is fully operational and ready for treating patients. The 60 MeV proton beam is generated from isochronous cyclotron AIC-144. The accelerated protons are extracted from the cyclotron chamber and transported by the beam delivery system to the therapy room. Flat (uniform) lateral dose distribution is realized by a single 25 µm scattering tantalum foil 12 meters from the isocenter and a set of collimators. It ensures uniformity of the dose distribution to within $\pm$1% over a 4-cm-diameter region [1]. The spreading in depth is realized by the range modulator propeller made by PMMA, which produces the Spread Out Bragg Peak (SOBP) with 15 mm plateau, in full range of proton beam.

In the preparation to commissioning of the facility the detail beam dosimetry studies have been performed. The methodology and results of beam dosimetry performed at IFJ PAN in preparation of the treatment of eye cancer was presented. At the facility the absolute dosimetry was performed according to the TRS-398 Code of Practice

(IAEA), the dosimetry protocol recommended for clinical application of various radiotherapeutical beams, including proton radiotherapy [2].
At the Institute of Nuclear Physics the absolute proton beam dosimetry was performed in the 10 x 10 x 10 cm^3 water phantom, in the middle of the Spread Out Bragg Peak, SOBP. The control dosimetry for patients was preceded in solid state phantom made in PMMA. The conformity between in water and in phantom dosimetry is better than 0.6%. Dose measurements in water in the middle of SOBP performed using Markus chamber PTW 23343 mounted in a 3D scanner and using cylindrical PTW 31010 chamber 0.125 cm^3 were consistent within 0.3%. Next, the intercomparison with the clinical dosimeters from the Charité - Universitätsmedizin Berlin (previously Hahn Meitner Institute) has been performed.
The relative in phantom dosimetry (lateral dose distributions with penumbra and depth dose distributions) was performed using ionizations chambers and diodes.

SECONDARY STANDARD DOSIMETRY LABORATORY AT INFLPR

F. Scarlat, R. Minea, A. Scarisoreanu, E. Badita, E. Mitru, E. Sima, M. Dumitrascu, E Stancu, C. Vancea,
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INFLPR has constructed a High Energy Secondary Standard Dosimetry Laboratory SSDL–STARDOOR – for performing dosimetric calibrations according to ISO 17025/2005 standards. This is outfitted with UNIDOS Secondary Standard Dosimeter from PTW (Freiburg Physikalisch-Technische Werksttaten) calibrated at the PTB-Braunschweig (German Federal Institute of Physics and Metrology). A radiation beam of the quality of Q used by our laboratory as calibration source are provided by INFLPR 7 MeV electron beam linear accelerator mounted in our facility. Nowadays there are more and more linear accelerator equipments used in radiation therapy practice due to their technical characteristics. Approach to clinical condition trough calibration to a high energy beam will improve quality of dosimetric chain used in routine dosimetry calibration in a radiotherapy laboratory. SSDL-STARDOOR is endowed with a MULTIDATA EuroStandard Dosimetry System compounded by: EuroStandard 3D Realtime Dosimetry System, Universal Waterphantom, Transport/Storage Cart, Electrometer, Notebook, Printer, In-air Scanning Frame and RTD Software Version 5.2 to perform absorbed dose distribution in 1D, 2D and 3D measured in water, air and film dosimetry. SSDL-STARDOOR has three principal aims: calibration of dosimetric equipment for third type laboratories, calibration of photon and electron beam, and testing of radiation beam characteristics. Dosimetric system from our laboratory alow calibration in wide range of energy for photons in 5 keV – 50 MeV region and electrons in 1 MeV - 50 MeV region from an electromagnetic spectrum. For future purposes our laboratory foresights to perform absorbed dose measurements for neutrons, protons and ions generated by RF classical accelerators in present and in the future - by the laser-driven plasma wakefield accelerators and laser – target interaction in relativistic regime ($1<a_e<100$, $a_e = |e|E/m_0\omega c = 4.8\ (\lambda/w_0)\ \sqrt{P[TW]}$) or in ultra-relativistic regime ($10^2 <a_e<10^5$, $a_e = 152\ (\lambda/w_0)\ \sqrt{P[PW]}$; 1 PW=$10^3$ TW =10^{15} W). SSDL-STARDOOR is offering calibration services for photon and electron beams, ionizing chambers and portable dosimetric instrumentation employed in various domains: education, research, industry, radiotherapy, radiation diagnostic, health physics/radiation protection and commercial. This paper is a detailed presentation of the quantity/equipment, range, best uncertainty, technique or reference standard.

