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Lectio Magistralis

BIOMEDICAL RESEARCH AT NEW HIGH-ENERGY PARTICLE ACCELERATORS

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At the Facility of Antiprotons and Ion research (FAIR) in Darmstadt [1], applied physics has been always part of one of the four pillars (APPA [2]). The necessity to transform the FAIR Biophysics Collaboration into a truly International, worldwide collaboration stems from the interest in the same activities in many new facilities (e.g. SPIRAL2, ELI, SPES, SEEIIST in Europe; FRIB in USA; NICA in Russia; RAON in Korea). The opportunities of the new accelerators can lead to breakthrough advances in space radiation research (where high energy is necessary) and medical physics (including particle radiography, minibeam radiotherapy, FLASH radiotherapy, use of radioactive ion beam) and production of new radionuclides for medicine [3]. These ideas have been discussed in the recent Biophysics Collaboration meeting and will be presented in this seminar [4].

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ABSTRACTS

SESSIONE 1

SPACE RADIATION

CHAIR: *Mariagabriella Pugliese*

DOSIMETRY IN THE SPACE: THE SHIELDING EFFECTIVENESS FOR THE RADIOPROTECTION OF ASTRONAUTS.

Filomena Loffredo [1], Emanuele Vardaci [2,3], Mariagabriella Pugliese [2,3], Marcello Serra [4] and Maria Quarto [1]

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The study of materials suitable for radiation protection of astronauts in space missions is always a topic of fundamental importance. The main aim of any radiation-protection program in space is to minimize crew's exposure to ionizing radiations. Unlike on the Earth, in the space the only countermeasure is the shielding. The space radiation field is a mix of radiations, Van Allen radiation belts, Galactic Cosmic Radiation (GCR) and Solar Particle Events (SPE)1,2. This work concerns with the effectiveness of shielding materials against radiations in space conditions, in particular for the Galactic Cosmic Radiation. The study was conducted by developing a simulation tool based on Geant4 framework3,4. The physics case reported here deals with the interaction of a 1 GeV proton beam (protons represent about 87% of the GCR flux with the energy spectrum peak around 1GeV) with a target added with boric acid or Gadolinium to deplete neutron escaping5. Charge, mass and energy distributions of secondary particles generated by the interaction are computed on the basis of different interaction models. It is found that the particles escaping the shielding material and reach a ionization chamber located in the opposite side of the shield are still mainly protons and neutrons. The added boric acid and or Gd acts as an effective neutron mitigating material5. However, the average dose does not change effectively because of the additional production of secondary particle after the interaction.

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VISUAL SYSTEM ACTIVATION BY IONIZING RADIATION: MODELLING THE IRRADIATION SETUP FOR WHOLE RABBIT EYE EXPOSURES

A. Mentana [1], G. Baiocco [1], I. Guardamagna [1], L. Lonati [1], A. Ottolenghi [1], M. Paci [2], S. Beninati [2], I. Borromeo [2], L. Di Fino [2], G. Romoli [2], W.G. Sannita [3], L. Narici [2]

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Cosmic radiation represents a major issue for human space exploration and several aspects of the risk assessment are under continuous scrutiny, in order to determine countermeasures to minimize the damaging effects on astronauts [1,2]. The earliest evidence of space radiation effects on brain function has been the phosphenes (flashes of light, LF) perceptions, reported by astronauts since the Apollo missions. The LF phenomenon and the underlying mechanisms have been largely investigated, showing that particles can initiate retinal processes capable of activating the visual system, including the visual cortex [3-7]. The recently reported effects of radiation on sensory channels other than visual suggest also a direct action of radiation on a neuron or neural networks and the possible mechanisms behind that kind of effect are under investigation [8]. In particular, ionizing radiation may influence the biological signaling mainly due to calcium ion homeostasis. In this context, the VISAIR project is conducting an experimental study in *ex vivo* whole rabbit eyes cultured in suitable medium to try to shed light on the activation of the visual system, using radiation with different LET/Z to analyze possible modulation of the effects with such parameters [9]. Modeling is needed to interpret the results and extrapolate findings to radiation rates relevant for space exploration. We here present results obtained with a software replica of the irradiation setup for the experimental *ex vivo* model of the whole rabbit eye that will be exposed to different radiation qualities of relevance for the space radiation environment, including heavy ions at different energies and a reference X-ray field. Preliminary results obtained with the Monte Carlo code PHITS on the characterization of the radiation field in the target organ include the spatial distribution of dose and LET distribution, as well as microdosimetric quantities, for further correlation with the observed biological endpoints.

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EFFETTI MOLECOLARI INDOTTI DALL'IRRAGGIAMENTO DI RODITORI IN TORPORE SINTETICO

Timna Hitrec [1], Walter Tinganelli [2,3], Fabrizio Romani [4], Palma Simoniello [5], Fabio Squarcio [1], Marco Luppi [1], Gaetano Compagnone [4], Alessio G. Morganti [6], Giulia Babbi [7], Pier Luigi Martelli [7], Rita Casadio [7], Roberto Amici [1], Matteo Negrini [6], Antonio Zoccoli [8,9], Marco Durante [3,10], Matteo Cerri [1,8].

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L'ibernazione/torpore è una strategia biologica utilizzata da alcuni mammiferi in condizioni ambientali avverse, caratterizzata da un'attiva riduzione del metabolismo, con conseguente diminuzione della temperature corporea. Tra le modificazioni tissutali tipiche dell'ibernazione, risulta di particolare interesse il considerevole grado di radioprotezione cellulare che si instaura (1). Questa caratteristica potrebbe rivelarsi utile in molteplici condizioni sia cliniche, come la radioterapia oncologica, che non, come l'esplorazione umana del Sistema Solare o in caso di esposizione a dosi elevate di radiazioni. Recentemente è stata sviluppata una procedura per indurre uno stato molto simile al torpore (torpore sintetico) in un animale non-ibernante, il ratto (2). Questa procedura consente per la prima volta di studiare se gli effetti positivi indotti dall'ibernazione siano riscontrabili anche in mammiferi non ibernanti, in un'ottica di applicazione all'uomo. I meccanismi alla base della radioprotezione indotta dal torpore non sono infatti ancora noti e diverse ipotesi sono state avanzate: dalla riduzione della quantità di ossigeno presente nei tessuti, all'arresto del ciclo cellulare, dalla riduzione della risposta infiammatoria, all'attivazione di meccanismi di riparazione del DNA più efficaci. In questo esperimento, abbiamo quindi valutato tramite RNAseq l'espressione genica nel fegato di ratti irradiati (raggi X, 3Gy) in torpore sintetico rispetto ad animali irradiati in condizioni di normotermia. Risultati preliminari di questo esperimento indicano che la risposta molecolare all'irraggiamento in torpore sintetico differisce sostanzialmente da quella in eutermia, aprendo una via verso la comprensione dei meccanismi molecolari alla base della radioprotezione indotta dal torpore, ed alle sue applicazioni traslazionali.

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ABSTRACTS

SESSIONE 2

RADIOBIOLOGIA - EFFETTI BIOLOGICI E MECCANISMI DI BASE

CHAIR: *Francesca Antonelli - Francesco Berardinelli*

RADIOBIOLOGICAL PROMISES OF NEW FRONTIERS IN PROTONTHERAPY

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By revisiting some old concepts and anecdotal evidence, such as radiation-associated immunosuppression and abscopal cancer regression, as well as discovering new dose rate-dependent phenomena such as the FLASH effect, radiobiology has recently proven that it may still be a source of potential benefit to human health by potentially improving existing radiotherapy (RT) modalities. Exploiting biology-based systemic responses, it has paved the way for a combination of conventional RT with immunotherapy[1]. Exploring temporal scales for the administration of curative radiation doses, it has hinted at the possibility for FLASH-RT regimes to limit normal tissue toxicity[2]. Protontherapy (PT) is already known to offer advantages over photon/electron-based RT but there exist margins for improving some of its inherent limitations. Not surprisingly, therefore, both the above-mentioned approaches are being investigated for PT[3,4]. Here we shall discuss the possibility to further the application of PT to radioresistant cancer by a binary strategy termed Proton-Boron Capture Therapy (PBCT) that employs a nuclear fusion reaction between low-energy protons and 11B to increase the biological efficacy of clinical proton beams[5]. Furthermore, we shall present recent data supporting this approach based on chromosome aberration analysis by FISH techniques as well as other cytogenetic endpoints (e.g. cellular premature senescence and micronucleus formation) and propose that combination of FLASH-PT and PBCT may expand the already favorable therapeutic window for PT.

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NORMAL FIBROBLASTS DIFFERENTLY INFLUENCE THE MOTILITY OF ASPC-1 PANCREATIC CANCER CELLS EXPOSED TO LOW OR HIGH LET RADIATION

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Radiotherapy represents a major treatment option for patients with pancreatic cancer being recommended as a postoperative adjuvant and neoadjuvant treatment although its benefits remain limited. Several experimental studies have demonstrated that ionizing radiation might promote migration and invasion of tumor cells highlighting the importance of interactions between tumor cells and their microenvironment1. In particular, it has been reported that, after photon irradiation, interactions between pancreatic cancer cells and surrounding fibroblasts play an important role in tumor progression and invasion[2,3]. Several Authors reported that carbon ions may decrease the migration and invasiveness of some cancer cells in vitro and in vivo[1,4,5].
In this study we evaluated for the first time the influence of the microenvironment on cancer cell invasion analysing the effects of untreated fibroblasts released factors on irradiated AsPC-1 pancreatic cancer cells using different doses of photons and carbon ions. In the presence of conditioned medium collected from 1 Gy and 2 Gy photon irradiated fibroblasts the number of migrated tumor cells statistically increased compared to fresh complete medium. When medium was taken from carbon ion irradiated fibroblasts a general trend not statistically significant in migration reduction compared to fresh complete medium was recorded. Medium collected from photon-irradiated fibroblasts increased the ability of AsPC-1 cells to invade the matrigel coat towards the lower insert. Conversely, medium from carbon ion-irradiated fibroblasts determined a strong decrease of invasiveness of pancreatic cancer cells bringing almost to zero the number of invading cells In conclusion, in our experimental settings the presence of soluble factors released by high or low LET irradiated fibroblasts differently modulated the invasiveness capability of irradiated pancreatic cancer cells depending on the type of irradiation used.

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COMBINATION OF CARBON IONS THERAPY AND HYPERTERMIA APPLIED TO PANCREATIC ADENOCARCINOMA CELL CULTURES

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We present a new therapeutic approach for the treatment of *in-vitro* pancreatic cancer BxPC3 cells, consisting in a combination of carbon ions/photons irradiation and hyperthermia. In our study the heating release is obtained by means of conventional procedure and magnetic fluid hyperthemia (MFH) mediated by magnetic nanoparticles (MNPs). Samples of iron- oxides based MNPs were synthesized and completely characterized. Preliminary *in-vitro* hyperthermia measurements on BxPC3 cells cultures incubating MNPs have been performed. Cell cultures irradiation with carbon ions was performed using the synchrotron-based clinical scanning beams at the Centro Nazionale di Adroterapia Oncologica (Pavia). Photon beam irradiation of cell cultures was performed using a 6 MV linear accelerator at Istituto Nazionale dei Tumori (Milano). The combined effect of hyperthemia and radiation was assessed using a clonogenic assay. BxPC3 cells were treated with three different protocols: (1) exposed to carbon ions/photons irradiation alone, (2) irradiated after the administration of MNPs and (3) treated with hyperthermia for 30 minutes at 42°C after irradiation (of samples previously incubated with MNPs). With respect to cells exposed to radiation alone, case (1), clonogenic survival (CS) decreases when cells uptake MNPs and undergo irradiation, case (2). A further decrease of CS is observed when hyperthermic treatment is carried for each exposure dose, case (3). This behaviour is due to the additional effect of hyperthermia with respect to the presence of magnetic nanoparticles and irradiation alone. The results clearly show a significant effect of hyperthermia for both irradiation protocols, which enhances the rate of cell death induced by of MNPs and/or irradiation. These encouraging results open the way to further *in vivo* investigations to finally test this new combined therapy (hadron irradiation and MNP assisted hyperthermia) in view of its translation to clinics.

"IMMUNOGENIC POTENTIAL OF CARBON IONS IN COMBINATION WITH IMMUNOTHERAPEUTIC DRUGS TESTED IN A MOUSE MODEL"

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Radiotherapy is one of the main treatments for cancers, which has experienced important improvements in the last years; metastatic disease still remains a problem. It is known that immune system plays a key role in the elimination of primary tumors and preventing tumor recurrence. Ionizing radiation is reported to be immunogenic, i.e. it may induce an immunogenic cell death in tumor cells leading to immunoactivation, in turn resulting in the shrinkage of out-of-field metastases. This phenomenon is known as abscopal effect. The right combination of radiotherapy with immunotherapy could be a strategy to induce durable responses and improve survival. Particle therapy with protons and especially carbon-ions is assumed to further increase the immunogenic effect. The aim of this study was to investigate the efficacy of X-ray and high-energy carbon ion therapy in a combination with immunotherapy. In this work we investigated the combination of radiotherapy, with either carbon ions or X-rays, and immune checkpoint inhibitors (CPI) (anti-CTLA-4 and anti-PD-1), in a syngeneic osteosarcoma mouse model (C3H/He mice, LM8 cells). Tumor cells were injected in both hind limbs of the mice. Following an initial growth period, one of the tumors was irradiated while the other was kept out of the irradiation field, mimicking the abscopal tumor. Macroscopic analysis on out-of-field metastases were carried out to investigate spontaneously formed lung metastases. Immune responses were investigated by histological analyses on the abscopal tumors screening. The results show that combination of carbon ion therapy and CPI lead to a reduced growth of abscopal tumors and reduced formation of lung metastases. In addition, in the abscopal tumors treated with combining therapy an immunogenic response resulting in increasing of infiltration of CD8+ cells was observed.
Combination of CPI with high-energy carbon ion radiotherapy could be a promising strategy for the treatment of tumor and metastasis.

DNA DAMAGES, GENE EXPRESSION AND MICROSCOPY: HOW AI- AND NEW FISH-BASED TECHNOLOGIES CAN SUPPORT GENOMIC RESEARCH AND CLINICAL GENETICS.

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Technology evolution has lately been on Artificial Intelligence, thus becoming a huge boost to new applications or even update existing ones, shaping and orienting them to new standards. MetaSystems have started working on implementing Artificial Intelligence on their microscope-based imaging systems as well, especially focusing their attention on the so-called Deep Neural Network, which has found a highly reliable application in metaphase analysis and karyotyping. The system capability to identify normal chromosomes and isolate abnormal ones within metaphases is turning to offer a great support to users. On the other side, innovation and expertise have also been used to dedicate our imaging systems to evaluate, automatize and quantitate gene expression on RNA transcript levels. Introducing and standardizing a new level of investigation (shifting it to the traditional DNA or proteins to their intermediate expression product) is increasing the amount of information collected both in Research and Clinical fields. MetaSystems have since long time been involved in new developments and automation for micronuclei assays, dicentric scoring, telomere length analysis, gene and chromosome aberration investigations with dedicated multifluorescence techniques and much more, related to the world of radiation biology; we are investing and eager to be preferred partners for longer times.

LA "PROTON BORON CAPTURE THERAPY" (PBCT) COME APPROCCIO PER AUMENTARE L'EFFICACIA RADIOBIOLOGICA DEI PROTONI IN MODELLI CELLULARI "IN- VITRO".

Marco Calvaruso [1,2], Luigi Minafra [1,2], Gaia Pucci [3], Francesco P. Cammarata [1,2], Gaetano Savoca [1,2], Valentina Bravatà [1,2], Giuseppe AP Cirrone [2], Giada Petringa [2], Lorenzo Manti [4,5], Giusi I Forte [1,2], Giacomo Cuttone [3], Giorgio Russo [1,2].

