MEDICIS-Promed Final Conference

Report of Contributions

https://indico.cern.ch/e/782482

Contribution ID: **1** Type: **not specified**

Introduction

Tuesday 30 April 2019 09:00 (30 minutes)

Presenters: Prof. PRIOR, John Olivier; Dr STORA, Thierry (CERN)

Contribution ID: **4** Type: **Oral**

The ISOLPHARM project at LNL: Production method of high specific activity radionuclides as radiopharmaceutical precursors

Friday 3 May 2019 09:50 (20 minutes)

At INFN-LNL (Istituto Nazionale di Fisica Nucleare –Laboratori Nazionali di Legnaro) a new facility for the production of radioactive ion beams is implemented, SPES (Selective Production of Exotic Species). This new facility, besides being operated for nuclear physics studies, may play a pivotal role in the production of medically relevant radionuclides by means of the ISOL (Isotope Separation On-Line) technique.
The production of the radioactive isotopes will be obtained by nuclear reactions induced by 40 MeV protons, accelerated by a cyclotron, that will collide on a target composed of 7 discs of carbon dispersed uranium carbide (UCx), properly spaced in order to dissipate the heat (8 kW) generated by the reaction. The uranium contained in the target material will be 238U, so that the produced radioactive isotopes will belong to elements having an atomic number between 28 and 57 (elements placed between nickel and lanthanum). In particular, most of the produced nuclides will be neutron-rich, so with an excess of neutrons with respect to the element stable nuclear configuration.
The core of the method is the possibility to obtain pure isobaric beams following mass separation; in this way no isotopic contaminations will be present in the beam and afterwards in the trapping substrate. Only potential isobaric contaminations can affect radiochemical and radionuclide purity, but proper methods can be developed to separate chemically different elements
The goal of the ISOLPHARM project is to provide a feasibility study for an innovative technology for the production of extremely very high specific activity beta emitting radionuclides as radiopharmaceutical precursors. This revolutionary technique will allow to obtain radiopharmaceuticals, impossible in most cases to obtain in the standard production facilities (neutron reactors or cyclotrons), with lower costs with respect to traditional techniques and reduced environmental impact.
The steps to be addressed for the preparation of the radiopharmaceutical are: 1) Trapping of the radionuclide of interest present in the beam by means of the construction and placement of a suitable substrate; 2) Preparation of a medicinal product compatible with the method of administration; 3) Agreement with the requirements of quality guaranteed by compliance with the principles of Good Manufacturing Practice (GMP) in the field of radiopharmaceuticals. The ongoing activities concerning a recent experiment focused on 111Ag, a study performed in collaboration of Padova and Trento Universities, will be presented.

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Session Classification: Accelerator techniques for medical isotope production

Track Classification: Accelerator techniques for medical isotope production

Contribution ID: **5** Type: **Invited**

Comparison of adequate LINAC acceleration techniques for e- and light ions

Friday 3 May 2019 11:20 (30 minutes)

The state of the art in linac architecture at the low energy front has been developed quite a lot during the last decades. Frequency ranges and choices among available key components like amplifiers, controls and magnets have been extended. Room temperature as well as superconducting developments with high reliability are available now. The Pro's and Con's of alternative layouts will be discussed for typical beams like electrons, protons, deuterons and alphas in the energy range from a few MeV and up to tens of MeV.

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Session Classification: Accelerator techniques for medical isotope production

Track Classification: Accelerator techniques for medical isotope production

Contribution ID: **6** Type: **Oral**

Highly enriched target material for the production of radiopharmaceutical isotopes: the use of electromagnetic separation

Friday 3 May 2019 10:30 (20 minutes)

One limitation of the production of some radioisotope for medical use is the possibility to obtain them with a sufficient purity, not only in terms of chemical contaminant, but also in terms of isotopes. Different production techniques are available but at least for some particular isotopes, enriched primary matter is mandatory in order to achieve sufficient isotopic purity and not produce prohibitive contaminants.
This difficulty can be overcome through different possible enrichment techniques, one of them being electromagnetic separation.

As for a "proof-of-concept"experiment, Tb isotopes production has been chosen. They can be produced through nuclear reaction (p,x) on Gd isotopes. The first step of this study is to measure the production rates of such pure isotopes and their achievable isotopic purity.
The talk will present possibilities related to the use of one of the last high performance electromagnetic mass separator in Europe, SIDONIE, located at CSNSM-Orsay-France [1-3]. After a description of the machine, some "proof of principle"experiments will be described, as well as some first results. Gd-158 has been chosen due to the possibility to detect and quantify it by prompt-gamma experiment and to measure its contamination with its neighbour, Gd-157. We have shown the possibility to obtain ratio 157Gd/158Gd from 10E-4 to 10E-5, with relatively high currents, leading to the possibility to produce highly enriched target materials.
Perspectives of this preliminary study will be presented to conclude the talk.

This work has been possible though the collaboration of D.Ledu, F.Pallier, U.Koester, I.Tomandl, F.Haddad and N.Michel.

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Session Classification: Accelerator techniques for medical isotope production

Track Classification: Accelerator techniques for medical isotope production

Contribution ID: **7** Type: **Oral**

Use of electrodeposition for the production of Tb-149

Thursday 2 May 2019 14:30 (20 minutes)

Terbium is an element having four radioactive isotope of interest for nuclear medicine: Tb-149 and Tb-161 for therapy and Tb-152 and Tb-155 for imagery. The production of Tb-161 isotope can be done efficiently with high specific activity in nuclear reactor using Gd-161 target, the isotopes of Tb-149, Tb-152 and Tb-155 can be produced in a commercial cyclotron using a proton beam with energies up to 70 MeV. Both Tb-152 and Tb-155 can be obtained with good yields from a natural gadolinium target. However, the production of Tb-149 is challenging because its production from a natural gadolinium target is very low. To improve its production, it is necessary to use enriched gadolinium either 152 or 154. The enrichment of Gd-152 or Gd-154 is under oxide form and this form can be problematic during irradiation because of its low thermal dissipation. In GIP ARRONAX, in Nantes, we have developed the solid target of gadolinium by the electrodeposition technique. Pure gadolinium coating is impossible in aqueous media due to its high standard potential, -2.279 V/ENH. Working in organic media is an alternative but remain difficult. We decide to use the EMMC technique, Electrodeposited metal matrix/metal particle composites. This technique consists to use the suspension particles of gadolinium salts in aqueous media and during the electrodeposition, these particles are trapped in the Ni deposit. Promising first results will be presented along with data on the characterization of the deposits through MEB-EDS and ICP-OES.

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Session Classification: Methods for production of novel radioisotopes for theranostics

Track Classification: Methods for production of novel radioisotopes theranostics

Contribution ID: **9** Type: **Oral**

Target concepts for the ISOLPHARM project

Thursday 2 May 2019 14:50 (20 minutes)

ISOLPHARM [1] (ISOL technique for radioPHARMaceuticals) is a project devoted to the discovery and development of high specific activity radiopharmaceuticals exploiting radionuclides producible with the future SPES (Selective Production of Exotic Species) ISOL (Isotope Separation On-Line) facility at INFN-LNL.
The strength point of such production method is the capability to produce a wide set of intrinsically carrier-free nuclides with high flexibility, since different radioisotopes can be extracted separately from the same production target by simply adjusting the settings of the electromagnetic separator.
In particular, ISOLPHARM could have the capability to provide nuclides with medically relevant decay properties but limited availability, such as 111Ag, 43Sc, 47Sc, 67Cu, 149Tb, 152Tb and 155Tb, once a suitable production target is identified.
In the presented work Uranium Carbide (UCx) is proposed as production target for 111Ag, Zirconium Germanide (ZrGe) for 67Cu, along with 64Cu [2], Titanium Carbide (TiC) or Titanium Boride (TiB2) for 43Sc and 47Sc, and Gadolinium Boride (GdB4) for 149Tb, 152Tb and 155Tb. The feasibility of the production of the desired nuclides was subsequently evaluated by means of Monte Carlo codes, in particular FLUKA and Geant4, and promising yields were calculated. Furthermore, in the case of the ZrGe target, provided the lack of experimental measurements on the natGe(p,X)64Cu and natGe(p,X)67Cu reactions, dedicated nuclear cross section studies were performed.
Furthermore, such study included also the performance of tests with stable counterparts of the desired nuclides, aimed to investigate the capability of SPES technologies to ionize, accelerate and selectively collect single isotopes of the elements of interest.