THERMOLUMINESCENT DOSIMETERS USED IN TELETHERAPY (A) AND SCINTIGRAPHY (B)

Zoe Ghitulescu[1, 2]
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The tissue equivalence (LiF) of the thermoluminescent dosimeters enables their use within teletherapy in measuring the absorbed dose on phantoms.
In order to set up and compare treatment doses of the inner skull tumors using a photon beam, a number of 22 preirradiated and calibrated TLD–100 was used and the mesurements were made using the small water phantom type 4322 PTW and the antropomorphical phantom Rando Alderson.

The two phantoms are exposed at the isocenter and respective to a lateral 6 MeV (6MV) photon beam under the reference conditions from the Varian's medical accelerator type Clinac 2300 C/D. The corresponding dose values for 15 MU established with the aid of the Farmer ionization chamber and of the TLD's average dose value are very close.

The absorbed dose values of 12.073 cGy, 12.05 cGy, 12.01 cGy for the z_3 depth (in Rando phantom) obtained with the TLD's method, analytical and by simulation are comparable with the considered reference value of 12.064 cGy measured with the Farmer ionization chamber. Thus, their relative deviations against the value measured with the Farmer chamber are less than 0.45% and the TLD's response is good in assesing the prescribed treatment dose.

In this study, there were placed also two TLD-100 on a patient aiming to obtain the surface dose of the patient's heart one hour later after he was injected with ^{99m}Tc – Sestamibi having the activity of 18 mCi. The method described in this paper is based on biological assumptions, on MIRD theory and on the SPECT-CT image acquisition.

The result obtained by TLD's reading of $\overline{D}_{TLD}$ = 6,17 mGy resembles to the calculated dose value of $D_{calc,TLD}$ = 5.99 mGy as shown in Table [4]. If compares the cumulated activity after 6 h from injection with the activity obtained through MIRD method it is suggested a rapid elimination of the radiotracer. According to calculated value of the measurement uncertainty listed in Table 5, the TL detectors are found to be accurate within 5% (1SD).

NOVEMBER 13 (Saturday)

Workshop program: 09:00-10:30 AM

IMAGING TECHNIQUES IN RADIATION ONCOLOGY

Dragos Cuzino
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Radiation therapy imaging especially computed tomography is the basis of treatment planning. In the near future, the role of other imaging methods like MRI and PET functional imaging will be more important. Medical imaging in radiotherapy and hadrontherapy must provide quantitative assesement for tratement planning. In particular, innovative molecules for PET imaging are in a phase of advanced study and will provide fundamental information for treatment planning on hypoxia and on thelocalization of tumours which are almost invisible to CT. In radiation therapy, the control of the dose distribution relies on off-line dosimetry and not on direct on-line measurements. For example, at GSI, an innovativetechnique– the in-beam PET – has been developed exploiting the fact that carbon ions form 11C nuclei by interacting with the patient's body . Since 11C is a positron emitter, its distribution can be measured by means of a PET camera installed in the treatment room and compared with the treatment planning. Studies are underway also to exploit the technique for protontherapy The precise determination of the range is essential in proton therapy and, being based on CT data, correction factors have to be applied in the treatment planning to calculate the density of the traversed material. Proton radiography can be used to obtain direct information on the range for treatment planning optimisation and to perform imaging with negligible dose to the patient. We also emphasize the role of medical imaging in monitoring radiotherapy response. In order to optimize radiotherapy planning we need a close cooperation between radiologist and radiotherapist and we need to establish common protocoals used in asa many centers of diagnostic imaging and therapy planning. Teleradiology, HIS and RIS must be used for the efficient implementation of the programmes.

RECEPTOR MEDIATED IMAGING FOR SENTINEL LYMPH NODE (RADIO)DETECTION

Dana Niculae[1], Ioana Patrascu[1], Ioannis Pirmettis[2], Cosmin Mustaciosu[1], Catalin Tuta[1], Gabriela Voicu[3]
1. Horia Hulubei National Institute for Physics and Nuclear Engineering, Bucharest Magurele, Romania

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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 ^{99m}Tc 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.