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La protonterapia (PT) è una modalità di trattamento radioterapico caratterizzata da un'elevata capacità balistica e da una maggiore conformità di dose rilasciata sul target. Un ulteriore aumento dell'efficacia biologica relativa (RBE) della PT, accompagnato da un incremento del "cell killing", può essere ottenuto sfruttando la reazione di fusione nucleare $p + 11B \rightarrow 3\alpha$. Tale reazione è alla base della Proton Boron Capture Therapy (PBCT) e consente di generare particelle alfa ad alto LET quando i protoni interagiscono con composti borati come il sodio borocaptato (NA2B12H11SH o "BSH") [1]. Al fine di valutare la risposta radiobiologica a livello molecolare in termini di risposta al danno al DNA (DDR) innescata dalla PBCT, abbiamo testato l'effetto del BSH in combinazione alla PT (2 Gy nella posizione mid-SOBP del fascio clinico avente un'energia di 62 MeV, presso l'INFN-LNS di Catania), mediante lo studio di espressione in immunofluorescenza della forma fosforilata dell'istone H2AX (γH2AX). Inoltre, tale analisi è stata accoppiata a quella di altre 5 proteine coinvolte nella DDR e in specifiche vie di segnale del riparo al DNA, attraverso tecnica Western Blot: la proteina X-Ray Repair Cross Complementing 6 (XRCC6/KU70), la Xeroderma Pigmentosum Group A- Complementing Protein (XPA), la Polymerase Beta (POLB), la Ataxia Telangiectasia and Rad3-Related kinase (ATR).I risultati ottenuti hanno dimostrato un effetto sinergico del BSH nell'indurre una maggiore DDR.Infine, abbiamo valutato come il pretrattamento con BSH potesse indurre una maggiore efficacia biologica della PT nella linea cellulare radioresistente di carcinoma pancreatico umano, PANC-1.I nostri dati dimostrano come il BSH sia in grado di: 1) indurre una maggiore attivazione dei meccanismi di riparo coinvolti nella risposta cellulare alla PBCT; 2) radiosensibilizzare e ridurre significativamente la sopravvivenza cellulare della linea PANC-1 rispetto alle cellule trattate con soli protoni.

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HYPOXIA IN PRECLINICAL MODEL OF GLIOBLASTOMA: PROTON THERAPY AND IMAGING ANALYSIS BY MICROPET/CT USING 18F-MISO AND 18F- FDG.

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Glioblastoma (GBM) is the most common and aggressive form of malignant astrocytic gliomas. The current GBM treatment techniques (surgery, chemotherapy and radiotherapy) produce minimal outcomes regarding extension of life expectancy [1]. Proton therapy (PT) is a type of precision radiation therapy that uses heavy particles - protons - to irradiate cancer cells. The proton beams are able to release the doses with extreme precision, saving the surrounding healthy tissue. PT is indicated for those tumors that do not sufficiently or adequately respond to traditional radiotherapy or for those that are localized to deep sites. Positron Emission Tomography (PET) is a molecular imaging technique usefully employed in preclinical and clinical studies. That accurately highlights tumor hypoxia area, using 18F-fluoromisonidazole (18F-FMISO) uptake evaluation [2], a radiotracer currently used in clinical practice [3]. Detection of tumor hypoxia is useful to optimize the dose painting so that biological rather than physical compliance for the administration of radiation to the tumor can be achieved. We conducted a pilot study to experimentally evaluate the variation of hypoxia in GBM treated with proton therapy by microPET imaging of orthotopic GBM xenografts in immunodeficient mice. Hypoxic tumor volume and the highest level of hypoxia in the GBM were measured before and after proton beam treatment by the combined use of 18F-FMISO and 18F-FDG. 18F-FMISO PET [4] imaging is promising in providing a complete description of tumor hypoxia levels and it reveals its efficacy as far as the preclinical evaluation and therapy planning is concerned. Development of reliable method to detect hypoxia in preclinical models may contribute to the discovery and production of novel targeted therapies in the treatment of malignant glioma through large-scale future preclinical studies.

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RAGGI X E DANNI AL DNA: LIMITI DELLA DOSE COME PARAMETRO PER GLI STUDI IN VITRO

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Circa 80 anni di studi di radiobiologia hanno chiaramente dimostrato che una maggiore dose di raggi X induce un maggiore danno al DNA. Questa relazione dose-effetto è stata parametrizzata con dei modelli matematici (il più usato è il lineare-quadratico) che si basano su fenomeni fisici e biologici. L'attenzione si è poi spostata sulla presenza/assenza di una soglia a dosi bassissime, sull'esistenza di una risposta adattativa e altro, ma la dose è sempre rimasta la principale (se non l'unica) quantità caratterizzante gli effetti di questo tipo di radiazione. Alcune ricerche hanno studiato l'influenza del rateo di dose. Pochissimi autori, invece, hanno studiato l'influenza dell'energia fotonica. Questi studi sono stati fatti, principalmente, confrontando i risultati di lavori pregressi, dove i ratei di dose erano diversi l'uno dall'altro. Malgrado questo fattore potenzialmente confondente, il risultato unanime è che, a parità di dose, raggi X con minore energia fotonica inducono maggiori danni al DNA. Nel nostro laboratorio abbiamo realizzato curve di dose-effetto relative a micronuclei (indicativi di danno al DNA) indotti in cellule irraggiate. Sono state usate tre diverse energie fotoniche e diversi ratei di dose. I risultati ottenuti confermano una correlazione inversa fra energia fotonica e RBE (Efficacia Biologica Relativa). Per spiegare questo fenomeno abbiamo ipotizzato che, poiché a parità di dose le cellule irraggiate con raggi X a minore energia ricevono un numero maggiore di fotoni, il numero di fotoni potesse essere un parametro importante. Rianalizzando i dati e ponendo come variabile indipendente la fluenza, invece della dose, abbiamo riscontrato che le diverse curve diventano pressoché identiche. La nostra conclusione è che il parametro principale per l'induzione di danno al DNA in vitro sia il numero di fotoni incidenti. Ciò avrebbe importanti ripercussioni per il trasferimento al campo della radioprotezione dei risultati di lavori in vitro.

THE USAGE OF DOSE AVERAGED LET VERSUS FULL SPECTRUM IN THE PREDICTION OF THE RBE

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The accurate prediction of relative biological effectiveness (RBE) is of crucial importance for delivering a treatment. The dose-averaged linear energy transfer (LET_D) is frequently used as a representative quantity for the biological effectiveness of a radiation field. In this study we will investigate whether the LET_D is an appropriate quantity to describe the RBE of broad spectra found in the mixed radiation field of protons and heavier ions treatments and discuss potential limitations. The Microdosimetric Kinetic Model (MKM) and its extensions, are ones of the most used to link experimental physical parameters to the RBE of ions [*Kase et al. (2006), Manganaro et al. (2017), Inaniwa et al. (2018)*]. While this approach gives reasonable RBE predictions in the major part of clinical cases, discrepancies were found between high Z ion beams and for such tumour nearby organs at risk, ultimately caused by the neglection of the stochastic nature of deposited specific energies. For this purpose, a modified stochastic MKM has been implemented in a research TPS and validated. The model uses the full energy spectra information allowing to evidence the differences between using distributions instead of average quantities to properly account for the inter-cellular energy deposition fluctuations and the inherently probabilistic nature of the cellular repair kinetics. The RBE is calculated at the voxel level for the full body, in two fictitious treatments: a prostate cancer and a pediatric brain tumor case, with proton and carbon ion beams. For each treatment, the corresponding RBE values are compared to those of strictly monoenergetic particles under track-segment conditions, characterized by a single LET = LET_D value. The analysis shows that the LET_D is not an accurate predictor for the RBE, especially for heavier particles, but also that this quantity can be still used as a physical predictor, even in the case of carbon, if a re-parametrization of the model is applied.

LIGHT QUALITY AND X-RAY TREATMENTS IMPROVE THE NUTRACEUTICAL PROPERTIES OF MUNG BEAN (*VIGNA RADIATA* L.) SPROUTS

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Sprouts are nutritious easy-to-produce food, suitable for cultivation in extra-terrestrial platforms as food supplement. In Space, plant exposure to ionising radiation, can alter morpho-anatomical development and change phytochemical content. These effects are more likely to occur when radiation exposure happens at the developmental stage of germinated seed. However, at very low doses, ionising radiation has been proved to induce some positive effects concerning plant physiological and morphological traits[1,2]. Moreover, the interaction with other microenvironmental factors (e.g. light quality and intensity, RH, T) during cultivation in controlled conditions, can be responsible for different sprout responses. In the present study, we used three X-ray doses (0.3, 10 and 20 Gy and a non-irradiated control, 0 Gy) to irradiate mung bean germinated seeds, with actively proliferating cells. These seedlings were grown for 9 days in a controlled environment under four light quality regimes (dark, white light, red light, red-blue light). This study aimed to evaluate whether sprout production under specific light wavelengths could mitigate the harmful effects of radiation and/or stimulate the induction of beneficial effects. Morpho-anatomical development of the sprouts was investigated through light-microscopy, while the content of flavonoids and isoflavones was quantified by HLPC. Main conclusions of this study are: 1) RB wavelength induces positive outcomes through the stimulation of antioxidant productions; 2) R wavelength offsets the harmful effects of radiation on morpho-anatomical traits, even at the highest X-ray dose. The overall results indicated that there is significant interaction between the two factors (radiation and light), suggesting that it is possible to induce specific traits in irradiated plants by opportunely manipulating light quality during plant growth.

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ABSTRACTS

SESSIONE 3

RADIAZIONI NON IONIZZANTI

CHAIR: *Antonella Sgura*

IL CORONAVIRUS SARS-COV-2 E LE RADIAZIONI NON IONIZZANTI TRA EVIDENZE SCIENTIFICHE E DISINFORMAZIONE

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Una grande quantità di informazioni riguardanti gli argomenti di salute, spesso provenienti da fonti non affidabili e veicolate in particolare dal web e dai social network, raggiunge quotidianamente la popolazione che ha difficoltà a distinguere le informazioni corrette da quelle scorrette. Per contrastare questo fenomeno, per il quale è stato coniato il neologismo "infodemia", l'Organizzazione Mondiale della Sanità ha individuato 29 argomenti connessi all'attuale pandemia di COVID-19 sui quali fornire una corretta informazione, tra i quali due si riferiscono alle radiazioni non ionizzanti, più precisamente alla radiazione ultravioletta (UV) e ai campi elettromagnetici a radiofrequenza.[1] L'utilizzo di lampade germicide UV-C è un mezzo consolidato per la disinfezione, utile per prevenire la diffusione sia per contatto che per trasmissione aerea di agenti infettivi quali batteri e virus. Se da un lato le evidenze di efficacia specifica nei confronti del coronavirus SARS-CoV-2 responsabile del COVID-19 si stanno ancora accumulando, dall'altro sono ben noti i rischi per la salute connessi alle esposizioni umane alla radiazione ultravioletta.[2] In questa relazione verranno quindi discussi i rischi di un utilizzo improprio di tali lampade, anche alla luce del fatto che sono state recentemente immesse in commercio, e molto pubblicizzate in occasione dell'attuale pandemia, lampade UV di dichiarata azione germicida e di diverse tipologie, destinate ad essere utilizzate da chiunque e non esclusivamente da parte di operatori opportunamente formati circa i rischi per la salute della radiazione UV e l'utilizzo degli opportuni dispositivi di protezione individuale. Per quanto riguarda i campi elettromagnetici a radiofrequenza, verranno discussi i presunti legami tra la recente tecnologia di telecomunicazioni mobili di quinta generazione (5G) e il COVID-19, in particolare quelli connessi a possibili effetti dei campi elettromagnetici a radiofrequenza sul sistema immunitario.[3]

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LA TECNOLOGIA 5G: UNA NUOVA SFIDA PER LE MISURE DI CAMPO NELL'AMBIENTE

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La tecnologia 5G utilizza tecnologie innovative basate su antenne il cui campo irradiato è ottimizzato in funzione delle condizioni di propagazione. Questa caratteristica rende la misura del campo elettromagnetico molto più complessa rispetto alle precedenti generazioni di sistemi cellulare. Obiettivo di questo contributo è discutere l'impatto dell'utilizzo delle varie soluzioni tecnologiche attualmente utilizzate nei sistemi 5G, quali le antenna a scansione di fascio, sistemi Single-User MIMO e Multi-User MIMO, e antenna massive MIMO, sulla misura del campo elettromagnetico nell'ambiente. Saranno inoltre presentare alcune metodologie recentemente proposte per la misura del livello di campo dei sistemi 5G.

Riferimenti: Adda, Sara, Tommaso Aureli, Stefano D'elia, Daniele Franci, Enrico Grillo, Marco D. Migliore, Settimio Pavoncello, Fulvio Schettino, and Riccardo Suman. "A Theoretical and Experimental Investigation on the Measurement of the Electromagnetic Field Level Radiated by 5G Base Stations." IEEE Access (2020).

PROTOCOL FOR A SYSTEMATIC REVIEW ON GENOTOXICITY OF RADIOFREQUENCY ELECTROMAGNETIC FIELDS IN VITRO

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Concern has been raised about possible adverse effects to human health due to exposures to Radiofrequency electromagnetic fields (RF-EMF), that have been classified by IARC [1] as possibly carcinogenic to humans, based on evidence that is weak and far from conclusive. Updated systematic reviews of the scientific literature on this topic are lacking, especially for mechanistic studies. Here we present a protocol for a systematic review of studies dealing with *in vitro* exposures to RF- EMF and assessment of genotoxicity that is one of the key biological indicators of carcinogenicity [2]. The protocol has been developed on the basis of the guidelines by the National Toxicology Program-Office of Health Assessment and Translation (NTP-OHAT) [3] and Office for the Report on Carcinogens (NTP-RoC) [4], and is reported according to the PRISMA-P [5] (Preferred Reporting Items for Systematic review and Metaanalysis Protocols) form. The methodological approaches suggested in those guidelines for hazard assessment of chemical agents have been adapted in this protocol to the peculiar features of RF-EMF studies (exposure characteristics, dosimetry, type of comparators), and transparent and objective methods have been defined for the processes of study eligibility, data extraction and analysis, risk of bias assessment and evidence appraisal. A pilot study has been performed to calibrate the search strategy developed for NCBI-PubMed search engine, and to optimize the forms for data extraction and risk of bias assessment.

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INHIBITION OF RF-INDUCED ADAPTIVE RESPONSE BY 3-AMINOBENZAMIDE

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The induction of adaptive response (AR) by Radiofrequency (RF) electromagnetic fields has been widely demonstrated by our research group on both primary (human peripheral blood lymphocytes, HPBLs) and immortalized cells (Chinese hamster lung fibroblasts V79, and human neuroblastoma SHSY-5Y cells), under different exposure conditions (900 MHz and 1950 MHz, variable waveforms, signals and bandwidth, specific absorption rate (SAR) from 0.15 to 1.25 W/kg), and against several chemical and physical agents[1-6]. Other research groups have reported similar observations *in vitro* and *in vivo*, under different exposure conditions, in different biological models, and by addressing several biological endpoints[7]. The mechanisms behind RF-induced AR still need to be elucidated, but the potentiation of oxidative stress defenses[5] and DNA repair processes[8-9] are possible candidates. In particular, the involvement of poly (ADP-ribose) polymerase-1 (PARP-1), a family of nuclear enzymes with a key role in the repair of DNA strand breaks and genomic instability, has been recently demonstrated[8-9]. In this study, HPBLs and V79 cells were exposed to 1950 MHz, UMTS signal, for 20 h, at SAR of 0.3 and 1.25 W/kg, respectively, and then treated with mitomycin-C (a DNA damaging agent), in presence and in absence of 3-aminobenzamide (3AB), an inhibitor of PARP. Following treatments, cells were tested for DNA damage by applying the cytokinesis-block micronucleus assay. In both cell lines, RF-induced AR was inhibited by the addition of 3AB. These findings provide further evidence of the involvement of DNA repair mechanisms in RF-induced AR, although further investigations are in order to get deeper into the action mechanisms.

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ABSTRACTS

SESSIONE 4

RADIAZIONI IN AMBITO CLINICO: ASPETTI DIAGNOSTICI

CHAIR: *Francesca Ballarini*

Francesco Paolo Cammarata

RADIAZIONI IN AMBITO CLINICO: VERSO LA MEDICINA DI PRECISIONE

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L'utilizzo delle radiazioni in diagnostica ha subito negli ultimi 30 anni un vero e proprio stravolgimento nei principi e metodi di rilevazione, di ricostruzione ed analisi di immagini, di utilizzo dei mezzi di contrasto e di radiofarmaci, tale da diventare oggi un elemento fondamentale per applicare realmente una medicina di precisione.

Le innovazioni sono molteplici ed in tutti i settori della radiodiagnostica e della medicina nucleare, ma ci concentreremo su tre di queste: 1) la svolta del digitale nel sistema di rilevazione PET, 2) il valore attuale della Radiomica e dei metodi di Intelligenza Artificiale (IA) nella diagnostica per immagini e 3) l'uso dei radiofarmaci diagnostici per la terapia radiometabolica.

Per il primo punto, sfruttando un sistema di rivelazione totalmente nuovo e molto piu' efficiente, si ottengono oggi immagini PET di altissima qualità, dove risoluzione spaziale, sensibilità e contrasto non sono comparabili alle immagini ottenute con le migliori tecnologie tradizionali PET. L'impatto di tale metodologia sui livelli di accuratezza diagnostica PET in oncologia è ancora da valutare, ma certamente è volto ad identificare e caratterizzare lesioni sempre piu' piccole metabolicamente attive, permettendo cosi' una terapia piu' mirata.