References
[1] F. Borgna et al., Appl. Radiat. Isot., 2017.
[2] F. Borgna et al., Molecules, vol. 23, no. 10, 2018.

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Session Classification: Methods for production of novel radioisotopes for theranostics

Track Classification: Methods for production of novel radioisotopes theranostics

Contribution ID: **10** Type: **MEDICIS-Promed ESRs**

HSA Er-169 production at ILL nuclear reactor and CERN-MEDICIS

Thursday 2 May 2019 16:00 (20 minutes)

Er-169 (half-life 9.39 d) is an almost pure β- emitter characterized by low energy electrons emission and few low energy and very low intensity gamma rays. It is currently produced in nuclear reactors through the neutron activation of Er-168, which is one of the 6 natural erbium isotopes. Er-168 is commercially available at around 98% enrichment level; nevertheless, the cross section of the reaction is quite low, entailing a dilution of Er-169 in high amount of stable Er-168. Thus, the low specific activity of the produced batches hinders its potential use for receptor-targeted radiotherapy. The combined use of nuclear reactor production and mass separation is proposed to overcome the low specific production of some carrier-added lanthanides, such as Er-169. The experiments performed at ILL nuclear reactor and CERN-MEDICIS facility showed the feasibility of the production method. The first production of high specific activity Er-169 has been performed with the collection of around 17 MBq. A specific activity increase from 1.3 GBq/mg to 235 GBq/mg at the time of mass separation was obtained. Nevertheless, the overall efficiency of the production method was around 0.2 %. Based on the first experiments, some improvements have been identified for the future amelioration. One is to optimize the position of the left slit maximizing the reduction of Er-168 atoms while minimizing the loss of Er-169 on the collection foil. The method identified for improving the efficiency, instead, consists in introducing the laser ionization in the mass separation process. The results achieved, as well as the future perspectives will be presented in more details. In parallel, it was shown that Er-169 can be produced and be available for preclinical studies. Thus, preclinical trials could be performed starting from mid-2019 in collaboration with hospitals and research centers.

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Session Classification: Methods for production of novel radioisotopes for theranostics

Track Classification: Methods for production of novel radioisotopes theranostics

Contribution ID: **11** Type: **Oral**

The MEDICIS facility –first operation year, current and future plans

Friday 3 May 2019 09:30 (20 minutes)

The MEDICIS facility mission is to become a European leading facility and CERN's main producer of non-conventional medical isotopes for research in cancer treatment and diagnosis. Current isotopes produced at MEDICIS include: 149Tb, 152Tb, 155Tb, 169Er and 165Tm and developments are being made to extend this list to 47Sc, 44Sc, 67Cu and 225Ac. The isotopes are either produced with CERN's 1.4 GeV proton beam (Tb, Tm, Sc, Ac, Cu) or they are provided as non-separated external sources from MEDICIS partners cyclotrons (Er, Tb, Sc).

MEDICIS first operation with radioactive beam started in May 2018 (after a short radioactive commissioning in December 2017). During 2018, more than 20 irradiations have been performed in more than 10 targets for machine development and experiments previously approved by the MEDICIS Collaboration board. Progress was achieved at a steady pace reaching the proposed milestones and isotope release efficiency goals successfully.

This year, a technical stop has been issued to maintain and upgrade the facility with radiochemistry capability and laser ionization (MELISSA), which is expected more than 10-fold in collected activities for Tb and Er. In April 2019 the facility will resume operation with external sources since CERN's protons are only available in 2021 (long shutdown).

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Session Classification: Accelerator techniques for medical isotope production

Track Classification: Accelerator techniques for medical isotope production

Contribution ID: **12** Type: **Oral**

Quantified nuclear medicine imaging of theranostic 155Tb

Wednesday 1 May 2019 10:00 (20 minutes)

There has been increasing interest in four radioisotopes of terbium with the potential for use in nuclear medicine: 161Tb emits therapeutic beta and Auger particles; 155Tb emits gamma-rays suited to Single-Photon Emission Computed Tomography (SPECT); 152Tb emits positrons suitable for Positron Emission Tomography (PET); and 149Tb emits alpha particles suitable for therapy. Their identical radiochemistry means they can be used as a theranostic set, combining therapy and diagnostic imaging with a single pharmaceutical. This allows for more personalised therapy, as more accurate patient dosimetry can be achieved.

This work focusses on the diagnostic isotope 155Tb. Samples of 155Tb were produced and collected at CERN-ISOLDE and MEDICIS and were sent to the UK National Physical Laboratory for new primary activity standard measurements. These primary standards permitted traceable activity measurements, which were applied to imaging conducted at The Christie NHS Foundation Trust. This provided the foundation for the first quantitative SPECT imaging of 155Tb.

Solutions of 155Tb were used to perform SPECT studies on a clinical scanner at The Christie NHS Foundation Trust, using energy windows centred on the 45, 87 and 105 keV gamma emissions. Validated Monte Carlo simulations of the full SPECT acquisition were performed to optimise the scatter correction for each window. Imaging measurements were used to compare the activity recovery given by each energy window, to determine the best imaging parameters for clinical quantitative 155Tb SPECT.

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Session Classification: Ovarian cancer (PARTII)

Track Classification: Preclinical research and development of new radiopharmaceuticals

Contribution ID: **13** Type: **MEDICIS-Promed ESRs**

Time-of-Flight study of molecular beams extracted from the ISOLDE RFQ cooler and buncher

Friday 3 May 2019 10:10 (20 minutes)

Molecular beams injected into the Radio-Frequency Quadrupole cooler and buncher (RFQcb), ISCOOL [1], at ISOLDE [2] have been studied under varying conditions. The extracted fragments were detected using the new Time-of-Flight (ToF) detector [3] placed approximately 10 meters downstream the extraction point of the RFQcb. When a beam of molecules is injected into the RFQcb and interacts with the buffer gas, collision-induced dissociation processes may occur. The process of molecular dissociation is of interest within medical applications, for example in CERN-MEDICIS and the MEDICIS-Promed project, where ^{11}C is studied as a possible treatment ion for hadron therapy [4]. In this case, carbon is extracted from the target material as carbon monoxide [5] since the molecule is more volatile than the atom. The objective of this work is to investigate if molecular dissociation occur inside the RFQcb when injecting ion beams of CO^+ and N_2^+. Two different buffer gases were used in the tests (pure helium or a mixture of helium and neon) and the radio-frequency field of the RFQcb was varied as the molecules, along with the dissociation fragments, were extracted from ISCOOL and detected using the ToF detector. The result of this work shows that the rates for molecular dissociation within ISCOOL were very small for both CO^+ and N_2^+, with the largest rates found for CO^+.