PET-CT FUSION IMAGING IN RESTAGING OF SUSPECTED RECURRENT OR RESIDUAL LUNG CANCER

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1 PET-CT Department Euromedic Fundeni. 2- Central Military Hospital "Dr Carol Davila" Bucharest
3-CT-MRI Department Euromedic Arad

Objective: To assess the diagnostic accuracy of PET-CT in postoperative assessment in patients with lobectomy or pneumectomy for lung cancer.
Matherial and method: Study lot was represented by 43 patients with lobectomy or pneumectomy for oncologic disorders which were assessed between april 2008-january 2010 in Euromedic Diagnosis Imaging Center for suspected recurrent or residual disease based on clinical, biochemical markers and radiological changes, at least 3 months after surgery. Confirmation was obtained mainly by clinical follow-up. Patients were required to fast and hydrate at least 6 hours before scan. Acquisition was performed 1 hour after iv injection of 3,7 MBq/kg bw of 18F-FDG, from tentorium level to proximal third of thighs, using a DISCOVERT ST scanner of 16 slices.
Results: From 43 patients, 41 had changes suggesting residual or recurrent disease. Lesion assessment included SUV analysis using a cut-off value of 2.5. Compared with standard imaging postoperative follow-up (CT), PET-CT changed postoperative staging in 18 patients by identifying malignant lesions omitted in CT (mainly local and lymph node recurrences) with immediate terapeutic approach being changed; also PET-CT excluded presence of recurrences in 2 patients as suggested by CT scan.
Conclussions: PET-CT fusion imaging is a high-performance tehnique with excellent results in postoperative restaging of suspected residual or recurrent lung cancer.

MOLECULAR IMAGING AGENTS FOR PET BASED ON GA-68

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Today the majority of PET studies are performed with F-18 radiopharmaceuticals requiring an on-site cyclotron or shipment from a site in close proximity to the place where the investigation is performed. Generator based radionuclides would allow easier availability and more flexibility in use. ^{68}Ge/^{68}Ga generators provide cyclotron-independent access to positron emission tomography (PET) radiopharmaceuticals. ^{68}Ga is a short lived positron emitter (half-life 67.6 min) and is coming from his parent ^{68}Ge, which have a half-life of 270.8 days. The 270 days half-life of the parent allows the use of the generator for a long period, potentially up to 1 year or even longer. The 67.6 half-life of the ^{68}Ga matches the pharmacokinetics of many peptides and other small molecules owing to rapid diffusion, localization at the target and fast blood clearance. The ^{68}Ga solutions eluted from the generator are usually containing small amounts of other cations. Before the radiolabelling of peptides with it, we have to purify the eluate. Because of the metallic impurities (Fe, Zn, breakthrough of Ge), the eluate has to be purified either on a cation exchange column, on an anion exchange column or both of them, combined. In this paper the results obtained after the purification on a cation exchange column, anion exchange column, both of them and fractioned elution will be presented.

Purification using anion resin and fractioned elution are feasible leading to a high quality eluate suitable for peptide radiolabelling

Workshop program: 11:00-14

ACCELERATORS IN HADRONTHERAPY - *(ED.)*

D. Sardari

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RELATION BETWEEN APOPTOSIS AND DELAYED LUMINESCENCE OF HUMAN LEUKEMIA JURKAT T-CELLS UNDER PROTON-IRRADIATION AND OXIDATIVE STRESS CONDITIONS

Irina Baran[a,*], Constanta Ganea[a], Ioan Ursu[b], Vincenza Barresi[c], Agata Scordino[d,e], , Francesco Musumeci[d,e], Salvatore Tudisco[d,e], Simona Privitera[d,e], Rosaria Grasso[d,e], Daniele F. Condorelli[c], , Virgil Baran[b], Eva Katona[a], Maria-Magdalena Mocanu[a], Raluca Ungureanu[a], Marisa Gulino[d,e], G.A. Pablo Cirrone[d], Giacomo Cuttone[d], Lucia Maria Valastro[d]

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We investigated the relation between apoptosis and delayed luminescence (DL) in human leukemia Jurkat T-cells undergoing various treatments. We used menadione, hydrogen peroxide and quercetin to induce oxidative stress conditions under different doses and treatment times. We irradiated Jurkat cells by using modulated beams of accelerated protons having energies up to 62 MeV, under a dose of 10 Gy distributed uniformly inside the cell suspension. We assessed cell proliferation, clonogenic survival and delayed luminescence of treated cells. Apoptosis and cell cycle distributions were measured by flow-cytometry. Irradiation with protons produced a modest increase in the apoptotic rate, but blocked the cell cycle at the G_2/M phase for at least 48 h after irradiation, suggesting the presence of severe DNA damage. The clonogenic surviving rate was below the resolution of our assay (0.12%), indicating that 10 Gy of protons induce massive necrosis in this cell system. Trypan blue exclusion tests confirmed high necrotic rates of 18.4% and 46.6% at 24 h and 48 h after irradiation, respectively. Delayed light emission of the living cells exhibited different characteristics when probed at 1 h or 24 h after irradiation. A 34% reduction of the DL quantum yield was observed in a specific DL time interval, 1-10 ms after the laser excitation of the cell samples after 1 h from irradiation, whereas the DL quantum yield exhibited an increase of 27% in the DL time interval 0.1-1 ms in cell samples probed 24 h after irradiation. The treatments using menadione, hydrogen peroxide and quercetin as oxidant agents potently induced apoptosis of Jurkat cells in a dose-dependent manner and consistently decreased the intensity of delayed photoemission. Our data