Radiomica e IA sono estesamente applicate alle immagini da qualche anno, sia come metodi di ricostruzione che di analisi delle immagini. In ambito clinico possono avere piu' di uno scopo: dare valore aggiunto alla diagnostica basata su analisi qualitativa; permettere una visione complessiva piu' accurata e veloce delle innumerevoli immagini generate dai moderni tomografi; identificare parametri di inquadramento diagnostico non altrimenti visibili ed importanti per la definizione di prognosi e trattamento; permettere lo studio di ampie popolazioni e 'big data' determinando nuovi algoritmi diagnostici 'personalizzati'. Attualmente, per arrivare ad un utilizzo cosi' esteso ed importante, è essenziale che questi metodi vengano validati attraverso un percorso che tenga conto non tanto di correlazioni casuali quanto di capacità predittiva dei metodi di IA superiore rispetto ai metodi tradizionali nel rispondere a specifici quesiti clinico-diagnostici anche su base individuale.

Infine, sebbene rappresenti una delle piu' antiche e consolidate metodologie di medicina nucleare, esiste oggi un rinnovato interesse per la terapia radiometabolica quando questa sia accompagnata da una specifica fase diagnostica. Si parla infatti di teranostica, ovvero dell'uso di uno stesso ligando di target molecolare specifico marcato con radioisotopi sia diagnostici che terapeutici. E' questo il caso del trattamento dei tumori neuroendocrini ormai entrato nella routine clinica e di altri nuovi trattamenti come quello dei tumori della prostata con PSMA.

Le 3 applicazioni riportate hanno vari elementi comuni (nuovo metodo, nuova tecnologia, nuove applicazioni) ma fondamentalmente rappresentano un enorme potenziale indispensabile alla definizione di nuove classificazioni delle patologie al fine di identificare trattamenti piu' specifici e mirati, verso quindi la medicina di precisione.

DOSE-TRACKING SOFTWARE: A RETROSPECTIVE ANALYSIS OF DOSIMETRIC DATA IN CT PROCEDURES

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The increasing use of ionizing radiation in healthcare is causing growing alarm about radiation protection of patients and the doses they receive during procedures[1,2]. Radiation dose assessment for patients in radiodiagnostics procedures is the subject of interest in view of the transposition into National Regulation of Directive 2013/59/Euratom. One of the most important focuses of the European Directive is the prescription to provide patient exposure information as an integral part of the examination report[3]. Dose monitoring systems are therefore essential for the collection of the dosimetric data[4]. In order to analyse potential and critical issues of these software, different systems, adopted at the Antonio Cardarelli Hospital in Naples, were compared. In particular, data, extracted from the DoseWatch software (GE Healthcare) and relating to four protocols adopted for computed tomography (CT), were retrospectively analysed for the purpose of identifying critical issues in the data acquisition and recording phase, optimizing the examined radiological procedures and determining local diagnostic reference levels (DRLs), as provided for in regulatory provisions for radiation safety. Multiphase examinations were also included in this study. Once the distributions of CT Dose Index ($CTDI_{vol}$) were determined for each acquisition phase and dose-length product (DLP_{tot}) for each examination, mean values and 75th percentiles were calculated for each distribution and then compared with the relevant national DRLs[5]. In addition, in order to improve protocol optimisation and dose reduction, the magnitude of the CT acquisition settings chosen in each procedure was evaluated. In conclusion, these systems allow accurate analysis of radiation dose according to equipment and protocol over time. For the application of optimization measures, a constant use of the dose-tracking software is required, which can be translated into actions on scan parameters and prospective data analysis.

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PREDICTIVE MODELS BASED ON RADIOMICS AND MACHINE LEARNING FOR LUNG CANCER RADIOTHERAPY DATA ANALYSIS

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Radiomics is an emerging field of research in the context of medical image analysis. It is based on the extraction and analysis of quantitative imaging features from medical images in order to exploit them in clinical decision support. Machine learning (ML) and deep learning (DL) approaches are widely employed to build predictive models based on radiomic features. We explored the predictive power of radiomic features extracted from the Radiotherapy planning thoracic CT in predicting the tumor histology, the tumor stage, and the survival time of patients with non small cell lung cancer (NSCLC). For this task, a subset of 130 subjects from the public dataset Lung1 Maastro NSCLC, and a proprietary dataset of 47 subjects (L-RT) collected in a collaboration between A.R.N.A.S. Civico Palermo, Università degli Studi di Palermo and INFN were considered. We highlighted the main challenges encountered when dealing with small datasets, which are generally characterized by more features per subject than subjects in the dataset. The best performances, expressed in terms of the area under the ROC curve (AUC), in histology classification of NSCLC the results obtained considering the Random Forest classifier is: AUC = 0.72 ± 0.11 if we restrict the analysis to stage I and II tumors. The results achieved in the overall stage classification of NSCLC by using Lung1 as training set and L-RT as test-set, are considerably above the random guess. In particular, the best performances are obtained by considering the SVM with linear kernel classifiers (AUC = 0.84 ± 0.03). Concerning the survival time prediction, quite satisfactory performances, expressed in terms of the mean absolute error (MAE), were obtained only in the training phase with the Random Forest Regressor (MAE = 5.0±0.3 months). This result is hardly generalizable to unseen test data. Thus, to enable more accurate and reliable performances, the enlargement of training and test data samples is foreseen.

L'IMPIEGO DELLA DIAGNOSTICA PER IMMAGINI PER IL COVID-19: LO STATO DELL'ARTE E IL DOCUMENTO ISS

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A gennaio 2020 un nuovo coronavirus, è stato identificato dal tampone rino-faringeo di un paziente. Questo patogeno è stato nominato SARS-Cov-2 e la malattia è stata chiamata COVID-19 dall'OMS. Ne è conseguito un grande fermento nel campo della ricerca scientifica, al fine di fornire alle comunità gli strumenti per superare questa sfida minimizzandone gli impatti negativi. Le istituzioni impegnate, tra cui l'Istituto Superiore di Sanità (ISS), hanno elaborato raccomandazioni indirizzate al pubblico e agli operatori sanitari. Il ritmo, senza precedenti, con cui sono emerse le pubblicazioni scientifiche relative alla pandemia COVID-19 ha reso la sintesi della conoscenza scientifica più importante che mai.
Individuare tutti gli aspetti rilevanti e di interesse per la comunità scientifica relativi all'uso della diagnostica per immagini in ambito COVID-19 è diventato un tema importante. L'uso dell'imaging TC nella diagnosi ed evoluzione del COVID-19 si è posto fin dall'inizio della pandemia come uno strumento diagnostico paragonabile alla tecnica di elezione ovvero la Reverse transcriptase-polymerase chain reaction (RT-PCR). La capacità della TC di risolvere casi di falsi negativi riportati dalla RT- PCR ha creato, soprattutto nella fase iniziale, molta confusione nell'utilizzo di questa tecnica fino ad ipotizzarne, impropriamente, l'uso come tecnica di screening di prima linea. La TC resta comunque il mezzo radiologico di elezione che permette, nei pazienti COVID-19, di evidenziare lesioni polmonari non visibili con altri mezzi diagnostici, di valutare la necessità di ventilazione, di individuare eventuali altre patologie e monitorarne il follow-up. In questo ambito l'ISS e la Società Italiana di Radiologia Medica (SIRM) hanno creato un gruppo di lavoro e elaborato un documento per fare luce su quanto emerso in letteratura sull'uso della TC, evidenziando possibili usi non appropriati verificatisi soprattutto in Cina nella fase iniziale della pandemia.

ABSTRACTS

SESSIONE 4

RADIAZIONI IN AMBITO CLINICO: ASPETTI TERAPEUTICI

CHAIR: *Francesca Ballarini*

Francesco Paolo Cammarata

L'INTELLIGENZA ARTIFICIALE IN RADIOTERAPIA, LA NUOVA FRONTIERA DELL'ADAPTIVE THERAPY

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Sono diverse le applicazioni dell'intelligenza artificiale (AI) in radio-oncologia (1). Sia gli organi a rischio che il target possono sono frequentemente soggetti a cambiamenti anatomici che possono essere causati dalla perdita di peso, da variazioni morfologiche e di movimento e dalla risposta al trattamento radiante (2); conseguentemente la dose effettivamente erogata si può discostare dalla dose precedentemente pianificata. Il tradizionale approccio per superare questo problema prevede di applicare dei margini di sicurezza al target aumentando però il rischio di tossicità (3). Con l'intento di ridurre questi margini di sicurezza è stata implementata l'IGRT (4). Laddove i cambiamenti anatomici comportano una significativa variazione di dose può essere utile poter "adattare" il piano di cura tenendo conto dei cambiamenti anatomici mediante l'Adaptive Radiotherapy (ART). L'AI entra in gioco nella Online ART (registrazione deformabile, autosegmentazione e planning) (5). Sono due le tipologie di Online ART: Hybrid e Real-time. Entrambe consentono il re-planning con il paziente su lettino di trattamento. La Hybrid ART consiste nell'utilizzare un piano di cura generato precedentemente per quel specifico paziente utilizzando una libreria di piani disponibili e scegliendo tra tutti quello che ha caratteristiche simili e accettabili per distribuzione di dose e DVH (6). La Real-time ART permette di ottenere un re-planning in tempo reale con il paziente sul lettino di trattamento utilizzando come sorgente la CBCT con notevoli vantaggi di fattibilità e di dati dosimetrici (7). Inizialmente ideata per gli MRI- LINAC, è stata recentemente attivata anche per gli altri LINAC (8). I limiti della metodica attualmente riguardano la tempistica richiesta (minimo 20-30 minuti) e l'accuratezza dell'autosegmentazione (soprattutto per i trattamenti del distretto testa-collo). Ulteriori miglioramenti sono attesi per inserire la Real Time-ART nella pratica clinica quotidiana.

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ISOLPHARM_EIRA: A NEW APPROACH TO CREATE HIGH PURITY RADIONUCLIDES FOR NUCLEAR MEDICINE APPLICATIONS

A. Andrighetto [1], S. Corradetti [1], M. Ballan [1], L. Morselli [1,2], A. Zenoni [3], V. Di Marco [4], F. Mastrotto [5], M. Lunardon [6], D. Maniglio [7], G. Russo [8], F. Cammarata [8], M. Asti [9] on behalf of the ISOLPHARM collaboration

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Radiopharmaceuticals are drugs containing radionuclides that are used in nuclear medicine for diagnosis or therapy of different diseases. The main difficulties associated with their use in clinical practice are the availability of radionuclides and the development of molecular systems for their specific localization in diseased sites. Radionuclides for this purpose are currently produced in cyclotrons or nuclear reactors, with issues being highly enriched target costs, low activity, production of undesired long-lived radioactive wastes and contaminants, expensive chemical separation routes. In this context, the ISOLPHARM[1,2] project at INFN-LNL (Istituto Nazionale di Fisica Nucleare-Laboratori Nazionali di Legnaro) has the aim of producing high purity radionuclides for nuclear medicine applications. Exploiting the Isotope Separation On-Line (ISOL) technique, radionuclides from many different regions of the nuclide chart will be produced with high specific activities, promising bases for innovative radiopharmaceuticals. One of such nuclides is certainly Ag-111, considered a potential radionuclide for therapy[3]. Its decay properties make it a promising candidate for internal radiotherapy. It is a β- emitter with medium half-life (7.45 d), convenient β- energy and medium tissue penetration (average β energy 360 keV and average tissue penetration 1.8 mm) and low percentage of associated γ-emission. The ISOLPHARM_EIRA INFN experiment, in the framework of ISOLPHARM, has three main goals, focused on the development of a Ag-111-based radiopharmaceutical: (i) test production of Ag-111 using standard techniques (neutron irradiation of natural Pd) and quality control, (ii) synthesis and characterization of chelators, linkers and targeting agents, (iii) biological characterization on cells. The final goals of the project are in vitro and in vivo studies. It this contribution, the ISOLPHARM project and its ongoing experimental activities will be presented.

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MONITORAGGIO INTER-FRAZIONE DEI TRATTAMENTI CON IONI CARBONIO AL CNAO

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In un trattamento di Terapia con Particelle (PT) i cambiamenti morfologici che si verificano nel corpo del paziente possono portare ad una dose rilasciata significativamente diversa da quella pianificata, impattando sull'efficacia del trattamento. Al giorno d'oggi un sistema in grado di verificare la conformità della dose rilasciata al volume tumorale con quella prescritta dal piano di trattamento non è presente nella routine clinica , e le variazioni morfologiche sono tenute sotto controllo eseguendo una TAC di rivalutazione dopo un numero di frazioni dipendente dalla patologia trattata. Il Dose Profiler (DP) [1] è un innovativo dispositivo progettato per il monitoraggio dei trattamenti con ioni carbonio al CNAO (Centro Nazionale di Adroterapia Oncologica, Pavia) sfruttando la rivelazione dei frammenti carichi prodotti dall'interazione del fascio principale con i tessuti del paziente. In questo contributo viene illustrata una tecnica recentemente proposta per l'individuazione di variazioni morfologiche, basata sulla misura e il confronto delle mappe di emissione dei frammenti (la cui produzione dipende dalla densità del materiale attraversato) nelle diverse frazioni. Il risultato del confronto fornirà un feedback sperimentale a supporto della decisione del medico di ripianificare il trattamento. La sensibilità del DP è attualmente sotto studio utilizzando i dati raccolti durante il trial clinico del sistema INSIDE [2] iniziato nel 2019 presso il CNAO (ClinicalTrials.gov: NCT03662373). È stata analizzata una prima serie di (10) pazienti che coinvolgono patologie testa-collo, osservando differenze significative in alcune delle mappe coerentemente con le informazioni fornite dalle TAC di controllo. In questo contributo verranno presentati i risultati finali, confrontati con una simulazione MC eseguita con il software FLUKA.

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PREVISIONI DI RBE MEDIANTE IL MODELLO BIANCA A SEGUITO DI IRRAGGIAMENTO *IN VITRO* E *IN VIVO* CON DIVERSI FASCI ADROTERAPICI

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Il modello biofisico BIANCA (*BIophysical ANalysis of Cell death and chromosome Aberrations*) è caratterizzato da due parametri liberi ed è basato su assunzioni che legano la formazione di lesioni critiche al DNA radioindotte alla produzione di aberrazioni cromosomiche e alla morte cellulare clonogenica. I parametri del modello sono stati inizialmente calibrati per produrre una tabella radiobiologica (coefficienti α e β di curve di sopravvivenza cellulare, in funzione del tipo di ione e della sua energia) per cellule V79, scelte come linea di riferimento. Dopodichè è stato sviluppato un approccio per produrre tabelle analoghe per altre linee cellulari, per le quali sia nota la risposta all' irraggiamento con fotoni. Questo passaggio non richiede nessun ulteriore aggiustamento dei parametri e permette, in linea di principio, di fornire previsioni per ogni linea cellulare di interesse. Tali tabelle possono essere lette da un codice di trasporto della radiazione e/o da un TPS (Treatment Planning System). In questo lavoro è stata creata un'interfaccia tra BIANCA e il codice MC di trasporto della radiazione FLUKA[1], per essere applicata alla previsione teorica di sopravvivenza cellulare e RBE (Relative Biological Effectiveness) in scenari di irraggiamento tipici dell'adroterapia. Nello specifico, è stato ottenuto un buon accordo con dati sperimentali di sopravvivenza di cellule CHO esposte in vitro[2] a differenti profondità lungo diversi Spread-Out Bragg Peaks di protoni, ioni carbonio e ioni elio. E' stato inoltre ottenuto un buon accordo con dati di RBE da protoni e ioni carbonio su effetti tardivi nel midollo spinale dei ratti[3], che rappresenta un modello per i danni sul sistema nervoso centrale nel trattamento dei tumori della regione testa-collo. Questo lavoro mostra che BIANCA, interfacciato con un codice di trasporto o un TPS, può essere utilizzato per predire l'RBE nei trattamenti di adroterapia, ponendo così le basi per future applicazioni cliniche.