References
[1] C. Babcock et al., Nucl. Instrum. Meth. Phys. Res. B 317 (2013) 484–487.
[2] R. Catherall et al., J. Phys. G: Nucl. Part. Phys. 44 (9) (2017) 094002.
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Acknowledgement
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Session Classification: Accelerator techniques for medical isotope production

Contribution ID: **14** Type: **Poster**

POLYAZA-MACROCYCLES WITH HANGING SULFIDE SIDE-ARMS: NOVEL POTENTIAL CHELATORS FOR 111Ag

Thursday 2 May 2019 17:20 (6 minutes)

ISOLPHARM-Ag is a branch of the SPES project (Selective Production of Exotic Species) aimed at the production of carrier free 111Ag for nuclear medicine application at INFN-LNL (Istituto Nazionale di Fisica Nucleare - Laboratori Nazionali di Legnaro). [1, 2]
Among all the radionuclides that will be produced by the future ISOL facility (Isotope Separation On Line), 111Ag is regarded as a very promising radionuclide for cancer therapy, thanks to its decay properties: it is a β⊠ emitter with a medium half-life (7.45 days), a convenient energy (360 keV) and medium tissue penetration. The decay of 111Ag also produces low energy ɣ rays (245 (1.24%) and 342 (6.7%) keV), which allow simultaneous therapy and in vivo monitoring of the delivered dose via SPECT. [3]
The application of 111Ag in radiopharmaceuticals is possible through the coordination of the radioisotope to a bifunctional chelator (BFC) conjugated to a targeting molecule that selectively binds over-expressed receptors on tumor cells. The choice of the BFC is a fundamental part of the design of target-specific radiopharmaceuticals since the chelator must guarantee high thermodynamic stability and kinetic inertia in physiological conditions to avoid the radioisotope release in vivo. The development of novel BFC for Ag (I) is demanding and very challenging because the aforementioned requirements for BFC are still an unsatisfied need in the case of silver.
In the present work, tetraazacyclododecane scaffolds with sulfur donating arms were designed and synthesized as novel possible BFCs for Ag(I). [4] Furthermore, their acid-base properties were investigated as well as their coordination chemistry in aqueous solution by potentiometric and spectroscopic techniques to obtain a prediction of the in vivo behaviour of the metal-ligand systems. The obtained high thermodynamic stability makes these ligands promising chelating agents for the future development of silver-based radiopharmaceuticals.

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4. Maecke et al., Angew Chem.; 1997, 36, 24: 2786-2787.

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Session Classification: Posters Session

Track Classification: Preclinical research and development of new radiopharmaceuticals

Contribution ID: **15** Type: **MEDICIS-Promed ESRs**

First step for PET aided hadrontherapy.

Thursday 2 May 2019 10:10 (20 minutes)

The benefit of hadrontherapy compared to conventional radiation therapy is the higher ratio between dose to tumor and dose to normal tissue. However, regarding depth dose distribution between charged particles and photons, effect of range uncertainty is more significant with charged particles. Thus, importance of understanding range uncertainty arises. There are many sources of uncertainty, such as beam range, CT –water equivalent penetration length conversion uncertainty, relative biological effectiveness (RBE) change, anatomical change of patient, etc. During hadrontherapy, positron emitting 11C and 15O are produced and the beam range can be measured with positron emission tomography (PET). However, 11C gives more PET signals than 12C and would give better analysis of beam range. 11C, which is used for PET imaging, is expected to have similar treatment characteristics compared to 12C. FLUKA simulation was done such that 11C beam energy will have 2mm intervals in water penetration depth range from 3 cm to 28cm. Additionally, one of the 12C Spread Out Bragg Peak (SOBP) plan was converted to 11C SOBP plan, and both physical and RBE weighted doses of this converted plan were calculated based on LEM I. The SOBP result shows the possibility to predict 11C RBE weighted dose based on LEM I. Additionally, we have summarized the calculations needed for developing a 11C ions based commercial treatment planning system (TPS), for both absorbed and biological dose, and found that the level of complexity is similar to 12C ions in terms of TPS implementation and database generation.

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Session Classification: Radioisotope beams in hadron therapy

Track Classification: Radioisotope beams in hadron therapy

Contribution ID: **16** Type: **MEDICIS-Promed ESRs**

Clickable Radioimmunoconjugates: Theranostic Agents for TEM1 Pre-Targeting

Tuesday 30 April 2019 16:00 (20 minutes)

The TEM1/endosialin is a receptor over-expressed in several human solid tumours and silenced in normal adult tissues, representing a suitable and potentially safe target for radioimmunotherapy of sarcoma.1,2 Taking advantage of the very fast in vivo kinetic of the click reaction between tetrazines (Tz) and trans-cyclooctene (TCO), we intent to explore a pre-targeting approach for the *in-vivo* recognition of TEM1 using a single chain fusion protein (scFv-Fc) that recognizes both the human and the murine TEM1. The optimization of the design of the final conjugates, using commercially available radioisotopes like 111In and 125I, included:

i) Evaluation of radioiodinated scFv-Fc's directed towards TEM1

A panel of TEM1 scFv-Fc's were labelled with 125I and evaluated to select the best candidate for pre-clinical studies. The evaluation comprised the *in-vitro* studies of their uptake and internalization in human and murine TEM1-positive tumor cells, the assessment of their binding affinity and quantification of specific versus nonspecific binding. Once the best scFv-Fc identified, biodistribution studies in tumor bearing mice were also performed.

ii) Evaluation of 111In-labelled tetrazine-containing macrocyclic chelators

A small family of macrocyclic chelators carrying tetrazine groups were synthesized and used to obtain clickable 111In-radiocomplexes for further targeting of TEM1 based on *in-vivo* click chemistry strategies. Their stability and pharmacokinetics were studied in normal mice.

The developed research work is expected to provide important insights for the development of TEM1-targeted radiopharmaceuticals, for which few studies have been reported so far but that can contribute to the rise of a more personalized approach in cancer treatment.

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Session Classification: Ovarian cancer (PART I)

Track Classification: Preclinical research and development of new radiopharmaceuticals

Contribution ID: **17** Type: **MEDICIS-Promed ESRs**

A novel dual-imaging probe for the detection of progressive ovarian cancer

Wednesday 1 May 2019 11:15 (20 minutes)

Ovarian cancer is the fifth most lethal cancer among women. Early detection is highly warranted in order to optimize therapy, and improve the overall prognosis. However, technologies for early detection of ovarian cancer are currently lacking.
Here, we describe the development of a new dual imaging probe for ovarian cancer. This imaging probe is based on folate as targeting moiety. Our probe is labeled with radioisotopes for positron emission tomography (PET), and a fluorescent dye for optical imaging. The radioisotope that we chose is gallium-68, which is coordinated using DOTA chelators. The dye that we chose is Cy5, which emits in the near-infrared (NIR) range, and which is advantageous for in vivo imaging due to the better signal-to-noise ratio.
To test our probe in vitro, we utilize the human ovarian cancer cell lines ES-2, which has a low expression of the folate receptor, and SKOV3, which has a high folate receptor expression. Moreover, ES-2 cells were stably transfecting it with a construct expressing the human folate receptor in a tetracycline-dependent manner.
The main advantage of this new dual imaging probe is the possibility to use each modality on its own, as well as in combination, which is anticipated to offer improved detection of ovarian cancer.