suggest the ability of superoxide anions to quench DL on the 100 μs - 10 ms scale and the relative insensitivity of DL to intracellular $OH^{\bullet}$ and H_2O_2 levels. By collecting the data obtained with all the treatments employed in this study, we obtained a strong anti-correlation between apoptosis of human leukemia Jurkat cells and UV-induced delayed photoemission on a specific time interval ranging from 100 μs to 1 ms after UV-excitation of the cell samples. Having in view the growing interest of using DL spectroscopy in clinical applications, this study brings useful insights into the biochemical mechanisms responsible for delayed luminescence of living cells and provides new data regarding the relation between DL and the cell status.

BIOLOGICAL EFFICACY OF C^{14} IONS. I*N VITRO* STUDIES.

E.L. Kadyrova[1], E.Yu. Grigorieva[1] , E.Yu. Koldaeva[1], M.G. Naidenov[1], A.D. Fertman [2], N.V. Markov[2], A.A. Lipengolz[3], V.N. Kulakov[3], A.A. Golubev[2]
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*Aim***.** The investigation of cytotoxic influence of heavy high energy C^{14}ions in tumor mammalian cells. It was used beam of carbon ions with the energy of 2400-3600 MeV, which was produced in accelerator complex of Institute of Theoretical and Experimental Physics (ITEP).
Materials and methods. There were used two standard test-lines of tumor cells – murine melanoma B16F10 (RPMI 1640 medium with 10% calf embryonic serum (CES), 4 мM L-glutamine and gentamycin) and Chinese hamster ovary cells (CHO-K1) - Ham's F_{12} Medium with 10% CES, glutamine, penicillin and streptomycin. For the estimation of cytotoxic affect of high energy carbon we used the test of colony formation. Control (non-irradiated cells) and irradiated cells were plated at 6-holes plates (2, 4 and 8 thousand cells per hole); at low doses of irradiation can observe the suppression or the stimulation of the growth of tumor cells. CHO-K1 line was plated the same (300 and 500 cells/hole). Every dose of irradiation was repeated not less three times. Every irradiated sample was plated into two holes. We calculated the amount of colonies after 3, 5 and 7 days of cultivation under the invert microscope (the magnification ×10). Minimum group of 20 alive closed contacted and similar morphology cells is the good colony.
Results. Tumor cells were irradiated by high energy ions C^{14} in the doses, equivalent to the range 1 - 13 Gy (namely 1,2,4,5,7,10 and 13 Gy), at two positions: «entrance» of Bragg's peak and «maximum» of Bragg's peak. After the irradiation cells were treated by Versen, pipetted, and we calculated the quantity of alive cells (immediately after the irradiation) by routine method with the using of trypane blue. Even during first hours after the irradiation in some experimental samples was observed a great decrease of alive cells in the comparison with non-irradiated ones. The efficiencies of both lines were very high (up to 98%). Comparative estimation of cell ability of two lines to form the colonies in dependence on absorbed dose of carbon (dose-effect curve) showed that for more expressed therapeutic effect of carbon it should be necessary more carefully to determine optimal dose of irradiation; it needs future investigations.
Conclusion. The experiments, carried out at two widely used tumor mammalian cell lines showed the perspective of high energy carbon ions using speed up at accelerator complex of ITEP) for the development of new methods in hadron therapy.

THE BIOLOGICAL EFFICACY OF C^{14}IONS. THE *IN VIVO* STUDIES.

E.Yu. Koldaeva[1], E.Yu. Grigorieva[1] , M.G. Naidenov[1] ,E.L. Kadyrova[1], , A.D. Fertman [2], N.V. Markov[2], A.A. Lipengolz[3], V.N. Kulakov[3], A.A. Golubev[2]
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Objective of study. The investigation of influence of heavy C^{14}ions on growth of murine transplanted melanoma. The energy of carbon flux produced in accelerator complex of Institute of theoretical and experimental physics was varied from 2 400 MeV to 3 600 MeV.