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2. *M.P. Carante et al. Phys Med Biol 2019, 64;215008.*
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PREVISIONE DI DANNI AL TESSUTO SANO PER FASCI ADROTERAPICI MEDIANTE IL MODELLO BIANCA

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Attualmente nella valutazione dell'RBE (Relative Biological Effectiveness) in adroterapia si considera come *endpoint* biologico la sopravvivenza cellulare. Ciò permette di valutare l'efficacia del fascio nella regione tumorale, nonché i danni a breve termine nei tessuti sani, che generalmente sono ben correlati con la morte cellulare. Tuttavia per il rischio di danni a lungo termine, inclusi i tumori secondari, può essere interessante integrare questo approccio valutando anche uno o più endpoint *ad hoc*. In particolare le aberrazioni cromosomiche (tipicamente i dicentrici) nei linfociti del sangue, che sono ampiamente utilizzate come *biomarkers*, possono essere utili per stimare il rischio associato a questo tipo di danni. A questo scopo il modello biofisico BIANCA (BIophysical ANalysis of Cell death and chromosome Aberrations) [1] è stato adattato per riprodurre dati sperimentali disponibili in letteratura sull'induzione di dicentrici in linfociti esposti a radiazioni di diverso tipo (fotoni, protoni, ioni Elio e ioni Carbonio) e diverso LET; ciò ha permesso di calibrare i parametri del modello. A seguito di questa calibrazione, senza nessun ulteriore aggiustamento dei parametri, sono state simulate un gran numero di curve dose-risposta che prevedono l'induzione di aberrazioni in funzione del tipo di particella e del LET in maniera sistematica, includendo anche valori di LET per i quali non sono disponibili dati sperimentali. Descrivendo ciascuna di queste curve in termini di coefficienti lineare e quadratico (e quindi di RBE) si produce un database radiobiologico che può essere letto da un codice di trasporto della radiazione e/o da un TPS (Treatment Planning System). Analogamente a quanto fatto in precedenza per l'RBE da sopravvivenza cellulare, interfacciando BIANCA al codice Monte Carlo FLUKA [2] si sono quindi poste le basi per il calcolo dell'RBE basato sull'induzione di dicentrici nei tessuti sani a seguito di irraggiamenti con fasci adroterapici.

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2. G. Battistoni, J. Bauer, T.T. Boehlen, F. Cerutti, M.P.W. Chin, R. Dos Santos Augusto, A. Ferrari, P.G. Ortega, W. Kozłowska, G. Magro, A. Mairani, K. Parodi,
3. P.R. Sala, P. Schoofs, T. Tessonnier, V. Vlachoudis, The FLUKA Code: An Accurate Simulation Tool for Particle Therapy, Front. Oncol., 6, 116 (2016)

PROTON PENCIL BEAM SCANNING REDUCES SECONDARY CANCER RISK IN BREAST CANCER PATIENTS WITH INTERNAL MAMMARY CHAIN INVOLVEMENT COMPARED TO PHOTON RADIOTHERAPY.

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Proton pencil beam scanning (PBS) represents an interesting option for the treatment of breast cancer (BC) patients with nodal involvement[1]. In this study, we compare tangential 3D-CRT and VMAT to PBS proton therapy (PT) in terms of secondary cancer risk (SCR) for the lungs and for contralateral breast[2]. Five BC patients including sovraclavear (SVC) nodes in the target (Group 1) and five including SVC plus internal-mammary-nodes (IMNs, Group 2) were considered. The Group 1 patients were planned by PT versus tangential 3D-CRT in free-breathing (FB). The Group 2 patients were planned by PT versus VMAT considering both FB and deep-inspiration breath hold (DIBH) irradiation. The prescription dose to the target volume was 50 Gy (2 Gy/fraction). A constant RBE=1.1 was assumed for PT. The SCR was evaluated with the excess absolute risk (EAR) formalism, considering also the age dependence and the cumulative EAR was finally computed[3,4]. According to the linear, linear-exponential and plateau dose response model, the cumulative EAR for Group 1 patients after PT was equal to 45±10, 17±3 and 15±3, respectively. The corresponding relative increase was found to be equal to 2.3±0.3, 2.2±0.2 and 2.4±0.2 for tangential 3D-CRT. Group 2 patients showed a cumulative EAR after PT in FB equal to 65±3, 21±1 and 20±1, according to the different models; the relative risk obtained with VMAT increased by 3.5±0.1, 5.2±0.1 and 5.1±0.1. Similar values emerge from DIBH plans. Contrary to photon radiotherapy, PT appears to be not sensitive to the age dependence due to the very low delivered dose. PBS PT is associated to significant SCR reduction in BC patients compared to photon radiotherapy. The benefits are maximized for young patients with IMNs involvement. When combined with the improved sparing of the heart, this might contribute to the establishment of effective patient-selection criteria for proton BC treatments.

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ABSTRACTS

SESSIONE 5

ASPETTI DOSIMETRICI E NUOVE TECNOLOGIE DI RADIATION DETECTION

CHAIR: *Silva Bortolussi - Mario Mariani*

DETECTORS FOR HADRONTHERAPY

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Because of the high dose gradients of proton and carbon ion beams parallel and perpendicular to the beam axis , high resolution detectors are to be used for measurement of depth dose distributions and lateral profiles in passive and active hadrontherapy facilities. Due to the LET dependence of the response of films and solid-state detectors, dosimetric measurements are mostly based on ion chambers.In this review new detectors are presented to be used as an alternative to the ionization chamber, characterized in collaboration between CNAO and LNS. A PR60020 silicon diode detector (PTW- Freiburg, Germany) was tested at INFN-LNS cyclotron on the scattered proton beamline (62 MeV) dedicated to ocular treatment; for the first time, the detector was also characterized in scanning proton beams accelerated by the CNAO synchrotron. Bragg peak curves closely matched those acquired with ionization chamber, relative differences being lower than 3% in peak-to-plateau ratios. Very good results were also found for SOBP dose measurements as in scattered and scanned proton beams. In conclusion, diode detector appeared suitable for relative dosimetry and absorbed dose determination in passively scattered and scanning clinical proton beams, particularly for very small fields used for ocular treatments. At the Centro Nazionale di Adroterapia Oncologica (CNAO Foundation), a two-dimensional high resolution scintillating dosimetry system has been developed and tested for daily Quality Assurance measurements (QA) in carbon ion radiotherapy with active scanning technique, for both single pencil beams and scanned fields produced by a synchrotron accelerator. The results of this study show the suitability of the scintillation detector for daily QA in a carbon ion facility with an active beam delivery system, with great time savings compared to film to films currently used.

A NOVEL HYBRID MICRODOSIMETER FOR RADIATION FIELD CHARACTERIZATION BASED ON TEPC DETECTOR AND LGADS TRACKER

M. Missiaggia [1,2,3], E. Pierobon [1], M. Castelluzzo [1], A. Perinelli[1], F. Cordoni [2,5], M. Centis Vignali [3], G. Borghi [2,3], V. E. Bellinzona [1,2], E. Scifoni [2], F. Tommasino [1,2], V. Monaco [4], L. Ricci [1,2], M. Boscardin [2,3], C. La Tessa [1,2]

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In microdosimetry, lineal energies y are calculated from energy depositions ε inside the microdosimeter divided by the mean chord length, whose value is based on geometrical assumptions on both the detector and the radiation field. We have developed a Hybrid Detector for Microdosimetry (HDM), composed of a tissue equivalent proportional counter (TEPC) and a 4-layers low gain avalanche detectors (LGADs)-tracker; this design provides a direct measurement of energy deposition in tissue as well as particles tracking with a submillimeter spatial resolution. The data collected by the detector allow to obtain the real track length traversed by each particle in the TEPC and thus estimates microdosimetry spectra without the mean chord length approximation. Using Geant4 toolkit, we investigated HDM performances in terms of detection and tracking efficiencies when placed in water and exposed to protons and carbon ions in the therapeutic energy range.

MODELLO DI CUTE SANA CRESCIUTO *IN-VITRO* PER VALUTARE IL DANNO DA RADIAZIONE

Ian Postuma [1], Claretta Guidi [1,2], Patrizia Sommi [1,3], Agostina Vitali [3], Cinzia Ferrari [1,4], Laura Cansolino [1,4], Chiara Magni [1,2], Setareh Fatemi [1], Nicolett Protti [1,2], Saverio Altieri [1,2], Umberto Anselmi-Tamburini [1,5], Sara J. Gonzalez [7,6] and Silva Bortolussi [1,2]

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Negli studi preclinici di terapie radiogene, la valutazione del danno da radiazione nel tessuto sano è più complessa rispetto al tessuto tumorale, per il quale viene studiato il tasso di mortalità cellulare in funzione della dose depositata. Nel caso del tessuto sano usare la mortalità come "endpoint" è una condizione limitante, poiché l'obiettivo non è valutare la letalità della terapia, ma stimare la probabilità che avvenga un effetto avverso che possa limitare la deposizione della dose al tumore, inficiando l'efficacia del trattamento clinico. Questo tipo di danno può essere valutato retrospettivamente su pazienti o in studi dedicati *in-vivo*. Tuttavia, questo approccio può essere complesso a causa dei costi e dell'iter autorizzativo.. D'altra parte, l'utilizzo di colture cellulari *in-vitro* non è rappresentativo della complessità di un tessuto. Per questi motivi, abbiamo effettuato uno studio preliminare per valutare il danno da radiazione dovuto a Boron Neutron Capture Therapy (BNCT) alla pelle sana utilizzando un tessuto cresciuto *in-vitro:* Reconstructed Human Epidermis (RHE) di EpiskinTM, abbiamo selezionato RHE poiché la pelle nella Boron Neutron Capture Therapy (BNCT) è un organo a rischio e spesso limitante per il trattamento clinico [1,2]. L'obiettivo di questo studio è valutare l'effetto della radiazione dovuta a un trattamento BNCT rispetto alla radiazione di riferimento (fotoni). Le curve dose-effetto servono ad estrarre dei parametri radiobiologici da usare per il calcolo della dose fotone-equivalente, ad esempio utilizzando il modello fotone- isoeffettivo [3]. Verranno presentati i risultati ottenuti irraggiando i campioni RHE con fotoni e con neutroni, in presenza e in assenza di boro e la dosimetria computazionale per la costruzione delle curve dose-effetto

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THE PAIR PRODUCTION IMAGING CHAMBER (PAPRICA)

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In Particle Therapy, safety margins are applied when planning the treatment in order to account for the multiple sources of beam range uncertainty. Reducing safety margins is fundamental in the treatment of tumors close to organs at risk and paediatric patients. Several range monitoring techniques are being investigated, all based on the detection of secondary particles produced in the nuclear interactions of the ion beam with the patient's tissue nuclei. Many efforts are focussed on the prompt photons detection. In this contribution, a novel range monitoring technique is proposed, based on the exploitation of the prompt photons pair production mechanism as prompt gamma imaging technique. The PAPRICA (PAir PRoduction Imaging ChAmber) project will be discussed: the chamber will reconstruct the prompt photons 3D spatial emission distribution, requiring an energy E>4 MeV to select the event population that is most correlated to the Bragg peak position. The PAPRICA detector will be able to monitor proton and carbon ion treatments, implementing neutrons background reduction strategies and profiting from the $e^{+,-}$ pair clear topological event signature. No collimation nor time of flight information on the detected photons will be needed. The PAPRICA detector design and the expected performances evaluated by means of a Monte Carlo simulation in a real case scenario will be presented.

RADIATION STABILITY OF THE COMPLEXATION CAPABILITIES OF THE PYTRI-DIOL EXTRACTION SYSTEM FOR ADVANCED SPENT NUCLEAR FUEL PARTITIONING

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The reduction of volume and hazards of the high-level waste and the optimization of natural resources exploitation and final repository environmental footprint could be pursued by the Partitioning and Transmutation of long-term radiotoxic U, Np, Pu and Minor Actinides (Am and Cm) contained in the Spent Nuclear Fuel. In the last decades, researcher's efforts have been dedicated to developing hydrometallurgical processes capable of efficiently and selectively recovering these elements for their multi-recycling. Among all, the promising innovative-Selective ActiNide EXtraction (*i*-SANEX) process aims at the selective Am and Cm recovery from the highly active raffinate, downstream the other actinides removal. To this aim, the *TetraOctyl-DiGlycolAmide* (TODGA) extractant and a hydrophilic complexing agent, *2,6-bis[1-(propan-1-ol)-1,2,3-triazol-4-yl)]pyridine* (PyTri-Diol) being the most promising, could be synergically used. Besides promising extraction selectivity and efficiency for Am and Cm, this system showed outstanding radiolytic and hydrolytic stability [1-2]. In this work, the selectivity for trivalent Am and Cm towards Eu, chosen as representative of the lanthanides, has been assessed by UV-Vis and Time Resolved Laser Fluorescence Spectroscopy (TRLFS) under relevant conditions: PyTri-Diol solutions were γ-irradiated (up to 200 kGy by 2.5 kGy/h ^{60}Co source) or aged (up to 100 days) in 0.44 mol/L HNO3 before complexometric titration experiments. The obtained results were compared with those of fresh PyTri-Diol solutions, in order to evaluate the impact of radiolysis and hydrolysis on metal-ligand complex formation. In accordance with the stability outlined by previous studies, also the complexation capabilities resulted to be unaltered [1]. These results further support PyTri-Diol as valid candidate for partitioning processes.
This work was supported by the European Commission (TALISMAN, SACSESS FP7 projects and by H2020-GENIORS project) and the Italian Ministry of Education, University and Research.

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THE RADIATION CHEMISTRY CHALLENGE TO UNDERSTAND FLASH RADIOTHERAPY MECHANISM

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The last couple of years have seen an unprecedented attraction of interest and an exploding amount of publications in the field of FLASH radiotherapy. This was driven by the idea to re-explore, with modern technical means, an approach introduced in the fifties - based on ex- ploiting radioprotective effects on a normal tissue, by ultrafast dose rate irradiation-, followed by a rapidly accumulating bunch of new promising data. Different types of radiation have been tested, from electrons to synchrotron radiation, including protons and heavy particle beams, at several conditions of instantaneous dose rate, total dose and pulse duration, return- ing not always a confirmation of the effect, but providing a remarkably consistent amount of in vivo data. Despite such an increasingly broad preclinical evidence of both significant normal tissue pro- tection (see e.g.[1]) and corresponding maintained tumor control (see e.g.[2]), still the mech- anistic ground of justification of the effect, which is vital not only for scientific purposes, but even for efficient control of the FLASH, especially in its fundamental differential impact be- tween normal tissue and tumor, is far to be unraveled. Among the several theories which were suggested from the very beginning to explain this effect, the high dose induced oxygen depletion and peroxide radicals recombination have at- tracted the major credit, and both of them are strongly related to radiation chemistry analysis. The different recent international attempts to unveil the mechanistic features of FLASH will be reviewed, with a focus on the GSI-TIFPA approach, based on an in-house developed radia- tion chemical track structure code (TRAX-CHEM)[3], allowing a nanoscale analysis of oxy- gen consumption by radiation [4] and its impact in the conditions of the FLASH dedicated experiment [5].

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EPR RESPONSE OF PHENOLIC SOLID STATE PELLETS FOR DOSIMETRY OF RADIO-THERAPEUTIC PHOTON AND ELECTRON BEAMS

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Among the various dosimetric techniques used for characterizing the radiation beams used in radiation therapy, the electron spin resonance (ESR) arouses increasing interest for applications in various therapy procedures. In this work, we report the ESR investigation of particular phenol compound (IRGANOX 1076) exposed to clinical photon and electron beams1. Phenol (IRGANOX 1076 - Sigma Aldrich) pellets were produced also with paraffin (10% by weight). Phenol pellets were exposed to clinical photon and electron beams at various energies produced by a linear accelerator (LINAC) with absorbed doses ranging between 0 and 13 Gy. ESR measurements were performed through a X band Spectrometer. Readout parameters were optimized to maximize the signal without excessive spectrum distortions. Basic dosimetric properties of phenolic dosimeters, such as reproducibility, dose-response, sensitivity, linearity and dose rate dependence were investigated. A satisfactory intra-batch reproducibility of the ESR signal of the manufactured dosimeters was obtained. The analysis of the ESR signal as function of absorbed dose highlights that the response of this material is linear in the dose range investigated (1-13 Gy) and is independent of the beam energy. The presence of an intrinsic background signal limits the minimum detectable dose to a value of approximately 0.6 Gy. Reliable and accurate assessment of the dose was achieved, independently of the dose rate. The dosimeters were tested by measuring the depth dose profile of a 6 MV photon beam.
Such characteristics, together with the fact that IRGANOX 1076 is almost tissue-equivalent, and the stability of the ESR signal, make these dosimeters promising materials for ESR dosimetric applications in radiotherapy.

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FEASIBILITY STUDY OF A WEARABLE INDIVIDUAL DOSE MONITORING APPARATUS FOR MOLECULAR RADIONUCLIDE THERAPY

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In Molecular Radionuclide Therapy (MRT), dose delivery depends on several interconnected key factors, and both radiopharmaceutical uptake and excretion can largely fluctuate from patient to patient [1][2]. A systematic measurement of the internal activity distribution in all the patients undergoing MRT would enable treatment improvements with an individualization of the activity to be administered. This personalization (recommended by 2013/59/EURATOM) would increase the local tumor control while sparing healthy tissues, and lowering toxicity. To this purpose a Wearable Individual Dose Monitoring Apparatus (WIDMApp) for continuous mapping of the radioactive agent transit and accumulation in the body is under study. The WIDMApp system is conceived as a wireless non-invasive multi- sensor network for in vivo radiation detection, combined with a simulation algorithm and a powerful data analysis tool to de- convolve the detected signal in contributions from each emitting volume/organ. The detecting elements will be embedded in a garment that can be comfortable worn by the patient during the entire MRT treatment in order to detect the activity for different organs/tissues 24/24h. WIDMApp will provide precise reconstruction of the biological time-activity trend in lesions and in healthy tissues over a large temporal interval, and with uncertainty well below those originating from activity quantification in conventional nuclear medicine imaging [3]. A Monte Carlo simulation of the multi-sensor apparatus, using anthropomorphic phantom [4] mimicking MRT treatments for metastatic thyroid cancer, was developed to test the feasibility of the network system and to calculate the expected signal. An algorithm to disentangle contributions to emissions of each emitting volume and to reconstruct time-activity curve for target and organs has been tested. The uncertainty due to sensor mispositioning was estimated, and impact of the number and size of the detectors was evaluated.