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Session Classification: Ovarian cancer (PARTII)

Track Classification: Preclinical research and development of new radiopharmaceuticals

Contribution ID: **18** Type: **MEDICIS-Promed ESRs**

Comparison between microPET-based and biodistribution-based dosimetry of a 152Tb-labelled antibody in tumour-bearing mice

Tuesday 30 April 2019 14:30 (20 minutes)

Aim. To assess the feasibility of mouse-specific, microPET- based dosimetry of an antibody labelled with 152Tb. Image-based absorbed dose estimates were compared with dosimetry results obtained from the extrapolation to 152Tb of a classical biodistribution experiment using the same antibody fragment labelled with 111In.
Methods. The scFv78-Fc fusion protein targeting TEM-1 was conjugated with the chelator CHX-DTPA, and then labelled with either 152Tb or 111In. Micro-PET images of four female mice bearing sarcoma were acquired 4, 24 and 48 h after the i.v injection of 152Tb-CHX-DTPA-scFv78-Fc. After count/activity camera calibration, time-integrated activity coefficients (TIACs) were obtained for the following compartments: heart content, lungs, liver, kidneys, intestines, tumor and whole body. For comparison, radiation dose estimates of 152Tb-CHX-DTPA-ScFv78-Fc were extrapolated from mice dissected 4, 24, 48 and 96 h after the injection of 111In-CHX-DTPA-scFv78-Fc (3–5 mice per group). Imaging-derived and biodistribution-derived organ TIACs were used as input in the 25 g mouse model of OLINDA2. Tumor absorbed doses were obtained using the OLINDA2 sphere model. Finally, the relative percent difference (RD%) between absorbed doses obtained from imaging and biodistribution were calculated.
Results: RD% between microPET-based dosimetry and biodistribution-based dose extrapolations were +12, −14 and +17 for the liver, the kidneys and the tumors, respectively. Compared to biodistribution, the imaging method significantly overestimates the absorbed doses to the heart and the lungs.
Conclusions: MicroPET-based dosimetry of 152Tb is feasible, and the comparison with organ harvesting resulted in acceptable dose discrepancies for body districts that can be segmented on CT.

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Presenter: Dr CICONE, Francesco

Session Classification: Ovarian cancer (PART I)

Track Classification: Preclinical research and development of new radiopharmaceuticals

Contribution ID: **19** Type: **Poster**

Production of Ac-225 at CERN-ISOLDE and prospects for CERN-MEDICIS

Thursday 2 May 2019 17:46 (6 minutes)

Over the last few years, several studies have proven the effect of targeted alpha therapy using Ac-225 and Bi-213 [1, 2, 3]. One of the crucial bottlenecks in upscaling these studies and moving to clinical trials is the availability of these isotopes. The current production methods cannot provide sufficient quantities of Ac-225 or its daughter Bi-213. Furthermore, some of these production techniques result in batches of Ac-225 with a lot of impurities which require advanced radiochemical separation techniques to be purified, and with limited specific activity (e.g. contamination from Ac-227). Therefore, the ISOL-technique is under investigation as a new production route for these isotopes, as it could provide both chemical and isotopic separation, to reach high purity and high specific activity. Recently, the first online radioactive Ac+ beams at CERN-ISOLDE have been produced with the Resonant Ionization Laser Ion Source (RILIS) [4]. Full characterization of the Ac+ beam has been performed.
Recent results on the beam production of Ac isotopes will be presented, focusing on Ac-225 and Bi-213 as medical radioisotopes. These measurements can be extrapolated to the CERN-MEDICIS facility as an indication of the batches that can be collected for medical research in the near future.

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[4] V.N. Fedosseev et al. Ion beam production and study of radioactive isotopes with the laser ion source at ISOLDE. Journal of Physics G 44:084006, July 2017.

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Presenter: Mr DOCKX, Kristof (KU Leuven (BE))

Session Classification: Posters Session

Track Classification: Methods for production of novel radioisotopes theranostics

Contribution ID: **20** Type: **MEDICIS-Promed ESRs**

Oxidation of uranium carbide targets at ISOLDE and radiochemistry infrastructures for the production of medical isotopes at MEDICIS

Saturday 4 May 2019 10:30 (20 minutes)

The Isotope Separator On-Line DEvice ISOLDE is a facility dedicated to the production of radioactive ion beams at CERN. With over 50 years of experience, ISOLDE is able to deliver more than 1000 different isotopes of 74 chemical elements used for experiments in various fields such as nuclear and atomic physics, material science and nuclear medicine.
Radionuclides are produced by irradiating thick targets made of refractory materials such as highly porous depleted uranium carbide with excess graphite (UCx). The microstructure of uranium-based materials was engineered to increase the isotope release efficiency. Due to their pyrophoric nature, UCx materials require extreme care in all handling procedures and are unsuitable in this form for long-term storage. Investments in new equipment have been made to investigate a safe and efficient process for the conversion of UCx into oxide. The procedures developed here could be transferred to other facilities worldwide, as a new waste disposal channel.
In the frame of the MEDICIS-Promed fellowship programme, infrastructures have been put in place for the safe collection, radiochemical process developments, packaging, and shipping of radioisotopes. The laboratory is expected to commission its radiochemical operations in spring 2019.
In this contribution, the oxidation kinetics of the next generation UCx target materials which depends highly on the starting microstructure will be discussed, and a layout of the MEDICIS laboratory will be presented.
This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No. 642889.

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Session Classification: Devices and Engineering for Radioisotopes Handling

Track Classification: Devices and Engineering for Radioisotope Handling

Contribution ID: **21** Type: **MEDICIS-Promed ESRs**

Production of intense mass separated ^{11}C beams for PET-aided hadron therapy

Thursday 2 May 2019 11:00 (20 minutes)

Within the Marie Skłodowska-Curie innovative training network MEDICIS-Promed, a ^{11}C based carbon therapy protocol is being developed. Replacing the stable ^{12}C beam with its radioactive isotope ^{11}C, therapy can be combined with on-line PET-imaging. The PET-images that are recorded simultaneous with the treatment, represent a 3D dose distribution map of the irradiation field, and thus, provide an on-line dose verification. One challenge for the realization of such a treatment protocol is the production of the intense radioactive ^{11}C ion beam. Effective treatments require beam intensities of $4 \cdot 10^8$ ions/spill delivered to the patient. Radioactive ion beam (RIB) production is a multiple step system with inevitable beam losses across the process chain. Consequently, optimization of the individual steps is required, to meet the desired beam characteristics for effective hadron therapy treatments. We will present a ^{11}C beam production system, based on the Isotope Separation On-Line (ISOL) technique that is currently being developed within MEDICIS-Promed. Key component for such an ISOL-type production system is the target-ion source unit. We developed a solid boron nitride (BN) target, manufactured by spark plasma sintering to improve the targets microstructure for fast diffusion and effusion times, aiming to enhance the isotope release properties. The target has been characterized and tested in various ways in respect of its feasibility and applicability in typical ISOL-type operational conditions. We will present and discuss results, such as temperature boundaries, operational limitations in oxidizing atmospheres and ^{11}C release efficiencies.

Acknowledgments
The authors would like to thank the MEDICIS-Promed ITN for the framework in which this work has been carried out. Furthermore, we want to express our gratitude to the collaborators and their corresponding facilities for the support during these studies. This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No. 642889. Further funding was received from Fonds Wetenschappelijk Onderzoek - Vlaanderen (Belgium) and from a KU Leuven START grant.