Materials and Methods. The study of C^{14}ions effect in melanoma B-16F10 bearing male mice C57Bl/6 was carried out. Weight of mice was 20-22 g, tumor suspension (6 mln. of cells per 0.3 ml of Hanks nutrient medium) was subcutaneously inoculated. The irradiation of experimental animals was conducted on 10-th day after tumor transplantation. At this day tumor volume was about 1 cm^3 . Doses of heavy ions were equivalent to 10 and 20 Gy. All experimental animals were given standard feeding. Daily after irradiation the measurement of three dimensions of tumor volume of both experimental and control (non-treated) mice were carried out. The increase of survival and per cent of growth tumor inhibition was estimated.

Results. There was shown that 10 and 20 Gy heavy ions irradiation were capable to essentially retard tumor growth comparatively with non-irradiated control (50 and 70%, respectively). The maximal difference was detected at 5-th and 7-th days after carbon ions irradiation (see table).

Efficacy of heavy C^{14}ions influence on melanoma B-16F10 bearing male mice C57Bl/6.

Animal group	Tumor volume V_t/V_0				Tumor growth inhibition %		
	3 day	5 day	7 day	14 day	3 day	5 day	7 day
контроль	2,2±0,3	5,8±0,1	11,8±0,2	43,6±0,1			
C^{14}, 10 Gy	1,4±0,1	3,1±0,9	5,7±1,2	27,6±3,2	36,14%	46,93%	51,80%
C_{14}, 20 Gy	1,3±0,1	1,7±0,3	3,1±0,2	17,4±1,5	41,57%	71,44%	74,13%

These experimental data have confirmed our preliminary data *in vitro*. The B16F10 cell growth in both cell culture and in total animal body was suppressed by C^{14} ions treatment. Expressed dose-effect dependence for tumor growth delay after C^{14} ions irradiation was shown. The retention of anticancer effect during more 7 days after C^{14} radiation therapy allows promising therapeutic efficacy. It is necessary for final evaluation of C^{14} ions irradiation efficacy to prolong further studies on human xenografts transplanted to nude animals and on large animals (dogs) with spontaneous tumors of various ethiology.

Conclusion. Our theoretical premises concerning the possibility of therapeutic efficacy at the use of impulse ion fluxes were confirmed in the *in vitro* and *in vivo* studies. Therefore continued investigation of this novel hadron therapy technique is too required.

TARGETED RADIONUCLIDE THERAPY (TRT) IN ONCOLOGY, BASED ON RADIOLABELLED PEPTIDES AND ANTIBODIES

Dana Niculae[1], Rodica Anghel[2], Valeria Lungu[1], Iuliana Gruia[2], Lorelei Brasoveanu[3], Valentina Negoita[2], Ioana Patrascu[1]

1. Horia Hulubei National Institute for Physics and Nuclear Engineering Bucharest - Magurele Romania
2. Institute of Oncology Prof Dr Al Trestioreanu, Bucharest, Romania
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Introduction: Radiolabelled antibodies with beta emitters offer a promising alternative for management of different malignancies (radioimmunotherapy). The development of the $^{188}W/^{188}Re$ generator, gives the possibility of having a radionuclide with therapeutic effect by virtue of its specific nuclear properties as: E_β=2,12 Mev, E_γ=155 keV, $T_{1/2}$=16.9 h and easy chemistry which allows to make similar labelling approaches to those used for ^{99m}Tc.

Aim: The aim of the present work was 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.

Methods: Direct labelling method was employed 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. Optimization studies of radiolabelling processes lead to 90 min. incubation time at 90 ^{0} C, ^{188}Re-labeling yields were 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 10^5 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 ^{188}Re-anti-MUC1 was evaluated by MTT method using MDA-MB-231 respectively MCF-7 cell lines. The citotoxicity of these two radiolabelled antibodies was also tested by MTT using HeLa cell lines after 24 and 48 h incubation time.

Results and conclusions: Radiochemical purity of ^{188}Re-VEGF and ^{188}Re-anti-MUC1 were higher than 95% while the specific activities of the radiolabelled antibodies were 100 mCi/mg.

The maximum binding of ^{188}Re-MUC1 to 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 (Fig 1). The ^{188}Re-MUC1 induces a cytotoxicity which decrease the HeLa cells viability up to 62.34% (at 48 h, 100 µCi).