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ELETTRETI E FONDO DI RADIAZIONE GAMMA: RISULTATI PRELIMINARI SULL'OTTIMIZZAZIONE DI UN SISTEMA DI MISURA DI GAS RADON

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Alla base di questa attività di ricerca c'è la necessità di far fronte alle esigenze dettate dall'imminente recepimento della direttiva Euratom 59/2013[1] sulla protezione contro i pericoli derivanti dall'esposizione alle radiazioni ionizzanti, in particolare all'obbligo di misure di concentrazione di attività di gas radon in tutti i locali aperti al pubblico, siti al piano terra. L'obiettivo del lavoro è mettere a punto un metodo di rivelazione passivo del radon semplice e di immediato, che consenta di effettuare misure accurate anche senza ricorrere a rivelatori che necessitano di trattamenti lunghi e strumentazione costosa. I rivelatori ad elettrete (E-Perm)[2] rispondono a questi requisiti, ma hanno lo svantaggio di essere sensibili non solo al gas radon ma anche al fondo gamma ambientale. Tale fondo viene misurato o con strumentazione attiva (camere a ionizzazione, contatori proporzionali) o passiva (dosimetri a termoluminescenza), per poi essere sottratto al fine di ottenere la concentrazione di radon effettiva. Nel presente studio sono stati utilizzati rivelatori ad elettrete, in configurazioni diverse, sia per la misura di gas radon che per il fondo gamma ambientale[3]. Vengono presentati i risultati del confronto tra i valori del fondo gamma ottenuti con le diverse metodologie di misura: contatore proporzionale, dosimetri a termoluminescenza ed elettreti.

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ABSTRACTS

SESSIONE 6

RADIOPROTEZIONE

CHAIR: *Valentina Dini*

PROGRAMMA NAZIONALE ENEA-MISE PER L'AFFIDABILITÀ DELLE MISURE DI RADIAZIONI IONIZZANTI BASATO SU CONFRONTI INTERLABORATORIO E PROVE VALUTATIVE (ILC/PT)

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Il Ministero dello sviluppo economico (MiSE) ha recentemente stipulato una Convenzione con l'ENEA per l'organizzazione e svolgimento di un programma triennale di Confronti Interlaboratorio (ILC) nel settore della misurazione delle radiazioni ionizzanti (RI) in campo medico ad ambientale. L'esecuzione tecnica del programma è stata affidata all'Istituto Nazionale di Metrologia delle Radiazioni Ionizzanti dell'ENEA (INMRI-ENEA) in qualità di Istituto Metrologico Primario Nazionale nello specifico settore delle RI. I fondi necessari per lo svolgimento del programma derivano dalle sanzioni amministrative irrogate dall'Autorità garante della concorrenza del mercato che, in linea con quanto richiesto dalla legge 23 dicembre 2000, n. 388, concernente "Disposizioni per la formazione del bilancio annuale e pluriennale dello Stato", sono da destinare ad iniziative a vantaggio dei consumatori. L'obiettivo finale del programma è quindi la tutela dei consumatori in ogni ambito mediante la promozione continua dell'affidabilità delle misure, permettendo a tutti i laboratori coinvolti di individuare le principali fonti di errore e migliorare le procedure sperimentali adottate. Le RI trovano ampio impiego in campo medico (radiodiagnostica e radioterapia) e sono di estrema importanza in quello ambientale (controllo della contaminazione radioattiva naturale ed artificiale dell'ambiente e degli alimenti a uso animale ed umano). Nel caso delle applicazioni mediche il consumatore è rappresentato dal paziente e dai suoi familiari. Nel caso dei controlli ambientali il consumatore è assimilabile a qualunque cittadino che vive nell'ambiente sottoposto a sorveglianza o che si nutre di prodotti generati in detti ambienti. La relazione descrive le motivazioni e i presupposti metrologici del programma nonché le tipologie di operatori attivi sul territorio nazionale. Affronta successivamente i criteri predisposti per l'organizzazione e svolgimento degli ILC, specificandone anche il valore nel settore degli accreditamenti. Viene infine riportato un quadro temporale del programma specificando gli elementi già definiti sul piano tecnico. La relazione sottolinea altresì l'utilità di mantenere per il futuro un programma di ILC stabile e continuativo al fine di avviare un percorso di miglioramento continuo della qualità delle misure e, quindi, dei servizi offerti al cittadino.

OPINION POOL RELATED TO RADIATION PROTECTION OR RADIATION RISK PERCEPTION: RESULTS OF THE EJP CONCERT WP5 SURVEY

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Among the activities of Work Package 5 of the CONCERT European Joint Programme, Task 5.3 was in charge of developing a survey to gauge the perception of radiation risk among a wide range of persons directly or indirectly involved in the radiation protection (RP) field.
The survey was developed and launched in 2017, translated in fifteen different European languages. The first general part of the survey included a section about the respondents'attitude towards science and technology, their satisfaction about the actors in the RP domain, and their opinion towards the communication channels about radiological and nuclear risk. In the second part of the survey, specific sections were included to address particular audiences (professionally exposed workers, patients exposed to radiation, people with a cultural interest for RP issues).
A total of 1961 replies were obtained. A brief description of the dissemination of the public survey will be presented, as well as the main results. A strong dependence of the perception of risk on nationality and on the familiarity with the ionizing radiation (IR) field was observed.

BRINGING TOGETHER MEDICAL AND NUCLEAR SCIENTIFIC COMMUNITIES TO IMPROVE PATIENT AND WORKER RADIOLOGICAL PROTECTION ACROSS EUROPE: STATE OF THE ART OF THE MEDIRAD PROJECT WP6

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The MEDIRAD project aims to enhance the scientific bases and the clinical practice of radiation protection in the medical field. The Istituto Superiore di Sanità (ISS) is involved in the WP6, whose final scope is the draft of recommendations for an effective protection of patients, medical workers and population. To promote a fruitful linkage between research and society, a Stakeholder Forum (SF) of 76 members (12 from Italy) from european and international societies was set up. A questionnaire based on the Research and Development objectives of MEDIRAD was developed and distributed among the SF members. Ten topics (priorities) turned out to be considered as the most relevant for the RP research among the SF members. Then, an effort was made to identify, *a posteriori*, these priorities among the 23 topics previously identified by the project partners (WPs 2-5) within the four thematic sections of the recommendations (Standardized European procedures for consolidating patient data repositories; Optimisation of ionising radiation based medical protocols for diagnostics or therapy; Optimisation of radiation protection for patients and medical workers; Future research and development priorities). An overview of the 23 topics identified by the WPs 2-5, critically linked with the priorities selected by the SF, will be presented.

NATURAL RADIOACTIVITY IN SOILS AND MATERIALS CHARACTERISTIC OF THE CAMPANIA REGION (ITALY)

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The subsoil of the territory of the Campania region (Southern Italy) is rich in pyroclastic materials coming from the eruptions of several volcanic systems of the region[1]. Many of these materials have been largely used in the past as building materials, and now they are still used, and are responsible not only for the radon release but also for the external γ-ray exposition[2]. This contribution shows the results of the characterization of radioactivity of various soils and materials both typical in the architectural constructions for public and private buildings of the Campania region. This characterization has carried out by performing: (i) γ-ray spectrometry, using of a Hyperpure Germanium detector, for the determination of the radioactivity content from 226Ra, 232Th and 40K in the analysed samples, in terms of activity concentration (Bq/kg)[3]; (ii) α-spectrometry of ionised descendants of 222Rn, collected in an electrostatic cell, to measure the emanated fraction of this radioactive gas[4]. Soils of different pedologic settings and origin, and material (natural and not) strongly used in buildings construction in the Campania region have been sampled and investigated. The results underline the differences among the radioactivity content and the capacity of the samples to emanate radon. Samples collected in volcanic areas of the region show their high radioactivity content[5]. Interesting result is that the occurrence of high value of activity concentration of 226Ra (direct parent of 222Rn) in the building materials not always correspond to high 222Rn emanation coefficient[6]. Results can be useful as input for the creation of a model for the identification of risk areas in Campania. The parameters computed in this study can contribute to the estimation of radon entry rates in living environments (according to the differential equations governing the Radon transport through diffusion and advection) to assess the health hazards of radon accumulation[7].

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OUT-OF-FIELD DOSIMETRY AND NEUTRON ACTIVATION IN THE IRRADIATION ROOM OF A BNCT CLINICAL FACILITY WITH ACCELERATOR

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Boron Neutron Capture Therapy (BNCT) is a radiotherapy that uses the high cross section of boron-10 for the capture of thermal neutrons. In a BNCT treatment, the patient is infused with a borated drug capable of targeting cancer cells, and then irradiated with low energy neutrons. The final effect is the selective killing of cancer cells thanks to the energy released by the high-LET particles produced in the capture reaction. Recently, the technology has been developed to allow the construction of BNCT clinical facilities based on accelerators, with the potential to spread the use of this therapy. The designs of such facilities requires several evaluations, especially about the neutron activation of the irradiated materials and about the out-of-field dosimetry. This work concerns a clinical BNCT facility based on a Radio Frequency Quadrupole proton accelerator, producing neutrons through the (p,n) reaction on a beryllium target and coupled to a Beam Shaping Assembly (BSA) with lithiated aluminum fluoride as the main constituent. Experimental and computational studies for the design of the facility are presented, on the material of the BSA, the dosimetry and neutron activation in the room. Aluminum fluoride was object of a detailed characterization regarding its composition and its response to neutron irradiation. The irradiation room was simulated using different Monte Carlo codes, with an anthropomorphous phantom to represent the patient in several typical treatment positions. Simulations of a clinical irradiation were performed, to study the distribution of doses in the air of the treatment room and in the healthy organs of the patient. The neutron activation of the BSA and the patient due to a treatment were also calculated, and the time evolution of dose values due to the residual activity was investigated. Overall, the feasibility of a clinical BNCT facility based on the RFQ proton accelerator coupled to a BSA of lithiated aluminum fluoride was confirmed.

POSTERS

RADIOBIOLOGIA

EVALUATION OF SRC INHIBITION COMBINED WITH X-RAYS IN NORMOXIC AND HYPOXIC GLIOBLASTOMA CELL LINES

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The radioresistance of GlioBlastoMa (GBM) is mainly determined by the occurrence of hypoxic regions, where the indirect effects of ionizing radiations (IRs) are largely reduced[1]. New molecularly targeted drugs represent a strategy to enhance the effect of IRs by increasing the damage in hypoxic cancer cells. SRC proto-oncogene non-receptor tyrosine kinase (c-SRC) is a key target, because it is involved in many hallmarks of GBM related to hypoxia [2]. In our previous works, a new inhibitor of c-SRC (Si306, Lead Discovery Siena) demonstrated a synergic effect with X-ray and proton irradiation in GBM cells, but hypoxia had not been taken into account[3,4]. In this study, we evaluated the radiosensitizing effect of Si306 in combination with X-rays irradiation, comparing normoxic (21% of oxygen) and hypoxic (1% of oxygen) conditions on U251-MG and U87-MG GBM cell lines. The surviving cells fraction after treatment was evaluated by clonogenic assay; in addition, γH2AX foci detection by immunofluorescence was performed to quantify the radiation-induced DNA double-strand break formation and the DNA damage repair ability. The role of c-SRC inhibition on migration was also evaluated by wound healing assay. Dose modifying factor and oxygen enhancement ratio demonstrated that Si306 exhibited a synergistic effect with X- ray, decreasing radioresistance induced by hypoxia. γH2AX quantification showed that the foci activation signal remained high at 24 hours after treatment with X-ray and Si306, compared to irradiation alone, both in normoxia and hypoxia. The addition of the Si306 molecule reduced the migration index of cells in both oxygen conditions. In conclusion, while further *in vitro* and *in vivo* investigations are required, our encouraging data confirms Si306 has a novel putative drug to overcome hypoxia radioresistance.

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RBE AND DETERMINISTIC DAMAGE EVALUATION FOR PROTON BEAM IRRADIATION IN HEALTHY MURINE MODELS.

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The use of beams of charged particles in therapy, such as protons, is motivated by the presence of the Bragg Peak which gives an inverted depth-dose profile. Consequently, to reach the prescribed dose, it is possible to combine different energy beams able to selectively reach the area corresponding to the tumor target producing what is called Spread-Out Bragg peak (SOBP). For these reasons, the damage caused to the healthy tissues surrounding the tumor is limited. When protons are near the Bragg peak, they are characterized by a higher LET than X- rays, which results in greater biological efficiency in killing cells. High values of LET are associated with a localized deposition of energy responsible for an enhanced and irreparable biological damage to the irradiation target. A very important parameter that allows to quantify this greater effectiveness is the RBE. The RBE of the proton changes with the increase of LET and therefore with the depth in a SOBP from ~ 1.1 in the input region, to ~ 1.7 in the distal. The literature shows similar in vivo studies using only heavy ions and neutrons, but few with the proton beam. Within MoVe-IT (Modeling and Verification for Ion Beam Treatment planning) research project, healthy C57BL6J mice were irradiated at spinal cord with single doses adapted by GEANT4 Monte Carlo simulation with two different LET configurations. To evaluate the variation of RBE, some biomarkers of neuronal damage and demyelination are under investigation by histopathological techniques and western blot detection of protein of interest. As side effect, skin injury arise with a homogeneous intensity, as a direct consequence of the proton-beam.

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PRIMO ESPERIMENTO DI *PROTON BORON CAPTURE THERAPY* (PBCT) SU MODELLO *IN VIVO* DI EMBRIONI DI ZEBRAFISH (*DANIO RERIO*) PRESSO LA SALA CATANA DEI LNS-INFN

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La reazione di fusione nucleare p + 11B → 3α, conosciuta come *Proton Boron Capture Therapy* (PBCT), è in grado di generare particelle α ad alto LET mediante l'uso di molecole contenenti 11B quali, ad esempio, il borocaptato di sodio (NA2B12H11SH or "BSH")[1] che, quindi, si comporta come agente radiosensibilizzante quando colpito da fasci di protoni. Tale metodo consente di ottenere un miglioramento dell'Efficacia Biologica Relativa (RBE) nei trattamenti di protonterapia. Un primo esperimento di messa a punto di PBCT su modello *in vivo* è stato condotto su embrioni di zebrafish (*Danio rerio*) presso la sala sperimentale CATANA (62 MeV – *conventional protons - horizontal beams*), LNS-INFN Catania, per valutare l'efficacia radiobiologica del BSH. Gli embrioni WT a 72 ore dalla fecondazione sono stati suddivisi in quattro gruppi (CTRL, BSH, RT, BSH+RT) e irradiati per ogni posizione del picco di Bragg (*plateau*, *mid-SOBP* e *distal*) con la dose di 5 Gy. L'incubazione con o senza la concentrazione ottimale di BSH (0.13 mg/ml, 80 ppm), precedentemente valutata, è stata effettuata 16 ore prima del trattamento. Il posizionamento degli embrioni lungo il fascio orizzontale della sala CATANA è stato effettuato inserendo gli embrioni in apposite bustine di plastica, incorniciate da un riquadro rigido, della dimensione di 25 x 35 mm e dello spessore di 30 µm, capaci di ospitare sino a 25 embrioni, ciascuna in un volume di 1 ml di E3 *medium* per assicurarne la vitalità. Il corretto posizionamento e la misura della dose effettivamente erogata è stato effettuato impiegando pellicole GafChromic. 30 minuti e 24 ore dopo l'irraggiamento gli embrioni sono stati sacrificati e fissati per la successiva valutazione del danno al DNA a doppio filamento, tramite *whole body immunostaining* per il *marker* ɣ-H2AX, e per la quantificazione dell'apoptosi tramite la ricerca della Caspasi 3 attivata. Le indagini biologiche sono tuttora in corso per attestare l'efficacia del pretrattamento in presenza di ^{11}B.