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Session Classification: Radioisotope beams in hadron therapy

Track Classification: Radioisotope beams in hadron therapy

Contribution ID: **22** Type: **MEDICIS-Promed ESRs**

Automated Laser Ion Source System for Production of Medical Radioisotopes

Friday 3 May 2019 14:50 (20 minutes)

The CERN-MEDICIS facility is aimed for the production of innovative medical radioisotopes. The dedicated electromagnetic mass separator allows to selectively extract a desired isotope from all others of the same element, what is inaccessible for chemical separation methods. It is foreseen to handle working materials, which are either irradiated at the CERN-ISOLDE target station or provided from external institutions. Radionuclides extracted using thermal ionization are accompanied with high contaminations of radioactive or stable isobars. Moreover, surface ion sources with a limited selectivity exhibits a rather low extraction efficiency for the isotopes of interest, making the total production process economically not profitable.

To provide both, selective and efficient ionization, a laser ion source is implemented at MEDICIS. The high elemental selectivity is achieved via multi-step laser resonance ionization, which in combination with mass separation allows to collect a mono-isotopic ion beam of the desired radionuclide. Therefore, for each element of interest, i.e. lutetium, terbium and erbium, a characterization of an optimum resonance ionization scheme was accomplished for two-step photoexcitation, representing a highly efficient ionization process suitable for large-scale production of radioisotopes.

The laser ion source system is based on Titanium:sapphire (Ti:Sa) lasers of Mainz design. As all characterized steps of ionization schemes for these lanthanides lay in the second harmonic emission range of Ti:Sa, an automated grating-tuned Ti:Sa laser with intra-cavity frequency doubling was developed. Two lasers of this design allow to rapidly switch between different ionization schemes, providing a possibility to extract several nuclides of interest from one source material or to make an express analysis of contaminants during the collection process.

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Session Classification: Devices and Engineering for Radioisotopes Handling

Track Classification: Accelerator techniques for medical isotope production

Contribution ID: **23** Type: **MEDICIS-Promed ESRs**

Role of THIK-1 in glioblastoma multiforme progression

Tuesday 30 April 2019 11:00 (20 minutes)

Glioblastoma multiforme (GBM) [World Health Organization (WHO) grade IV astrocytoma] is the most malignant form of brain tumors, carrying a poor prognosis and high rate of recurrence. During the course of the disease, microglia and brain macrophages are both recruited by the tumor microenvironment via the release of several chemoattractants and contribute considerably in several aspects of glioma development and therapeutic resistance. Microglia are the resident mononuclear macrophages of the CNS and are heterogeneously distributed in non-overlapping regions throughout the brain and spinal cord. In the healthy adult CNS, microglia exhibit a 'resting'phenotype, characterized by small cellular bodies from which thin ramified processes are extended. The transition from the 'resting'to the 'activated'state under pathological conditions, such as inflammation or disease, implies not only functional but also morphological alterations. Advances in our understanding of microglial physiology and in our understanding of the complex interactions between microglia and tumor cells in GBM can elucidate their role in glioma progression and indicate potentially interesting druggable targets. Here, we plan on investigating the two-pore domain potassium channel THIK-1 (Tandem-pore domain Halothane-Inhibited K+ channel; Knck13) as such a target. THIK-1 is expressed almost exclusively by microglia in the brain, and plays a key role in regulating microglia ramification, processes baseline motility and release of interleukin-1ß. Considering that the standard treatment for GBM is surgery followed by adjuvant radiotherapy and chemotherapy, we aim to look at the curative perspectives of THIK-1 under the scope of brachytherapy, which is a form of internal radiation using stereotactic techniques.

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Session Classification: Lessons learned from recent targeted radiotherapy treatments

Track Classification: Preclinical research and development of new radiopharmaceuticals

Contribution ID: **24** Type: **Oral**

Characterization and optimization of a versatile laser and electron-impact ion source for radioactive ion beam production at ISOLDE and MEDICIS

Friday 3 May 2019 11:50 (20 minutes)

The CERN-MEDICIS facility delivered its first radioactive batch for research in May 2018. Based on the ISOL method for radioactive ion beam production, MEDICIS relies on the CERN PS-Booster for target irradiation, but, unlike ISOLDE, it is not coupled 'on-line'to an isotope extraction system. Instead, targets are typically irradiated (while cold) at the ISOLDE proton beam dump location and then rapidly transported to MEDICIS for isotope extraction. This key difference presents a unique challenge in terms of ion source operation: ISOLDE targets are outgassed before use and the isotope release and in-target production occurs concurrently. Conversely, for MEDICIS, production occurs first and it is the isotope extraction and target outgassing that occurs simultaneously. Furthermore, to preserve the sample and maximize the specific activity, the sample extraction should occur in a fraction of the time that was required for its production.

In this presentation, a newly developed VADLIS with tunable extraction voltage is introduced. This ion source is capable of efficient electron-impact (VADIS) or laser ionization (RILIS). A factor of >2 increase of the efficiency in RILIS-mode has been demonstrated for gallium (off-line) and magnesium, molybdenum and mercury ion beams (on-line). In this work, it will be shown how this modified VADLIS could offer a significant ion capacity advantage (μA vs nA) with respect to the hot-cavity RILIS.

We will also show how particle-in cell software have been used, along with experimental data, to gain a deeper insight into the VADIS performance. The effect of the magnetic field on the electron, ion and electrical potential field distributions inside the anode cavity will be discussed. The simulations provide for the first time a plausible explanation of some experimental observations which imply that the VADIS is not simply an electron-impact ion source, and that the interplay of ion and electron dynamics in the plasma must be considered.

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Session Classification: Accelerator techniques for medical isotope production

Track Classification: Accelerator techniques for medical isotope production

Contribution ID: **25** Type: **Oral**

TARGETS DEVELOPMENT AT CERN: MEDICIS LARGE CONTAINER

Saturday 4 May 2019 09:30 (20 minutes)

CERN-MEDICIS is a CERN facility dedicated to the production of isotopes for medical research in a very pure form. Such radioisotopes are produced in ISOLDE target production area by taking advantage of the 1.4Gev proton beam with low energy degradation which is still available after ISOLDE target interaction before reaching the dump. MEDICIS targets are designed to be larger than ISOLDE standard targets in order to be able to account for proton beam scattering after the ISOLDE target. After the irradiation step, the target units are moved to the MEDICIS front-end, where they are heated to temperatures higher than 2000℃. One of the main goals of the target development is to have a temperature homogeneity in all over the surface of the container and ion source and transfer line, avoiding the cold spots where the isotopes can condense and are thus lost during the extraction process.
For the ISOLDE targets, to achieve that, a special thermal insulation is proposed to be placed around the container, transfer line and ion source. To this moment, in ISOLDE targets (small container), thermal screens from Ta, W and Mo are used as a thermal insulation. This solution has proved to be unstable at high temperatures as the efficiency decreases during the heating cycles. In order to improve the thermal insulation of the targets, new industrial alternatives (rigid/flexible carbon foam or ZrO2 advanced ceramic insulation etc.) are studied and aimed to give a more stable-efficient result over time.
The MEDICIS target 673M (large Ta container with rigid carbon foam as thermal insulation and with Ta-rolls & graphite spacers inside the container) has been designed, built and tested online (target up to 1000 A and ion source up to 270 A) giving us useful results for the future research and development of the targets.

Keywords: CERN, MEDICIS, Targets, Development, Isotopes production

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Session Classification: Devices and Engineering for Radioisotopes Handling

Track Classification: Devices and Engineering for Radioisotope Handling

Contribution ID: **26** Type: **Oral**

Technical Design Report for a Carbon-11 Treatment Facility

Thursday 2 May 2019 09:50 (20 minutes)

The particle therapy is a major contributor to the medical application of accelerator technology and may yet be improved by the use of radioisotopes as beam species, which would allow a better traceability of the applied dose.
The Medicis-Promed network leads an initiative to study the possible technical solutions for the implementation of Carbon-11 radioisotopes in an accelerator-based particle therapy center. The result of this study is a Technical Design Report (TDR) for a Carbon-11 Treatment Facility.
The TDR starts from summarizing the medical advantages of using Carbon-11, it elaborates the required facility layout and performance, and it proposes upgrade options for existing particle therapy centers.
We present here the TDR content and conclusions, and we discuss the next steps.