The results also show that for 0.3 – 0.6 µg antibody there is maximum binding of ^{188}Re-anti-VEGF to expressive tumour cell receptors. The graph of the induced radiotoxicity of ^{188}Re-anti-VEGF registers a decreasing of the MDA-MB-231 cells viability, at 50-100 µCi, up to 90%; the cytotoxic effect of the ^{188}Re-anti-VEGF on HeLa cells was also high.

NOVEMBER 14 (Sunday)

Workshop program : 9:00-10:30 AM

THE ROLE OF HYPERBARIC OXYGEN IN RADIOTHERAPY

Ion Bogdan Cristian

Hyperbaric and Diving Medicine Institute, Bielefeld – Germany, Hyperbaric and Diving Medicine Institute, Constanta – Romania

The applications of hyperbaric oxygenation in oncology are:

In the first place hyperbaric oxygen fights against the complications of radiotherapy. Radiation therapy is often accompanied by endothelial damage in irradiated territory, and the result is radiation vasculitis, and implicit the considerable depreciation of the irradiated tissues, hyperbaric oxygen is the only method that allows rapid angiogenesis, recovering the capillary bed in the affected territory.

Both chemotherapy and radiotherapy, takes place without complications at patients who have received hyperbaric oxygenation in parallel, by increasing the body's regenerative capacity by releasing angiogenic peptides.

The synchronization of tumor cells effect. Tumor mass, characterized by an exacerbated increase, presents ischemic or necrotic foci, however, hypoxic, without reactivity both in chemotherapy and the radiotherapy. Hyperbaric oxygenation allows homogenization of the tumor, combating intratumoral ischemic areas, increasing tumor sensitivity to radiation, in general.

Hyperbaric oxygen has a strong effect of increasing the concentration of TNF in the body with immunomodulation enriching the patient's immune capacity.

Hyperbaric oxygen is a potent antibiotic effect particularly for intracellular microorganisms (mycoplasmosis, toxoplasmosis, etc.), sterilizing the patient's body, thereby improving the immune response.

THE EFFECTS OF HYPERBARIC OXYGENATION IN IRRADIATED TISSUE REHABILITATION

Ion Bogdan Cristian

Hyperbaric and Diving Medicine Institute, Bielefeld – Germany, Hyperbaric and Diving Medicine Institute, Constanta – Romania

Hyperbaric oxygenation therapy uses "oxygen" as medicine allowing its distribution to tissues in certain diseases, in large amount, by increasing environmental pressure. Increasing environmental pressure leads both to increasing the amount of oxygen dissolved in plasma (quantitative growth) and the radius of penetration of oxygen in the tissues (qualitative growth).

Hyperbaric oxygenation is combating edema. Unlike other drugs that cause the reduction of edema with hypoxia, hyperbaric oxygen reduces edema with hyperoxia. Normally, the ischemic tissues become gradually hypoxic because of progressive edema, leading to increase edema and ischemia. Vasoconstriction is a key element in tissue edema and thus release of cellular edema.

Hyperbaric oxygen, even in normal oxygenate tissues, especially in hypoxic tissues leads to a angiogenesis reaction, taking place the formation of new functional capillary in hypoxic tissues and thickening of the capillary network in normoxic tissues with beneficial effects on their functionality. Angiogenesis occurs as a result of hyperbaric oxygen stimulation of the platelets and macrophages activity, respectively PDGF secretion and VEGF and FGF, but also other angiogenic peptides.

The activation of macrophages and leukocytes effect with immune response is essential to improve both primary cellular immunity, and also by secretion of specific factors in the processes of regeneration and post necrotic repairs. Besides increasing the secretion of PDGF and FGF, hyperbaric oxygen stimulates the secretion of TNF, which is essential in inducing the autoimmune response in anti-tumor protection and cellular immunity. TNF plays a major role in the anti-tumor protection so that there is a great need to study the involvement of hyperbaric oxygen in anti-tumor treatment.

One of the main concerns in studies on stem cells is the method of propagation of these adult stem cells and reinjection of their own for repairing damaged tissues. PENN study is a milestone in stem cell research because at present we know that exposure to hyperbaric oxygen for 40 hours at least 2 ATA lead to a global increase in their circulating adult stem cells (CD34) by eightfold.

LASER – ACCELERATED PROTON AND ION BEAMS FOR RADIOTHERAPY.