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IMPROVED PARTICLE RADIATION RESEARCH FACILITIES AT CNAO

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CNAO is one of the four centres in Europe, and six worldwide, offering treatment of tumours with both protons and carbon ions. Since its start in September 2011 almost 3000 patients have been treated. Besides clinical activity, CNAO has also research as institutional purpose. In this framework a room dedicated to experimental activities will be available soon to allow external researchers to perform activities related to radiation biophysics, radiobiology, space research, materials research and detector development. The CNAO synchrotron provides energies up to 400 MeV/u for carbon ions (corresponding to a Bragg peak depth of up to 27 cm in water) and up to 227 MeV for protons (corresponding to a Bragg peak depth of up to 32 cm in water). The maximum proton energy available is 250 MeV. The minimum extraction energies are about 63 MeV and 115 MeV/u, for protons and carbon respectively, corresponding to particle range of 30 mm. An additional ion source is under installation and additional ions will be made available in the experimental room within 2022. The beam distribution in the CNAO experimental room is based on the same active scanning system in use in the treatment rooms. According to the needs of the experiment to be performed the experimental beamline can be arranged in four different configurations depending on the space required downstream the target or the dimensions of the scanning field. Furthermore, access to biological laboratory with all the necessary equipment is provided. Furthermore, in the next 2 years the research area will be expanded and rooms dedicated to microscopy, cell handling, cytology/histology and small animals preparation will be accessible. Indeed, thanks to the nearby animal house facility and the strong collaboration with the University of Pavia, in CNAO is also possible to carry out *in vivo* irradiations of small rodents, after technical evaluation and approval by the local ethical committee.

EFFETTI DEGLI ANALOGHI DEL COMPOSTO RHPS4 IN COMBINAZIONE CON RADIAZIONI IONIZZANTI SU LINEE CELLULARI DI CARCINOMA MAMMARIO

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Il composto RHPS4 appartiene ad una classe di agenti in grado di stabilizzare strutture secondarie alternative del DNA, note come G-quadruplex (G4), situate in regioni del genoma ricche in guanina, come telomeri e promotori. Nonostante studi precedenti abbiano mostrato che RHPS4 sia in grado di incrementare in modo sinergico la risposta al trattamento con radiazioni ionizzanti (RI) in linee di glioblastoma umano e che tale effetto sia correlato con la sua capacità di indurre disfunzione telomerica, il suo possibile utilizzo terapeutico è stato fortemente limitato da effetti indesiderati sul sistema cardiovascolare. Recentemente, sono stati sintetizzati analoghi di RHPS4 (nominati 190, 761 e 785) che riducono gli effetti off-target ma ritengono effetti cellulari simili a quelli della molecola di origine. In questo lavoro, tali ligandi sono stati testati in trattamenti singoli e in combinazione con RI in tre linee di carcinoma mammario (MCF7, MCF7-Y537S Tamoxifen-resistenti e HCC1937 mutate in *BRCA1*) e in una linea epiteliale non tumorigenica di ghiandola mammaria (MCF10A). Saggi di inibizione della crescita cellulare mostrano effetti antiproliferativi più marcati nelle linee tumorali rispetto alle linee di controllo e indicano RHPS4 e 190 come i composti più efficienti in trattamento singolo. Inoltre, tutti i composti sono in grado di ridurre significativamente i livelli proteici di CHK1 e RAD51, proteine note per il loro ruolo nella risposta allo stress replicativo e riparazione del danno al DNA. Tuttavia, il trattamento combinato con RI non ha evidenziato marcati effetti radiosensibilizzanti a differenza di quanto osservato con RHPS4 in cellule di glioblastoma. Tale differenza può essere giustificata dalla resistenza delle linee di carcinoma mammario alla disfunzione telomerica indotta dai ligandi e indica che gli effetti antiproliferativi siano principalmente ascrivibili all'inibizione di CHK1 o ad ulteriori target extratelomerici non ancora caratterizzati.

P53 INHIBITION INCREASES TELOMERIC RECOMBINATION IN X-IRRADIATED NORMAL FIBROBLASTS

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Unlimitedly proliferating cancer cells need to acquire a telomere maintenance mechanism (TMM) to counteract telomere shortening through multiple rounds of replication. The large majority of cancers (80–85%) maintain telomere length by expressing telomerase whereas the other ones (15-20%) use the Alternative Lengthening of Telomeres (ALT) pathway [1]. Telomerase is a reverse transcriptase that adds simple repeated sequences at the chromosome ends [2]. Instead, ALT mechanism is based on homologous recombination (HR) dependent exchange and/or HR dependent synthesis of telomeric DNA [3]. Previous studies demonstrated that human fibroblast after ionizing radiation exposure, are able to activate ALT mechanism. Indeed, both protons and X-rays induce telomere length modulation, causing the ALT activation instead of telomerase activation, probably as a response to DNA damage induced by these radiation [4,5]. Whereas telomerase-positive tumors can have or have not mutations of the tumor suppressor protein p53, all ALT cell lines are p53-deficient [6]. The aim of this study is to investigate if the absence of p53 alone in normal cells is sufficient to induce telomere recombination after X-rays treatment instead of telomerase activation. For this reason, in this study we have decided to use human normal cells (primary fibroblasts) that have not any type of mutation. We also put under the same conditions fibroblasts ectopically overexpressing telomerase, in order to investigate if telomerase interferes or prevents the activation of this mechanism. Preliminary results display an increased induction of telomere recombination through p53 inhibition after 3 Gy of X-rays exposure. However, cells overexpressing telomerase and p53 inhibited, show a lower telomere recombination level compared to the normal counterpart, after treatment. These data confirm that DNA damage activates a TMM and suggest that the switch between the two mechanisms could be influenced by the p53 protein.

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ROLE OF STAT3 EXPRESSION IN 2D CELL CULTURES AND 3D-ORGANOIDS EXPOSED TO RADIO-INDUCED GENOTOXIC STRESS

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Many nuclear transcription factors (NTFs) translocate to mitochondria, however, their function is poorly understood. Mitochondrial DNA (mtDNA) is different from nuclear DNA and NTFs are unable to activate the mitochondrial transcriptional program, nevertheless, it has been reported that several NTFs, including STAT3 are able to bind DNA. Here we report our preliminary results on the effects of STAT3 expression (in the wild and mutated form) on gene expression regulation during the genotoxic response to ionizing radiation of mouse cells grown in 2D or in 3D gut organoids from mouse crypts to model in vivo multicellular intestinal architecture.

DEFECTS IN NEUROGENESIS AND CHANGES IN MIRNA PROFILES IN OUT OF FIELD HIPPOCAMPUS AFTER PARTIAL- BODY IRRADIATION OF MICE

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Our previous work, showing that brain and skin cancer development in genetically sensitive mice is increased by radiation exposure of distant tissues, highlighted the importance of communication between irradiated and non-irradiated tissues in cancer induction. To test the potential contribution of "out-of-target" irradiation to non-cancer pathologies we have interrogated the hippocampus. Impairment of hippocampal neurogenesis is frequently observed after whole-brain exposure, and it is regarded as the most important mechanism of radiation-induced cognitive dysfunction. For our purposes, C57BL/6 female mice were whole body (WBI) or partial body (PBI) irradiated with 2 Gy of x-rays or sham irradiated (SI). PBI consisted in the exposure of the lower third of the mouse body, whilst the upper two thirds were shielded. Brains were collected 15 days post-irradiation from WBI, PBI and SI mice and, through a methodology based on a combination of morphological cellular features and immunohistochemistry with stage-specific neurogenesis markers, we investigated dysfunction in the dentate gyrus. Our findings demonstrate that PBI causes defects in the dynamic transition among neural stages, nearly identical to those induced by WBI. Alterations, involving self-renewal and proliferation, point to disturbance in the control of progression of neural stem cells into neurons. In parallel, given the emerging importance of miRNAs as part of the gene regulatory networks governing adult neurogenesis and in the cellular response to stress, we carried out miRNome analysis by NGS in dissected hippocampi. We detected a marked overlap of miRNA expression profiles in WBI and PBI hippocampi. Overall, our results demonstrate that the shielded hippocampus exhibits molecular/cellular alterations nearly identical to those induced by WBI. These results may have important implications in clinics and radiotherapy. The SEPARATE project has received funding from the Euratom research and training programme 2014-2018 in the framework of the CONCERT [grant agreement No 662287]

RADIATION-INDUCED ACTIVATION OF MATRIX METALLOPROTEASES IN COLORECTAL ADENOCARCINOMA CELLS

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Matrix metalloproteases (MMPs) are degradation enzymes that allow cells to migrate through the extracellular matrix: e.g. MMP2 and MMP9 are zinc-dependent endopeptidases that degrade collagen IV and lamina in the basal membrane; MMPs generate new binding sites for tumor cell receptors that stimulate migration and invasion of normal tissues, leading to metastasis. Recently, it has been shown that these proteins can also be localized at the nuclear level, taking on new regulatory roles including apoptosis induction[1,2] through the increased Annexin V binding, associated with the PARP cleavage. MMP-2, indeed, cleaves PARP generating two distinct degraded fragments of about 66 and 45 kDa. In our Radiation Biophysics and Radiobiology laboratory we have started an extensive experimental characterization of the response to X-rays (up to 10 Gy) of Caco-2 cells: this cell line is derived from human colorectal adenocarcinoma, usually adopted as an intestinal barrier model and recently characterized as radio-resistant. Colorectal cancer is among the three top cancer types for incidence and the second for mortality, usually managed with surgery, chemotherapy and radiotherapy. In addition to classically radiobiology-related endpoints (clonogenic survival; cell cycle distribution, necrosis and apoptosis, micronuclei) we performed gelatine zymography analysis, to evaluate MMP2 and MMP9 activity, which has been much less investigated as a function of radiation dose and time after exposure. Furthermore, we also investigated the possible dependence of MMP activation in presence of an immune response[3], using a co-culture model of Caco-2 cells with PBMCs. We here focus on these preliminary results, also discussing the limitation of gelatine zymography analysis for a precise quantification and addressing the possible correlation of MMP2 and MMP9 activity with apoptosis induction.

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THE LACK OF P21 SENSITIZES COLON CANCER CELLS TO RADIATION-INDUCED APOPTOSIS.

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Radiation therapy is the most-effective cytotoxic therapy available for the treatment of localized solid cancers. With the introduction of charged particle radiotherapy (proton therapy), the area of irradiated healthy tissue surrounding the tumor was further decreased. The aim of this study is to investigate the role of p53 in both X-rays and proton therapy treatments. p53 is a transcription factor with a key role in stress-depended regulation of DNA repair, cell cycle arrest, cellular senescence, and apoptosis.
As a model, we used 3 isogenic derivatives of the colon cancer-derived cells HCT116: parental, *TP53*-/-, and *CDKN1A*-/- (coding for p21). To uncover treatment-specific biological effects, we analyzed cellular responses to irradiation, focusing on DNA damage, p53 targets activation, apoptosis induction, and 3D culture disaggregation.
As expected, X-rays caused DNA damage as early as 4 hours after treatment in all cells, detected by the formation of γ-H2AX foci. Interestingly, 24 hours post-treatment, parental cells repaired the radiation-induced damages more rapidly in comparison with p53 null cells. Moreover, the p53 null clone showed a higher apoptotic rate, indicating that p53-/- cells could be more radiosensitive in respect to p53+/+ cells. To better mimic the shrinkage effect of radiation therapy on solid cancers, 3D spheroids were used. HCT116 parental, p53-/-, and p21-/- cells spontaneously formed spheroids in ultra-low attachment plates. Notably, while parental spheroids showed a reduction in diameter 13 days after the treatment, but still maintained a proper 3D organization, the p53-/- and p21-/- spheroids completely disaggregated. Moreover, the viability of p53-/- and p21-/- spheroids drastically dropped in response to X-rays, and analysis of PARP cleavage highlighted an increase in apoptosis particularly in p53 and p21 null cells. These results suggest that the absence of p53-dependent responses through p21 enhances the sensitivity to irradiation.

POSTERS

ASPETTI DOSIMETRICI

CARATTERIZZAZIONE DI DOSIMETRI A TERMOLUMINESCENZA (TLD-100) PER APPLICAZIONI IN RADIOTERAPIA

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I dosimetri a termoluminescenza (TLD) rappresentano dispositivi versatili e funzionali, utilizzati per verifiche dosimetriche in ambito radioterapico. La proprietà di quasi tessuto equivalenza (Zeff = 8.2) e le ridotte dimensioni (~ mm) li rendono utili per la dosimetria *in vivo*, essendo facilmente inseribili in fantocci antropomorfi o acqua equivalenti.1-3 Al fine di utilizzare i TLD per una misura di dose precisa e accurata, occorre implementare un protocollo rigoroso di caratterizzazione e calibrazione, utilizzando gli stessi fasci ed energie impiegati per i trattamenti sui pazienti. In questo studio sono stati caratterizzati e calibrati 3 lotti di TLDs-100 (LiF:Mg,Ti), esponendoli a fasci di fotoni da 6 MV e 15 MV presso la facility dell'Istituto Nazionale Tumori "Fondazione Pascale" di Napoli e con un fascio di protoni monoenergetico da 100 MeV presso il Centro di Protonterapia di Trento. Per determinare il fattore di sensibilità S=R/Rmedia per ogni TLD, ciascun lotto è stato inserito in un apposito alloggiamento in fantoccio acqua equivalente ed esposto a una dose pianificata di 2 Gy sul target. Le curve di calibrazione per le diverse qualità ed energie di fascio sono state determinate esponendo, per ogni lotto, diversi gruppi di TLDs-100 a dosi comprese tra 0.5-15 Gy per i fotoni e 0.5-20 Gy per i protoni.
I risultati per ogni lotto evidenziano linearità della funzione dose-risposta per dosi inferiori a 10 Gy ed una tendenza sopralineare superato tale livello, sia per i fotoni che per i protoni, in accordo con le previsioni teoriche.

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IL RUOLO DELLA TECNICA ED-XRF NELLA DETERMINAZIONE DELLO SPESSORE DI MATERIALI DI RIVESTIMENTO

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Con la tecnica di fluorescenza di raggi X s'identificano gli elementi chimici e si determinano le loro concentrazioni dello strato superficiale di un campione. L'analisi spettrale può anche consentire la stima dello spessore del rivestimento di un substrato. Quest'ultimo aspetto è di grande interesse nel campo dei beni culturali[1] per lo studio di oggetti che hanno una struttura stratificata, specie con metalli preziosi. Tale indagine fornisce informazioni sulla tecnica utilizzata nella realizzazione, su possibili interventi di restauro, sulle modalità di conservazione e sull'identificazione di possibili falsificazioni. Spessori di rivestimento dell'ordine delle decine di micron possono essere determinati sia misurando l'intensità dei raggi X di fluorescenza generati nel rivestimento che nel substrato. Nel primo caso, un aumento dello spessore del rivestimento comporta un aumento dell'intensità dei raggi X prodotti in esso[2-4]; mentre, nel secondo caso, si ha una diminuzione dell'intensità dei raggi X prodotti nel substrato perché attenuati dallo strato di rivestimento[5-8]. Lo scopo del presente contributo è la determinazione della natura e dello spessore dello strato ricoprente di un oggetto metallico mediante un'analisi delle linee caratteristiche di fluorescenza utilizzando uno strumento portatile commerciale ED-XRF. Esso è già stato utilizzato efficacemente in varie applicazioni per studiare pigmenti[9], monete antiche[10] e lamine d'argento[11]. Qui, viene eseguita un'analisi sistematica di diversi substrati rivestiti di oro e argento con uno strumento non appositamente adattato al tipo di misura, quindi, senza un segnale monocromatico, lenti confocali e la possibilità di scegliere determinate energie di lavoro. Inoltre, vengono usati vari possibili rapporti delle linee caratteristiche di fluorescenza e viene discussa la loro efficacia nel determinare lo spessore di oro e di argento in campioni d'interesse storico-artistico.

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RADON IN ACQUA DESTINATA A CONSUMO UMANO: MISURA E DISTRIBUZIONI IN ALCUNI POZZI DELLA REGIONE CAMPANIA.

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In questa indagine sono riportati i valori di concentrazione di gas radon nelle acque destinate al consumo umano. Il razionale è la cogenza di una normativa nazionale, il D.Lgs. n.28/20161, che definisce i criteri di misura e la tipologia di acque da analizzare indicando i valori di parametro ai fini di una efficace radioprotezione dei consumatori. Questo aspetto è di grande interesse per la salute pubblica dato che oltre al rischio di tumore ai polmoni dovuto all'inalazione di gas radon in aria2,3, vi è quello da ingestione. Ad oggi, pur non esistendo una stretta correlazione causa-effetto per altri tipi di tumori, l'ingestione di radon è di grande interesse scientifico4-7. Per l'analisi di mappatura di concentrazioni di radon in acqua, sono stati selezionati alcuni pozzi di raccolta dislocati in tutto il territorio della Campania e sono state eseguite misure in campioni di acqua utilizzando il sistema ad elettrete E-Perm® 8. Il lavoro riporterà una mappatura delle concentrazioni di radon ed alcune considerazioni riguardo l'influenza dei parametri ambientali sulla concentrazione di gas radon disciolto in acqua.