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Presenter: PENESCU, Liviu (Abstract Landscapes)

Session Classification: Radioisotope beams in hadron therapy

Track Classification: Radioisotope beams in hadron therapy

Contribution ID: **27** Type: **Poster**

Orthogonal Click Chemistry for Synthesis of Dual-targeting Agents Towards αvβ3 Integrin and Folate Receptors for Molecular Imaging

Thursday 2 May 2019 17:26 (6 minutes)

Folate-based radiopharmaceuticals were applied for targeting the folate receptor (FR) positive malignant tissue while cyclic Arg-Gly-Asp (c(RGD)) peptides were used to target αvβ3 integrin which is overexpressed during tumor angiogenesis. Combination of these two different targeting motifs in one molecule could be utilizable for dual-targeting. Here, we present the introduction of folate and c(RGD) motifs to chelator fusarinine C (FSC) in a "one-pot"employing orthogonal "click" reactions. All heterobivalent compounds were then evaluated for dual-targeting of FR and αvβ3 integrin.

Starting with [Fe]FSC functionalized with alkyne and maleimide, thiol-maleimide click reaction with c(RGDfK)-(PEG)4-SH was performed, followed by Cu(I) catalyzed azide-alkyne cycloaddition (CuAAC) with folate-(PEG)3-N3 and subsequent iron removal. Stability, binding affinity (IC50), distribution coefficient (logD) and protein binding were investigated. Internalization assays were performed in FR-positive cancer cells (KB) and human melanoma αvβ3-positive cells (M21).

Orthogonal click reactions were successfully applied for a one-pot synthesis of heterobivalent conjugates. Products were obtained in moderate yields and could be radiolabeled with [68Ga] in quantitative radiochemical yields. All conjugates revealed high hydrophilicity (logD = -3.46 to -3.83) and low protein binding. Dimeric c(RGDfK) and dimeric (folate) conjugates showed higher specific uptake in vitro than monomeric counterparts. Biodistribution studies and microPET/CT imaging in tumor-bearing mice are ongoing.

This study shows the possibility of applying orthogonal click reactions for introducing different targeting vectors to one chelator scaffold in a one-pot synthesis with high selectivity and without purification in each step. This finding may stimulate new strategies for designing the dual-targeting agents for diagnostic, therapeutic, and theranostic applications.

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Session Classification: Posters Session

Track Classification: Preclinical research and development of new radiopharmaceuticals

Contribution ID: **28** Type: **Oral**

Extraction chromatography method for the separation of 155Tb from radionuclide impurities for primary standardisation, nuclear data measurements and SPECT imaging

Thursday 2 May 2019 15:10 (20 minutes)

Radioisotopes of terbium (149, 152, 155, 161Tb) have been identified as a potential theranostic quartet for use in nuclear medicine. Any such radiopharmaceutical based on the radioisotopes would be required to have a low (< 0.1 %) level of radionuclidic impurities, therefore it is crucial that chemical separation techniques are developed to ensure these thresholds are met while maintaining a high yield of the terbium radioisotope.
155Tb (t½ = 5.32 d) offers promise as an imaging tracer in single photon emission computed tomography (SPECT), with initial pre-clinical studies indicating excellent image quality even at low doses. The administration of 155Tb prior to a therapeutic terbium isotope would give a theranostic pair with identical chemical properties; this is particularly advantageous as it facilitates the application of personalised medicine.
155Tb prepared by high-energy proton spallation at the CERN ISOLDE and MEDICIS facilities contains radioactive 139Ce16O following on-line mass separation, plus possibly stable zinc and/or gold impurities depending on the employed collection foil. A highly efficient radiochemical purification method has been developed using ion-exchange and extraction chromatography resins in two column separation steps to successfully isolate 155Tb with a chemical recovery of 95 % and an isotopic purity exceeding 99.9%.
155Tb sources collected at CERN and chemically purified at NPL have been used at NPL for activity standards, nuclear data measurements and quantitative SPECT imaging to underpin future clinical use of this radioisotope.

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Presenter: Dr IVANOV, Peter (NPL)

Session Classification: Methods for production of novel radioisotopes for theranostics

Track Classification: Methods for production of novel radioisotopes theranostics

Contribution ID: **29** Type: **Invited**

IBA accelerators for medical radio-isotope production

Friday 3 May 2019 09:00 (30 minutes)

In this contribution, an overview will be given of the different cyclotrons and electron accelerators produced by Ion Beam Application (IBA, Louvain-la-Neuve, Belgium) for radio-isotope production. The 3 main cyclotrons for radio-isotope production are distinguished by their maximum beam energy : the Cyclone KIUBE delivers protons up to 18 MeV, the Cyclone 30(XP) delivers protons from 15 up to 30 MeV, whereas the XP version delivers protons (15-30 MeV), deuterons (8-15 MeV) and alpha beams (30 MeV). Finally, the Cyclone70(XP) delivers protons from 30 up to 70 MeV and the XP version adds 35 MeV deuteron and 70 MeV alpha beams. The main components of the cyclotrons and their technical specifications will be described, with emphasis on their relevance for the radio-isotope production.
Illustrative examples of radio-isotope production techniques will be given for each cyclotron. In some cases, the economic viability of the production scheme and technique will be discussed.
The electron accelerators by IBA (all of the "rhodotron"-type) are being upgraded at this moment and their prospective use in the radio-isotope production cycle will be discussed and compared to alternative production methods (linear accelerators, nuclear reactors, ...).

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Session Classification: Accelerator techniques for medical isotope production

Track Classification: Accelerator techniques for medical isotope production

Contribution ID: **30** Type: **MEDICIS-Promed ESRs**

Uranium Carbide Target Development

Thursday 2 May 2019 17:00 (10 minutes)

Content
Background: Radioactive ion beams at ISOLDE are produced by the interaction between an intense proton beam with a thick target material [1]. Micrometric UCx-based targets are the current reference at ISOLDE, but a significant increase on the yields of exotic isotopes is expected to be obtained from nanostructured and porous UCx targets.
Key Method: Electrospinning is a top-down technique of making fibers [2]. In this method, a high tension is applied between two electrodes, a needle connected to a syringe and an aluminium collector. A polymer solution is inserted in the syringe and ejected at the tip of the needle, being held by its surface tension and subjected to the high electric field to form a Taylor cone. After discharging, the polymer solution undergoes a bending instability and elongation process, which allows the jet to become thinner, leaving a solidified fiber on the collector.
Experimental Results: uranium precursor nanofibers were prepared by the electrospinning method. The solutions for electrospinning were prepared by dissolving a uranium salt (acetate, acetylacetonate, and formate) and cellulose acetate in glacial acetic acid and 2,4-pentanedione solvents in 2 : 1 ratio. The fibers were heated up to 550 o C in argon atmosphere with a heating rate of 1 o C / min to decompose the polymer. The obtained material was further heat-treated at 1750 o C for 2 h in vacuum to carboreduce the oxide. The final material is composed of small-sized grains, with an average below 10 nm.