F. Scarlat, R. Minea, A. Scarisoreanu, E. Badita, E. Sima, M. Dumitrascu, E. Mitru, E Stancu, C. Vancea, 1, N. Verga-2

1- National Institute for Laser, Plasma and Radiation Physics – INFLPR, Bucharest, Romania, 2- University of Medicine and Pharmacy “Carol Davila”, Bucharest, Romania

Progress made in the ultra-intense short pulse laser technology has led to obtaining some very high acceleration gradients of the order 10-100 GeV/m, by comparison with the conventional accelerators based on radiofrequency where the gradient of the acceleration fields is of the order 10-50 MeV/m. Starting from these considerations, the made progress and from the existing requirement of a target for the nuclear transmutation, this article is presenting an evaluation and some talks on the possible parameters for a proton laser accelerator. Plasmas, which are gases of free ions and electrons, can support large electric fields – a characteristic that can be used to accelerate particles to relativistic energies over much shorter distances than is possible with current technologies. Plasma wakefield acceleration, either laser driven which have advantage of high electric field (100 GeV/m over distances of a few cms) or electron – bunch driven which has permit a medium electric field (50 GeV/m over 1 metre), has been demonstrated to hold great potential. In present there is a proposal to excite plasma with a proton bunch. The proton driven plasma wakefield acceleration for 1 TeV proton bunch has been already investigated in computer simulations (Caldwell et al., 2009). In contrast to plasmas driven by electrons, the proton driven plasma can accelerate electrons to the TeV scale in one stage. Direct laser acceleration of protons to relativistic energies ($E_{0,p}$ > 938 MeV) requires intensity $I_p = 4.6 \times 10^{24}$ W/cm^2 x $(1\mu m/\lambda)^2$, corresponding to the dimensionless amplitude $a_e \equiv (|e|.E/ m.\omega.c) = M/m \approx 1836$, where E, λ and ω are the electric field, wavelength, and frequency of the laser radiation, e and m are the electron charge and rest mass, c is the light speed, and M is the rest proton mass. In plasmas, because of collective effects, protons can gain relativistic energies at much less intensity about $I_p = 10^{21}$ W/cm^2 x (1μm/λ)^2. Starting from the above, in this paper we discuss the laser - accelerated proton and ion beams parameters for hadrontherapy

CONCEPT FOR A LINAC-BASED SEEDED FEL PROJECT AT INFLPR

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The FEL proposal is the result of a research contract financed in Romania for to extend the applications of electron accelerators - 7 MeV linac, 11.5 MeV microtron, 31 MeV betatron and 40 MeV medical betatron – built in the National Institute for Lasers, Plasma and Radiation Physics (INFLPR), Romania. This paper is a presentation of the concept and system parameters for Linac-based Free-Electron Laser Project at INFLPR. The project has considered the recent advances of technologies in the domain of accelerators, lasers, undulators and seeded operation with HGHG. The Project proposal has also considered the frequency domains from Infra-Red to Hard X-rays, dividing it in 5 spectral domains, following that the scientific community in Romania should establish which domain still stay and which is the first to start, function of the application. By now, our local experience in building and application of charged particle accelerators and the use of laser systems have been considered for accomplishing a FEL which may generate coherent radiation in the Infra-Red and Ultraviolet/Vacuum –ultraviolet wavelength, in the first stage, the final milestone being to obtain coherent ionizing radiations in the HXR range.

ELECTRON PARAMAGNETIC RESONANCE SPECTROSCOPY: NEW TOOL IN HADRONTHERAPY

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The electron paramagnetic resonance (EPR) spectroscopy is a physical method of observing resonance absorption of microwave power by unpaired electron spins in a magnetic field. The EPR spectroscopy has many applications; two of them could be used in hadrontherapy. The first one is related with the possibility of the EPR to obtain the irradiation dose. The radiation produces free (unpaired) electrons, and the EPR signal intensity is proportional to the spin concentration and so to the total dose. The second application is related to the capability of the EPR to measure the free radicals species, which for example in proton therapy this species are the key in DNA damage.