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XRF ANALYSES ON MOSAIC TESSERAE OFTHE PALATINE CHAPEL OF PALERMO

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A first archaeometric study was carried out on the mosaic wall decoration at the Palatine Chapel aimed at identifying the raw materials used for the creation of the different coloured glass and metallic foil tiles. For the first time, a technical-material study of the precious mosaic decorations that decorate the walls of the Palatine Chapel in the Royal Palace of Palermo was proposed and carried out. This unique site, built at the behest of King Roger II of Sicily in 1129 and completed in 1143 AD, was registered by UNESCO in the WHL since 2015. Investigations were carried out using X-ray fluorescence spectrometry and scanning electron microscopy on glass tesserae used in the original mosaic surfaces and/or restoration areas. XRF *in situ* measurements were performed by using a mobile micro-XRF spectrometer for elemental analysis (Bruker Biospin ArtTAX 200), equipped with a low-power X-ray tube using a molybdenum anode as target. For the study of the non-coloured vitreous matrices (bottom and top glass layer called "*cartellina*" of the golden tesserae) the XRF analytical data were integrated with those performed on some samples analysed in scanning electron microscopy (SEM-EDS). The results of the investigations have allowed the identification of the chromophore chemical elements, the executive techniques, verifying the original areas or subsequent mosaic integration over time, and confirming the hypotheses established on the stylistic analysis proposed by art historians. This work was funded by the project coordinated by Ruggero Longo and aimed to "Valorizzazione e fruizione del Palazzo Reale di Palermo" (Po-Fesr 2014-15) and partly by the Project MIUR PON03PE_00214_2 "Sviluppo e Applicazioni di Materiali e Processi Innovativi per la Diagnostica e il Restauro di Beni Culturali (DELIAS)" provided by the National Ministry of Education and Research (MIUR).

PRACTICAL ROLE OF POLYMERIZATION INHIBITORS IN POLYMER GEL DOSIMETERS

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Chemical gel dosimeters are prominent candidates for the direct determination of highly conformal tridimensional dose distributions1, typical of modern radiotherapy treatments. Pre-treatment dosimetric quality assurance is fundamental to achieve the full clinical potential of radiotherapy, while at the same time limiting side effects deriving from exposure of healthy tissues. The lack of recognized tools capable of performing direct 3D dose measurements in this setting is the driving force promoting the research in the field of chemical gel dosimetry. In this study, the dose response of a modified version of the acrylamide-based polymer gel dosimeter PAGAT has been characterized. The response of this dosimeter derives from radiation initiated free radical polymerization between acrylic monomers dispersed in a tissue equivalent gel matrix2, resulting in the formation of polymeric domains which can be measured via different techniques, *e.g.* UV-Vis spectrophotometry or MRI3. The dose range in which the dosimeter expresses a linear response is directly proportional to polymerization efficiency. In this study, the role of two polymerization inhibitors, hydroquinone and nitrobenzene, used individually or in combination with each other, was studied. The addition of these compounds leads to a lower polymerization yield, allowing to control the linear dose response range of the dosimeter, and to tailor it to the dose range of interest of the particular clinical application under examination. Obtained results indicate that an accurate control of inhibitor concentration can lead to a significant extension of the useful dose range, from approximately 5 Gy for the reference composition up to 15 Gy when inhibitors are added, with no significant detriment on other parameters such as accuracy, precision, dose resolution and temporal stability of the dose response.
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THE DOSIMETRY FOR *IN VITRO* BNCT RADIOBIOLOGICAL STUDIES

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BNCT dose is due to a mixed field, whose components have different biological effectiveness. The conversion of absorbed dose into photon-equivalent dose is important for dose prescription and to predict the clinical outcome of the treatment, based on the experience in dose-response gained in traditional photon-therapy. The calculation of photon-equivalent dose values has been traditionally obtained using fixed RBE/CBE factors, derived from in-vitro or in-vivo studies. Recently, other models have been proposed, such as photon-isoeffective dose, based on the evaluation of the whole dose-effect radiobiological curves instead of fixing an endpoint. Regardless of the model adopted to express BNCT dose in photon-equivalent units, a robust BNCT dosimetry relies on sound radiobiological data. For example, the survival of tumour cells as a function of dose when irradiated with neutrons only, with neutrons in presence of boron and with a reference photon beam are a typical tool to explore BNCT effectiveness in comparison with photon therapy. Recently, other in-vitro models have been explored to study BNCT safety and effectiveness. In Pavia, a long experience exists on the in-vitro BNCT studies, and we have explored the importance of dose calculations to construct the dose-effect curves. Detailed Monte Carlo calculations assessing the most suitable transport strategies, together with dedicated boron measurements for each irradiation experiment lead to accurate dose calculation. This work shows the effect of non-correct assumptions in dose calculations and of poor boron concentration knowledge in the determination of mixed-field dose, comparing the difference in the curves when different calculations strategies are applied.

DEVELOPING A PORTABLE DEVICE FOR ILLICIT RADIOACTIVE MATERIALS MONITORING: THE SICURA PROJECT.

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The regional government of Lazio (Italy) funded a two-years project, called SICURA, aimed at developing a new portable device to be employed in the prevention of radiological terrorism and illicit trafficking of radioactive material. Efforts were spent to fulfill the following characteristics: low cost, attractive for industry, portable, sensitive to photons and neutrons, capable of both gamma dosimetry and spectrometry, and compliant with relevant international standards. The radiation sensitive elements of the device are a Tallium-doped Cesium Iodide scintillator and a Cadmium-Zinc- Telluride semiconductor for X and Gamma rays, plus a Helium-3 proportional counter for neutrons. Dedicated electronics readout was developed. This communication presents the design of the SICURA measuring system, its MCNP simulation and the comparison with the results of the characterization campaign.

DATING OF BRAZILIAN SHELLS THROUGH ELECTRON PARAMAGNETIC RESONANCE

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The chronology of the formations of coastal planes in Brazil has been investigated by a large number of geologists. Among few possible mechanisms, one that drew major attention is the relative marine sea level fluctuation in the past. Before 1974 geomorphological, biological and sometime pre-historical arguments were used but after 1974 an extensive radiocarbon dating has been carried out by several authors and has allowed to obtain information about sea level variations, especially in Holocene period for southeastern and southern coast (Suguio & Martin 1978). For the northeastern coast of the state of Rio de Janeiro, sea level fluctuation curves were observed during a period between 8,000 years ago and present (Castro et. al. 2014): the maximum sea level occurred between 3,000 and 6,000 years ago. During that period, the region was under the sea. Then there was a proliferation of very large number of mollusks and oysters. The death of such mollusks produced a layer of shells inside the soil before the sea level receded to the present one. In the present work, we report dating procedure of these shells by using the electron paramagnetic resonance. The first step of the analysis was the definition of the optimal procedure for sample preparation. At this aim the analysis of the sample composition was carried out by X-ray fluorescence (XRF) measurements and an accurate analysis was study on the effect of the chemical etching with varying typology and concentration of acid to be used for removing the external layer of shells which are affected by alpha particles.
The EPR measurements were performed by applying the accumulated dose method. This method allows to extract the radiation dose the shells were exposed to and then, through the knowledge of the annual dose rate, the age of the shells. Furthermore, a comparison of the EPR dating results with radiocarbon method was performed. The Authors acknowledge funding also from the Project MIUR_PON03PE_00214_2 "Sviluppo e Applicazioni di Materiali e Processi Innovativi per la Diagnostica e il Restauro di Beni Culturali (DELIAS).

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X-RAYS AS USEFUL TOOL FOR CONTROL PHYTOCHEMICALS IN TOMATO FRUITS

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Tomato fruits are an essential source of antioxidants useful in counteracting free radicals and preventing the occurrence of several diseases1. The increasing demand for functional food promotes researches aimed to find cultivation practices enhancing phytochemical production. Ionising radiation (IR) is successfully utilised in breeding programs to improve plant productivity and quality2, in terms chemical composition of edible organs3 and crop shelf life4. This study evaluates the effects of different X-rays doses (0.3,10,20,50,100 Gy) on flowering, fruit set and biochemical traits (i.e. antioxidants, carotenoids, phenols and sugars) of *Solanum lycopersicum* L. cv. 'Microtom' plants. The radiosensitivity of plants at different phenological stages was assessed on seeds, and plants at vegetative, flowering and fruit ripening stages. The irradiation at the seed stage increased fruit production compared to control; at the vegetative stage it determined a decreasing in flower and berry production, which was prevented at doses of 50 and 100 Gy. The irradiation at the flowering stage did not alter the ripening at low doses but prevented the berry development at higher doses. The bioactive compound production in fruits was affected by dose and plant phenological stage. Plants irradiated at flowering stage showed the highest amount of carotenoids, cis-lycopene, lutein and □-carotene in fruits. The irradiation at ripening stage produced fruits more reach of total phenols (rutin, naringenin and caffeic acid). A dose-dependent increment of sugars was found in fruits regardless of the developmental stage. The results indicated that irradiation at the seed stage ensures fruit production also at very high X-rays doses, while at flowering and ripening stages, doses that do not prevent fruit formation induce a phytochemical increase. Our research confirms IR as a promising tool for control and modulation of bioactive compounds in tomato.

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PRELIMINARY STUDY OF THE SENSITIVITY TO PHOTONS AND NEUTRONS OF AN IONIZATION CHAMBER FOR THE MEASUREMENT OF GAMMA DOSE IN MIXED FIELDS

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A Monte Carlo study of an ionization chamber for gamma dose measurement in mixed neutron and gamma fields is proposed. This measurement is problematic because neutrons interact with chamber materials producing an unwanted gamma background through radiative capture and inelastic scattering reactions. To minimize this effect, graphite has been chosen for the walls and CO2 for the filler gas; in fact, the radiative capture cross sections at thermal energies are less than 10 mb and 1 mb for C and O respectively; inelastic scattering cross sections have thresholds around 3 and 5 MeV, and those with charged particle production start above 6 MeV. The chamber has a cylindrical geometry with an external diameter and height of 1.64 cm and 2 cm; the wall thickness is 3 mm and the filling gas pressure is 10 atm.Simulations were carried out with the Monte Carlo MCNP6 code to evaluate the sensitivity of the chamber in terms of current intensity per neutron and gamma fluence; the energy interval studied ranges from thermal energies up to 10 MeV, for neutrons, and from 50 keV up to 5 MeV for gamma. The chamber has been designed for mixed fields inside the core of a nuclear reactor such as the 250 kW Triga of the Lena of the University of Pavia, and in those present in the treatment beams of Boron Neutron Capture Therapy (BNCT). The simulations have shown that the contribution to the current in the reactor core due to the neutrons is less than 3%; and the thickness of the walls guarantees the conditions of electronic equilibrium; moreover, the walls and the gas are tissue-equivalent for photons and perfectly coupled to each other.The work was carried out in the framework of a collaboration between the Department of Instrumentation and Control of the Comisión Nacional de Energía Atómica (CNEA) of Buenos Aires, which has designed and realized a prototype of the chamber, the Department of Physics and Lena of the University of Pavia and the INFN (Enter_Bnct project).

RECYCLING METALLIC WASTE IN NUCLEAR DECOMMISSIONING BY DEVELOPING ADVANCED DECONTAMINATION PROCESSES

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The heavy burden of nuclear waste is currently the driving force for the development of advanced technologies for treatment and conditioning of radioactive materials. The decommissioning of a nuclear facility generates a huge quantity of contaminated metallic materials to be managed. Innovative processes point to reduce metallic waste volume before disposal, and release materials after treatment for recycle. An advancement of the PHADEC process based on the phosphoric acid decontamination of metallic waste is under study to obtain further volume savings of the final waste.[1] This process is basically based on: acidic dissolution of the superficial contaminated layer, subsequent oxidation of the dissolution solution, electrochemical precipitation and vitrification of the dried iron phosphate precipitate. The research work aims to evaluate the potential role of solid compounds in the electrochemical precipitation step in order to enhance decontamination and recycle of the dissolution solution. First, screening tests were conducted to point out the most promising co-precipitation agents and to set up the best experimental conditions. The decontamination process was performed at lab-scale by adding the co- precipitation agent as powder to the iron phosphate solution coming from the dissolution and oxidation steps before electrochemical precipitation. Stable Co, Cs, Sr and Ni have been chosen as representatives of the radionuclides present in the metallic dissolution liquor. Several experiments were carried out by using barium sulfate, calcium phosphate and polyphosphate at different concentrations (0.1, 0.3, 0.5 M). The first results showed a good abatement of contaminants from the iron phosphate solution. Calcium polyphosphate at low concentration seems very promising. The ongoing tests aim at optimizing the concentration of the selected co-precipitation agent to improve the decontamination yields. The experimental details and the main results will be presented.

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DOSIMETRIC CHARACTERIZATION OF PVA-GTA FRICKE GEL FOR DOSIMETRY IN PHOTON BEAM RADIOTHERAPY BY MRI AND OPTICAL TECHNIQUES

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The use of synthetic gel matrices prepared with poly(vinyl-alcohol) (PVA) cross-linked by glutaraldehyde (GTA) contributed to enhance the interest toward radiochromic Fricke gel (FG) dosimeters. Purpose of this study is the characterization of the dosimetric properties of PVA-GTA-FG. Also, we study the dependence of the dosimetric response of PVA-GTA-FG both on the irradiation temperature and on temperature changes possibly occurring between the irradiation and readout phases. These properties were investigated by means of magnetic resonance imaging (MRI) and optical absorbance (OA) measurements1,2. Xylenol Orange (XO) FG dosimeters were uniformly irradiated with 6 and 15 MV X-rays generated by a LINAC. UV-Vis absorbance spectra collected at consecutive times post-irradiation showed that a time of approximately 15 minutes is sufficient to reach a stable value of the absorbance, indicating the achievement of a chemical equilibrium in the complexation processes between Fe3+ and XO. The analysis of the change of the absorbance spectra shape with the dose demonstrated that a linear dose-response curve of PVA-GTA-FG dosimeters is obtained in the entire investigated dose interval 0.5-15 Gy by choosing properly the wavelength used for the OA measurements. Furthermore, PVA-GTA-FG dosimeters proved to be nearly tissue-equivalent and characterized by a response independent on the energies and dose rates in the investigated intervals. The results did not reveal any significant dependence of the sensitivity of the dosimeters on the irradiation temperature in the investigated interval 20°C-35°C. By contrast, auto-oxidation phenomena confirmed to be a critical aspect for FG dosimeters, also in case of use of PVA matrix. The extent such phenomena, that might impair the accuracy of dose estimations, proved to critically depend on the temperature at which FG dosimeters are subjected before and after irradiation, as well as on the duration of possible thermal-stress.

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UTILIZZO DI DOSIMETRI A TERMOLUMINESCENZA IN BRACHITERAPIA

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I dosimetri a termoluminescenza (TLD) sono ampiamente utilizzati nella pratica clinica per verifiche dosimetriche grazie alle loro caratteristiche che corrispondono ai requisiti ideali per l'uso standard. Infatti i TLD sono solidi e di piccole dimensioni, facilmente maneggevoli e posizionabili, mostrano una buona risoluzione e sono riutilizzabili. La risposta TL è lineare in un'ampia regione di dose, tipicamente da pochi µGy a decine di Gy.1 Scopo del seguente studio è investigare la possibilità di utilizzare i TLD per verifiche dosimetriche in seguito ad un trattamento di brachiterapia (radioterapia interna), che costituisce un campo di utilizzo delle radiazioni ionizzanti a scopo terapeutico per lesioni tumori, in cui la dosimetria non è ancora una pratica standard.2 L'esperimento è stato condotto presso la facility dell'Istituto Nazionale Tumori "Fondazione Pascale" di Napoli. Utilizzando un fantoccio antropomorfo realizzato con elevata fedeltà e accuratezza anatomica in materiali tessuto equivalenti e una maschera che ospita cateteri abitualmente utilizzati per la veicolazione e l'alloggiamento della sorgente radioattiva, è stato simulato un trattamento con sorgente di Iridio 192. La dose pianificata sul *Clinical Target Volume* (CTV), localizzato sul cranio, è pari a 3.5 Gy. 20 TLD-100 sono stati fissati nei distretti di interesse ossia sul CTV, sull'occhio destro, sull'occhio sinistro e sul cranio al fine di verificare la correttezza della dose pianificata e la dose assorbita da organi e tessuti sani. Dai risultati ottenuti si evince una buona risposta dei TLD al fascio di radiazioni utilizzato per il trattamento pertanto, sfruttando la maneggevolezza e le piccole dimensioni dei TLD, si pensa di poter investigare ulteriormente la loro funzionalità come dosimetri per considerare l'applicazione di protocolli di controllo di qualità pre-trattamento oggi ancora non ben definiti in brachiterapia.