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Presenter: Prof. GONÇALVES, António (Professor)

Session Classification: Posters Session

Track Classification: Methods for production of novel radioisotopes theranostics

Contribution ID: **31** Type: **Oral**

Production of actinium-225 at JRC Karlsruhe

Friday 3 May 2019 12:10 (20 minutes)

The targeted treatment of cancerous tumors by alpha-emitting radionuclides has shown remarkable efficacy in recent clinical trials. It is likely that this treatment option will ultimately be applicable to a wide range of cancers and other diseases, subject to the development of specific carrier molecules. Currently Ac-225 is mainly produced from natural ingrowth in existing stocks of Th-229. An anticipated wider application for radiotherapy will require many orders of magnitude more radionuclide than can currently be produced. Consequently, following up on earlier experimental work at JRC, we are pursuing alternative production methods. In particular, the production by irradiation of Ra-226 with medium-energy protons at cyclotrons will be investigated. In this talk, past experience with proton irradiation of Ra-226 at JRC Karlsruhe will be reviewed. In addition, short- and medium-term plans for future work in this direction will be presented.

Authors: Dr KELLERBAUER, Alban (European Commission, Joint Research Center (JRC)); Dr BRUCHERTSEIFER, Frank (European Commission); Dr MALMBECK, Rikard (European Commission); Dr MORGENSTERN, Alfred (European Commission)

Presenter: Dr KELLERBAUER, Alban (European Commission, Joint Research Center (JRC))

Session Classification: Accelerator techniques for medical isotope production

Track Classification: Devices and Engineering for Radioisotope Handling

Contribution ID: **32** Type: **Poster**

Clicklabe Bombesin Antagonists for Prostate Cancer Theranostics

Thursday 2 May 2019 17:32 (6 minutes)

Our goal is to contribute for the development of new strategies for prostate cancer theranostics, based on bombesin (BBN) analogues with very high affinity and specificity for the GRP receptor (GRPr) and on a multistep pretargeting strategy. To achieve this goal, we have opted by in vivo inverse-electron demand Diels-Alder (IEDDA) reactions between BBN antagonists carrying a trans-cyclooctene (TCO) bioorthogonal reactive group and recognizing the GRPr that is overexpressed at the surface of tumor cells and clickable tetrazine-containing radiocomplexes. We have hypothesized that the prior administration of a non-radioactive antagonist, followed by the injection of a clickable radioactive complex with optimized pharmacokinetics, can be an efficient alternative to spare the kidneys from unwanted radiation effects, which often represent an obstacle in Peptide Receptor Radionuclide Therapy (PRRT).
In this communication, we will report on the radiosynthesis, biodistribution, pharmacokinetics and in vitro/in vivo stability of a small family of tetrazine-containing 111In-DOTA and 111In-DOTAGA complexes, as well as on their use for the in vitro labeling of a BBN antagonist carrying a TCO moiety linked to the peptide through different linkers. Cellular uptake studies of the resulting radioconjugates in human prostate cancer PC3 cells will be also presented, including blockade experiments with cold BBN analogues. These studies are expected to identify the best-performing clickable DOTA or DOTAGA chelator and BBN antagonist for further in vivo evaluation within the pretargeting strategy and using 177Lu as a trivalent therapeutic radiometal suitable for PRRT.

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Presenter: Dr PAULO, Antonio (Centro de Ciências e Tecnologias Nucleares, Instituto Superior Técnico, Universidade de Lisboa)

Session Classification: Posters Session

Track Classification: Preclinical research and development of new radiopharmaceuticals

Contribution ID: **33** Type: **Oral**

Laser-enhanced aerodynamic isotope separation for making medical radio-isotopes

Thursday 2 May 2019 16:20 (20 minutes)

Abstract: Aerodynamic isotope separation in a free gas jet is enhanced by 2 orders of magnitude by laser-induced isotopically selective condensation. The method is quite generally applicable and is demonstrated for separating S, Br and Si isotopes. The separation of Mo isotopes is discussed in detail for the production of 100Mo for the 100Mo(p,2n)99Mo reaction and the production of 99mTc for SPECT. Other possibilities including the enrichment of 44Ca from 2% natural abundance, to more than 90%, for PET scanning via 44Ca(p,n)44Sc are discussed, where β+ of 44Sc has a half life of 4h.

Authors: MONOT, R. (EPFL/Physics); Prof. HUBERT , Vandenbergh (EPFL)

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Presenter: Prof. HUBERT , Vandenbergh (EPFL)

Session Classification: Methods for production of novel radioisotopes for theranostics

Track Classification: Methods for production of novel radioisotopes theranostics

Contribution ID: **34** Type: **Poster**

Multifunctional Gold Nanoparticles as Nanoseeds for Targeted Chemoradiotherapy of Glioblastoma Multiforme (GBM)

Thursday 2 May 2019 17:40 (6 minutes)

Gold nanoparticles (AuNPs) can play a pivotal role in the design of new theranostic tools for cancer treatment. This is due to their appealing properties for medical application such as, biocompatibility, easy functionalization with molecular vectors and good biological half-life. Additionally, AuNPs can also be explored as multifunctional platforms for targeted-delivery of radionuclides and chemotherapeutic drugs. Herein, we will report on the synthesis, characterization and biological evaluation of AuNPs decorated with Pt(IV) prodrugs, a DOTA-based chelator for coordination of medically relevant trivalent metals (e.g. 67Ga, 111In, 177Lu)1 and a bioactive peptide (bombesin (BBN) analogue or substance P (SP) derivative) that recognizes the gastrin releasing peptide receptor (GRPr) or the NK1 receptor overexpressed in GBM cells. Some of the SP-containing AuNPs were also labeled with 125I profiting from the presence of a Tyr residue in the peptide sequence. The studies included the assessment of cellular uptake and cytotoxic activity in GBM U87 cells for the designed multifunctional nanoparticles, aiming to obtain a first insight on their suitability for targeted chemoradiotherapy of glioblastoma.

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Session Classification: Posters Session

Track Classification: Preclinical research and development of new radiopharmaceuticals

Contribution ID: **35** Type: **Oral**

γ-MRI: new imaging technology with hyperpolarised radiotracers

Saturday 4 May 2019 10:10 (20 minutes)

Our project is devoted to a new medical imaging modality based on a revolutionary technology combining the sensitivity of γ detection and the spatial resolution and flexibility of MRI. This modality, the so-called γ-MRI, goes beyond the present technological paradigms in molecular imaging. It is not just a hybrid approach joining two separate modalities into one complex machine (like for PET-MRI machines), but a single new modality, simultaneously achieving the high spatial resolution of MRI and the high-sensitivity of SPECT in faster scan times.

The key innovation in this new approach is the hyperpolarization of radio-elements with lasers. Since this process does not require ultra-high MRI magnetic fields or fast coincidence detection of gamma rays as in PET, γ-MRI can be performed using machines that are less complex and less expensive than the present state-of-the-art devices, especially hybrid ones. This disruptive approach of a more accurate and widely available molecular imaging technology will open new avenues for patient care and for the medical imaging market.

In this contribution I will talk about the principles of γ-MRI, our results so far and about the plans for the coming months.

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Presenter: PALLADA, Lina (CERN)

Session Classification: Devices and Engineering for Radioisotopes Handling

Track Classification: Devices and Engineering for Radioisotope Handling

Contribution ID: **36** Type: **Poster**

Advanced High Field Superconducting Cyclotron for Medical Isotopes Productions

Thursday 2 May 2019 17:58 (6 minutes)

Radioisotopes are one of the essential cornerstones of modern medicine. They may be used for both diagnostic and therapeutic purposes. Here we present full describtion of a 12 MeV compact high field superconducting cyclotron with a magnetic field 2 times higher than conventional H- cyclotrons that has been developed recently. This cyclotron will be a modern, state of the art design, which, because of the higher magnetic field, is smaller, lower maintenance, lighter weight and lower power consumption than any other machine available. The purpose of this cyclotron is to provide a sustainable supply of the critical Imaging Isotope F-18 and N13, to eliminate the need for supply from other production facilities for small centers. In addition, this cyclotron will be the most advanced version of the most common isotope production cyclotron used world-wide, we plan to commercialize it for international sales.