LASER ACCELERATED HADRON & ELECTRON BEAMS: REQUIREMENTS FOR THE CETAL PW LASER FACILITY

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Lately, there is an increasing number of multi-terawatt and petawatt laser interaction facilities being built, as the potential for fundamental and applied physics studies (and, among these, potential applications in hadrontherapy) is extraordinary promising.
However, in order to set up such a facility, the need for a detailed understanding of the potential radiological hazards is required and their impact on personnel is of major concern. Under different experimental circumstances an ultrahigh intensity laser facility can generate significant dose equivalent levels originated from the bursts of high energy photns (X and gamma rays), neutrons, miuons, etc. These are produced as a result of a highly focused laser spot (about10 μm focus wide or less) on a target (gas jet, semi-solid or solid target) at intensity level above 10^{18} W/cm^2. The interaction with the target will generate in the latter large numbers of electrons of high energy, which in turn generate via Bremsstrahlung large amounts of X and γ radiation in the target, in the materials inside the experimental chamber and in the walls of the experimental vessel. Under these conditions, it has been estimated (for the Astra Gemini facility, for instance) that the unprotected dose level can reach as high as 900 Sv / year.
The present paper shows our estimation of the radiation protection required for the CETAL PW laser facility, based on the experience gained in other facilities, the estimation of the occupancy and of the laser characteristics and using FLUKA simulations to estimate the worst case doses.

Workshop program (Round table & Concluding remarks): Research groups - ROMANIAN RESEARCH & DEVELOPING TOPICS ON RADIOTHERAPY INCLUDING HADRONTHERAPY

SRH
SOCIETATEA ROMANA DE HADRONOTERAPIE
ALMAS STREET NO. 34, 1ST DISTRICT, BUCHAREST, CP 012837, ROMANIA
www.rsh.ro

- REVIEW -

The 1st Romanian Society of Hadrontherapy (RSH) Workshop

"RADIOTHERAPY WITH NEUTRON AND PROTON BEAMS AS INTER- AND MULTI- DISCIPLINARY R&D"

PREDEAL, ROMANIA
February 27-March 01, 2009

February 26th
Welcome dinner (8:00 PM)
February 27th
History and "geography" of hadrontherapy

	Title	Author	min	
1	ENLIGHT, position and role in Europe	M. Dosanjh	20	
2	Protontherapy at PSI. More than 20 years of experience	R. Schneider	20	
3	Romania, a new country in the European and international circle of hadrontherapy	N. Verga	20	60

Protontherapy and neutron therapy, what is necessary and sufficient?

	Title	Author	min	
1	A proton therapy facility; large or small	F. Vernimmen	20	
2	Extreme Light Infrastructure (ELI) and hadrontherapy	D. C. Dumitras	30	
3	Absolute and relative dosimetry of proton and carbon ion beams on active and passive particle facilities	L. Raffaele	20	
4	In-vivo proton beam shaping using static magnetic field.	D. Sardari	20	80

Inter- disciplinary and multi- disciplinary R&D

	Title	Author	min	
1	Monte Carlo simulation for hadrontherapy	Maria Grazia Pia	20	
2	Investigation of Bragg peak tail in Carbon ion therapy	P. Saidi	20	
3	Quantifying the Depth-Dose curve in hadron therapy: a computational approach.	D. Sardari	20	
4	Computer codes ALICE, SRIM, and TRIM, their application in hadrontherapy.	P. Saidi	20	

Inter- disciplinary and multi- disciplinary R&D

	Title	Author	min	
5	Specific research projects in the framework of ENLIGHT: PARTNER, ULICE and ENVISION	M. Dosanjh	20	

6	Radiobiology of radiosurgery	F. Vernimmen	20	
7	Investigations on the concept „Complementary alternative medicine" (photodynamic therapy) and nuclear medicine	R. M. Ion, R.C.Fierascu, I. Dumitriu	20	160

February 28th

Clinical and economical in protontherapy and neutron therapy

	Title	Author	min	
1	Lecture on proton therapy	E. Luchin	20	
2	Long term results of proton radio surgery for AVM's, meningiomas, and acoustic neurinomas	F. Vernimmen	20	
3	Secondary effects in hadrontherapy	N. Verga	20	
4	The results of treating a large series of salivary gland tumours	Clare Stannard	20	

	Title	Author	min	
5	Lecture on proton treatment of meningiomas or other tumors at the skull base	E. Blomquist	20	
6	The results of smaller series on: advanced breast ca. endometrial sarcoma, large irresectable neck nodes, - and maxillary sinus tumours	Clare Stannard	20	
7	Radiation Therapy: Past, Present and the Future	A. Arbabi	20	120

March 1st

2 - Workshop program (Round table & Concluding remarks): 10:00-12:00 AM (Conference hall / hotel)

A small **exhibition** will be held near conference hall (Siemens Romania, Canberra Packard Central Europe) for *the whole period of workshop*.