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POSTERS

RADIAZIONI IN AMBITO CLINICO
RADIOPROTEZIONE

PRELIMINARY COMPARISON BETWEEN AUTOMATED AND MANUALLY PLANNED TREATMENTS FOR BRAIN METASTASIS

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Over the last years, radiotherapy has evolved significantly in term of treatment plans complexity and accuracy of the delivered, moreover it has become the first therapeutic choice in some lesions and in general it is present in several adjuvant and neo-adjuvant protocols. This trend suggests that in future the number of patients who will receive radiotherapy will continue to increase especially for treatments such as Volumetric Modulated Arc Therapy (VMAT). This technique involves a rotating treatment filed around the isocenter, typically located in the volume tumor target, which is continuously modified in dose rate and shape by a multileaf collimator, therefore it allows a good tradeoff between tumor coverage and Organs At Risk (OAR) sparing. Due to the high degrees of freedom involved in this technique, a computer based inverse approach is used: the medical physicist imposes the objectives and constraints depending on the patient's anatomy and the algorithm implemented in the adopted Treatment Planning System (TPS) search for the best solution. Therefore, the parameter setting biases the plan quality by making the treatment strongly operator dependent. However, some of the steps involved in the planning activity can be automated reducing human arbitrariness and ensuring quality uniformity among different medical centers. Brain is a common metastatic pathway regardless of the primary tumor location[1], and in case of multiple lesions the whole brain radiotherapy (WBRT) is typically adopted, nevertheless the VMAT could be used in order to avoid useless radiation to the brain reducing neurocognitive degeneration[2,3,4]. This work is aimed to test and compare treatments generated with auto-planning module against human-driven plans by using RayStation treatment planning systems for hypothetical brain lesions located in proximity of the brainstem, chiasm and eyes by evaluating the target conformity and the dose to the OARs[5].

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NUCLEAR REACTION MODELING OF 52GMN PRODUCTION FOR MULTIMODAL IMAGING

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MultiModal Imaging is an innovative technique that consists in the combination of diagnostic exams based on different physical processes to obtain a unique image with more detailed clinical information. The possibility of a simultaneous use of PET and MRI could be achieved by using a particular radioisotope: 52gMn. To optimize its production, different nuclear reactions, including p(52Cr,n)52gMn, d(52Cr,2n)52gMn[1] and α(NatV,x)52gMn, are theoretically investigated in this study. Considering three nuclear reaction codes (Talys, Fluka and Empire), an analysis of the cross sections is performed to identify the energy window corresponding to the maximum production of 52gMn with respect to its contaminants. The study is carried out using statistical instruments to describe the variability of the Talys models and to estimate a theoretical reference value for the integral yield[2]. The analysis gives a preliminary idea of the purity of the product of the considered reaction. After fixing the irradiation conditions (current, incoming energy, target thickness, irradiation time), a computation of the production rates and time evolution of the produced radioisotopes is performed, leading to the definition of two quantities: the Isotopic Purity (IP), which depends on the number of the produced nuclides; the RadioNuclidic Purity (RNP) which depends on their activities[3]. This process leads to the identification of the most promising reaction in terms of production yield and purities. In particular the (α,3n) reaction is shown to be a very competitive channel, thanks to the theoretical estimations and to the lower cost of the target. This reaction, which is not even mentioned in the literature[4] for this purpose, could thus represent a new approach for the production of 52gMn, in view of MultiModal Imaging applications.

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THEORETICAL STUDY FOR A ^{117M}SN PRODUCTION EXPERIMENT WITH A 30 MEV A-BEAM

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^{117m}Sn has been identified as a promising radionuclide due to the emission of both conversion electrons, E =126.82 keV (65.7%), 129.360 keV (11.65%), 151.56 keV (26.5%), and gamma-rays, E = 156.02
keV (2.113%), 158.56 keV (86.4%) [1], suitable for therapy and diagnosis, respectively. At present this radionuclide is produced only in nuclear reactors with a low-specific activity [2], therefore new possible production routes are under investigation. In this study we assess the reactions ^{nat}Cd(α,x)^{117m}Sn and ^{nat}In(α,x)^{117m}Sn, considering a 30 MeV α-beam, provided by the HIL U-200P cyclotron in Warsaw. Theoretical study of cross sections and yields are performed using the nuclear reaction codes Talys (v.1.9) and Fluka (v. 2018.2.dev) as a guide for experimental measurements. A statistical analysis of the variability of the models and the related theoretical error has been also evaluated [3]. For both targets, ^{nat}Cd and ^{nat}In, we identify the optimal irradiation parameters to obtain the maximum production of the radionuclide ^{117m}Sn, minimizing the co-production of contaminants. Results suggest that the activities produced with the two targets are comparable, but a higher radionuclidic-purity could be achieved in the case of ^{nat}In target.

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MONTE CARLO SIMULATION OF AN ELECTRON BEAM GENERATED BY A MOBILE IORT ACCELERATOR

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IORT is a technique that, after the surgical tumor removal, delivers a dose of ionizing radiation directly to the surgery bed. This procedure helps to eradicate the microscopic residual tumor cells that surgery can left over. The dose is provided by an electron beam produced by a miniaturized LINAC accelerator with energy between 4 and 12 MeV [1]. This single application can either be used as a boost to increase tumor local control or, in the most favorable cases, replaces the radiotherapy treatments. The mobile electron linear accelerator NOVAC 11 (SIT, Aprilia, Italy) [2] has been tested and simulated. NOVAC 11 maximum energy is 10 MeV which allows treating targets with a thickness up to 2.6 cm inside the 90% isodose (3.0 cm inside the 80% isodose). The device, that is able to successfully deliver the treatment in 100 seconds only, can be installed in any standard operating room with no need of lateral shielding or structural modifications to the operating theater. In the present work the experimental dosimetric characterization of the linear accelerator has been compared to a Monte Carlo simulation with FLUKA [3], for different energies (6, 8 and 10 MeV). In particular the accelerator beam optics that begins from the titanium window (at the end of the vacuum guide) and finishes at the end of the PMMA applicator has been simulated to evaluate the dose released by the electron beam, with two different applicators, at different applicator depth. The agreement between experimental and simulation results is extremely good (both for PDDs, profiles and Output Factor). Furthermore, it has been determined the ratio between the accelerated electrons and the dose delivered; beam current at the exit of the accelerating guide has been measured by means of a Faraday cup. Finally, the consistency between the measured dose at Dmax and the dose estimation provided by the simulation has been evaluated, with a good agreement.

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EXTERNAL CALIBRATION AND PERFORMANCE ASSESSMENT OF THE DRIFT CHAMBER DETECTOR ADOPTED IN THE FOOT EXPERIMENT

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In current treatment planning systems adopted in charged particle therapy, nuclear inelastic interactions between the projectile and the target material nuclei are not properly considered due to the uncertainties of calculation models and a lack of the experimental data needed for benchmarking. Different studies1 have shown that fragmentation of the projectile and/or of the target nuclei may produce a non-negligible amount of dose deposition outside the planned target volume. The main goal of the FOOT (FragmentatiOn Of Target) experiment is to measure the double differential cross sections with respect to kinetic energy and emission angle of fragments produced in nuclear interactions of ions with energies relevant for charged particle therapy. The FOOT data will be eventually exploited to improve the treatment planning systems, to study the nuclear interaction models and to be adopted as benchmark for the Monte Carlo simulation codes. In the FOOT experimental setup, a drift chamber detector is adopted to measure the incoming beam direction and position, identifying also pre-target fragmentation events. The space-time relations calibration and the performance assessment of the drift chamber have been conducted at the Trento protontherapy facility with proton beams at 228 and 80 MeV of kinetic energies, exploiting an external tracking system composed of different layers of microstrip silicon detectors. The resulted overall hit detection efficiency is 0.929 ± 0.008. The detector spatial resolution has been evaluated to be 150 ± 10 μm and 300 ± 10 μm for the higher and lower beam energies, respectively. In addition, the upper limit on the drift chamber resolution has been found to be of 60 ÷ 100 μm. The procedures adopted for the drift chamber calibration and to analyse its performance will be presented together with an overview of the FOOT experiment.

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LEARNING NUCLEAR CHEMISTRY AND RADIOCHEMISTRY THROUGH A MASSIVE OPEN ONLINE COURSE

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The progress made in developing innovative teaching and learning methods enables to have available new approaches to attract the interest of young generations on disciplines not so widespread but essential for addressing current challenges of modern society. Thanks to the support of the European MEET-CINCH project (*A Modular European Education and Training Concept In Nuclear and RadioCHemistry*), Politecnico di Milano developed the Massive Open Online Course (MOOC) "Essential Radiochemistry for Society" focused on various applications of Nuclear Chemistry and Radiochemistry (NRC) in relevant areas of our society. The MOOC is available at the Polimi Open Knowledge platform (https://www.pok.polimi.it/).
The MOOC, specifically designed for bachelor students in scientific matters, aims to present NRC in an engaging way, to make the student realize the involvement of NRC in everyday life and to highlight the benefits that NRC could introduce, despite the negative perception and mistrust that are still present in many people.1 The MOOC is organized in five weeks, each one presenting the main applications of NRC for environment, health, industry, nuclear energy and society, respectively. A specific pedagogical framework has been created to guide the student in an engaging and effective learning path. Different lesson formats, such as video, article and infographic, have been developed to explain, as example, the use of radiation in nuclear medicine, on food, for sterilization purposes, on cultural heritage for its preservation, and so on. The MOOC as self-paced learning experience or used in flipped classroom could represent a precious opportunity in several situations, such as the current pandemic. The development process of the MOOC as well as the feedback coming from the first pilot edition are presented and discussed.
This work was supported by the European Commission within the H2020 MEET- CINCH project (https://www.cinch-project.eu).

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RADIATION DOSE ESTIMATES IN DIGITAL BREAST TOMOSYNTHESIS COMPARED WITH FULL-FIELD DIGITAL MAMMOGRAPHY: A BRIEF ANALYSIS

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Breast cancer is reported as the second most common cancer in the world. The estimate for 2018 is 59,700 new cases of breast cancer [1]. The distribution of the incidence of breast cancer is high especially in industrialized countries, followed by developing countries. The development of effective screening programs allows to lead the survival to 84% in developed countries. Early diagnosis, in the context of these programs, is carried out using X-rays and the equipment used for this purpose is constantly updated to improve the detection capability for the same dose delivered.
Nowadays, next to full-field digital mammography (FFDM), 3d technology is available on modern mammography devices, such as Digital breast tomosynthesis (DBT). Some studies show that the use of DBT, combined with FFDM, or as a stand-alone technology, allows for a better diagnostic performance than FFDM alone [2,3]. In addition to the diagnostic capacity, of course, the dose to the population participating in the screening programs must also be investigated. Considering that the different manufacturers of digital mammography equipment uses different technologies to reconstruct pseudo-3d images, it is essential to check the radiation dose of various equipment available in healthcare facilities. The purpose of this work is to verify the radiation dose for a particular mammography device used in both FFDM and DBT procedure.

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END-TO-END TEST IN STEREOTACTIC RADIOSURGERY TREATMENTS THROUGH HELICAL TOMOTHERAPY

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In this study the accuracy of the dose delivered in an Intracranial stereotactic radiosurgery (iSRS) session by a non-conventional radiotherapy machine, the TomoTherapy Hi-Art System, was investigated using an "end-to-end" test. This is performed by means of alanine Electron Paramagnetic Resonance (EPR) pellets. The response of these dosimeters is compared to that of gafchromic films, which are particularly suitable for two-dimensional dose verification providing accurate estimate of the distribution and of the gradients of the absorbed dose.
Dose verifications were made using alanine dosimeters placed in an anthropomorphic head phantom (Alderson Rando Phantom) under different treatment conditions in case of both single and multiple brain tumors. 1.25 mm slice kVCT scan of the phantom was used to generate SRS plans on the TomoTherapy Planning Station platform, prescribing dose at the 95% isodose level of the "PTV" using different combinations of pitch and Modulation Factor. Before each session, a MVCT was performed for setup verification.
Commercial alanine dosimeters (Synergy Health, Germany) were irradiated in various positions of the phantom. EPR measurements were carried out through Bruker ECS106 spectrometer working at about 9.7 GHz. The dose values measured through alanine dosimeters and gafchromic films show a good agreement with the dose values calculated by the TomoTherapy Treatment Planning System, for both organs at risk and tumors. Alanine absolute dose measurements showed to be useful for the dosimetric validation of HT SRS treatments.

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NATO SCIENCE FOR PEACE AND SECURITY (SPS) PROJECT "*BIOPHYMETRE*" NOVEL BIOLOGICAL AND PHYSICAL METHODS FOR TRIAGE IN RADIOLOGICAL AND NUCLEAR (R/N) EMERGENCIES

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The Project entitled "Novel biological and physical methods for triage in radiological and nuclear (R/N) emergencies" *(BioPhyMeTRE*) has been recently approved within the NATO Science for Peace and Security (SPS) Programme. The project focuses on innovative biological and physical dosimetry methods allowing a rapid screening/triage of potential victims by using inexpensive and user-friendly analytical procedures and devices. The proposed biological method combines the two most standardised biological dosimetry methods into a more exhaustive "two-in-one" assay allowing the simultaneous scoring of chromosome aberrations and micronuclei on the same slide, while the physical method focuses on the use of a low cost, portable mini photo-luminescence reader for the individual dose assessment by using personal objects.Both methods will be validated through the set-up of calibration curves and inter-laboratory comparisons to verify their reliability for triage in R/N emergencies. Moreover, automation systems for the novel biological protocol will be evaluated.
The biological and physical dosimetry methods proposed in "BioPhyMeTRE" project, once fully developed and validated, could represent useful tools for the categorization of subjects overexposed to ionising radiation in R/N emergencies. The project, coordinated by the Italian National Agency for New Technologies, Energy and Sustainable Economic Development (ENEA) of Italy, involves the Institute of Radiation Safety and Ecology (IRSE) of National Nuclear centre of Kazakhstan, the National Health Institute (ISS) of Italy and Ruđer Bošković Institute (RBI) of Croatia.
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STUDIO DELLA PERCEZIONE DEL RISCHIO NEL TERRITORIO CAMPANO

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Il radon è un gas radioattivo di origine naturale che fa parte della catena di decadimento radioattivo naturale dell'uranio ed è quindi presente nella crosta terrestre. Esso tende a diffondersi ed accumularsi negli ambienti confinati, dove può raggiungere concentrazioni elevate e potenzialmente pericolose per la salute. L'OMS ha classificato tale gas tra le sostanze che presentano un'evidente cancerogenicità per l'uomo, inserendolo nel gruppo 1 della classificazione dell'IARC, ed ha stabilito che esso rappresenta la seconda causa di cancro ai polmoni dopo il consumo di tabacco. Data l'importanza di questa tematica, il quadro normativo ha subito una importante evoluzione fino all'emanazione della Direttiva europea EURATOM 59/2013[1], che detta le "Norme fondamentali di sicurezza relative alla protezione contro i pericoli derivanti dall'esposizione alle radiazioni ionizzanti" che sarà a breve recepita dall'Italia. La nuova normativa, oltre ad obbligare gli Stati Membri a definire dei livelli di riferimento nazionali per le concentrazioni di radon in ambienti chiusi al di sotto di un valore fissato, richiede l'adozione di un Piano d'azione per il radon, che prevede una serie di azioni coordinate per la riduzione del "rischio radon". La Direttiva invita ad adottare le misure necessarie ad individuare le zone particolarmente a rischio, dette *radon prone areas,* e ad incentivare le misure della concentrazione di questo gas nei luoghi chiusi. Al fine di migliorare l'efficacia del Piano d'azione per il radon, è utile verificare le nozioni diffuse tra la popolazione riguardo al rischio da radiazioni[4]. Lo scopo del presente lavoro è quello di fornire dati relativi alla consapevolezza della popolazione circa i pericoli derivanti dall'esposizione alle radiazioni di origine naturale e artificiale. Tali dati potrebbero rappresentare uno strumento molto utile per migliorare le campagne di sensibilizzazione alla popolazione in merito al rischio di esposizione al radon.

1. *Direttiva 2013/59/EURATOM del Consiglio del 5 dicembre 2013, Gazzetta ufficiale dell'Unione Europea,17.1.2014.*
2. *WHO Handbook on Indoor Radon. 2009, Geneva, Switzerland.*
3. *Bochicchio, F. Radiat. Prot. Dosim., 2011, 146(1–3)2–5.*
4. *Giancarlo Sturoni, AIRP - Atti del XXXIII Congresso Nazionale di Radioprotezione Torino, 20 - 23 settembre 2006 ISBN 88-88648-05-4.*