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Presenter: Dr AYASH, Alrashdi (Director of the National Accelerator Technology center at KACST)

Session Classification: Posters Session

Track Classification: Accelerator techniques for medical isotope production

Contribution ID: **37** Type: **Oral**

Pushing the frontier of medical isotope production at TRIUMF

Friday 3 May 2019 14:30 (20 minutes)

With over five decades of experience in the production of accelerator-based isotopes for science, TRIUMF also ensures that Canada remains on the leading edge of research and development of isotopes applied to nuclear medicine. TRIUMF's medical isotope program is primed to develop alternative tools and methods to meet the growing demand for life-saving isotopes, and advance the design and production of cutting-edge radiopharmaceuticals.

Together with the on-site commercial partner BWXT, formerly Nordion, already now TRIUMF delivers approx. two million patient doses of medical isotopes which are used for imaging and treatment around the world every year. The new Institute for Advanced Medical Isotopes (IAMI) - a multi-institutional research hub and facility focusing on radiopharmaceutical development and advanced isotope development –will serve as a conduit for isotopes produced using not only its own TR-24 cyclotron but also other TRIUMF's accelerators spanning the energies from 13 MeV all the way up to 520 MeV. The Advanced Rare Isotope Laboratory (ARIEL), TRIUMF's flagship project, with its symbiotic medical isotope production target positioned behind the proton ISOL target and state-of-the-the-art isotope handling infrastructure, will produce and develop isotopes for next generation-radionuclide therapies for metastatic cancers. Finally, with its high-energy proton irradiation and ISAC-I facilities, TRIUMF is already uniquely positioned to enable access to mass separated, isotopically pure Ac-225, by delivering batches for animal and clinical trials.

In this contribution, I will highlight the recent technical developments at TRIUMF which enabled the production of some of the most demanded medical isotopes (Ac-225, Tc-99m, etc), and discuss future plans in detail.

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Presenter: GOTTBERG, Alexander (TRIUMF)

Session Classification: Devices and Engineering for Radioisotopes Handling

Track Classification: Devices and Engineering for Radioisotope Handling

Contribution ID: **38** Type: **Oral**

Development of 213Bi-labelled somatostatin analogues: Finding the optimal match between radiometal and chelator

Tuesday 30 April 2019 15:40 (20 minutes)

Objectives: Targeted α-radionuclide therapy is a promising cancer therapy that allows targeted irradiation of primary tumour and its metastases. 213Bi-DOTATATE targeting the somatostatin receptor has been reported to delay growth in small and large volume endocrine tumours in mice (1,2). However, DOTA chelator has poor labelling kinetics and radiochemical purity with Bismuth-213. It appears that 3-p-*C*-NETA and 3-p-*C*-DEPA are the best current alternatives to DOTA for fast radiolabeling kinetics and excellent *in vivo* stability with Bismuth-213. As they are not commercially available, here we present the synthesis of 3-p-*C*-NETA-NO2 and 3-p-*C*-DEPA-NO2 to allow efficient one-step radiolabelling of 213Bi-somatostatin analogues for therapeutic applications (1–4).

Approach: This synthetic route was adapted from Song *et al.* and was inspired by the high efficiency and regiospecificity of the ring opening reaction of aziridinium **9** (3) Treatment of **1** with mild reducing agent BH3-THF afforded **2** (89%) followed by bromination with PBr3 to afford **3** (82%). The bromine was substituted by diethyl acetamidomalonate to provide **4** (60%) followed by hydrolysis to provide the amino acid **5** (52%). This product was esterified to enhance easy reduction to amino alcohol **7** (79%). Iodination of **8** using imidazole and PPh3 followed by intramolecular rearrangement to provide the aziridinium salt **9** (81%) and subsequent regiospecific ring opening of **9** with di-*tert*-butyl-2,2'-(1,4,7-triazonane-1,4-diyl)diacetate and tri-*tert*-butyl-2,2',2"-(1,4,7,10-tetraazacyclododecane-1,4,7-triyl) triacetate will provide 3-p-*C*-NETA-NO2 and 3-p-*C*-DEPA-NO2 respectively.

Conclusion: An already established synthetic scheme has been modified using mild reaction conditions to reach better reaction yields. These bifunctional chelators will be used to obtain a second generation of 213Bi-somatostatin analogues.

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Session Classification: Ovarian cancer (PART I)

Track Classification: Preclinical research and development of new radiopharmaceuticals

Contribution ID: **39** Type: **Oral**

Production of Classical and Theranostics Radionuclides

Saturday 4 May 2019 09:50 (20 minutes)

Trend of producing radionuclides for medical applications for both diagnostic and therapeutic purposes is on the rise. Amongst all medical radioisotopes, Mo-99/Tc-99m is the power hub of all nuclear medicines as it is being used in 80% of the nuclear procedures worldwide. I have been involved in production of Mo-99/Tc-99m Generators for the last twelve years in Pakistan. My institute is providing radioisotopes (Mo-99/Tc-99m generators, I-131, Lu-177 etc.) across all the country and fulfilling the national demands. However due to the shortage of nuclear reactors worldwide (shut down of major reactors after finishing life), shortage of Tc-99m is foreseen in near future. As an alternative of reactor produced classical isotopes, researchers are looking for alternatives. Recently MEDICIS, CERN (a new facility) has started to produce non-conventional / exotic medical radioisotopes, which would eventually be used as diagnostic, therapeutic and theranostics pairs.
Radiochemistry is extremely important for the removal of impurities, which may implant on the foils along with the required isotope. A method for the separation of lanthanides has been developed and tested at MEDICS and will be performed for the radionuclidic purification in future isotope implantations. Column chromatography will be carried out by using strong macroporous cation exchange resin for separating the lanthanides.
Purified Radioisotopes will be shipped to the partner institutes / hospitals for labelling it with some chemical compounds for further research and development.

Author: KHAN, Moazam Mehmood (Pakistan Atomic Energy Commission (PK))

Presenter: KHAN, Moazam Mehmood (Pakistan Atomic Energy Commission (PK))

Session Classification: Devices and Engineering for Radioisotopes Handling

Track Classification: Devices and Engineering for Radioisotope Handling

Contribution ID: **40** Type: **Oral**

Towards the labelling of heat-sensitive biomolecules with terbium radionuclides: Chelation studies of DOTA-NHS with natural Tb and 161Tb

Tuesday 30 April 2019 14:50 (20 minutes)

Introduction: Targeted radionuclide therapy using 161Tb is a promising approach for β- and Auger electron therapy.1 Moreover, the availability of the diagnostic radionuclides 152/155Tb is of interest in a theranostic setting.2-4 Heat-sensitive biomolecules (e.g. antibody fragments, etc.) are increasingly being used as carriers in radiometal-based radiopharmaceuticals. These molecules, however, require mild radiolabeling conditions. In this study, we evaluated DOTA-NHS as potential bifunctional chelator for mild Terbium radiolabelling.

Methods and results: Cold complexation studies were performed with DOTA-NHS (1 eq.) and natural TbCl3 (0.5 eq.) in 0.1M acetate buffer, pH 4.7 at 25 ℃. The complexation was evaluated using high-resolution mass spectrometry (UV-HRMS-ESI-TOF, Bruker Maxis Impact). Complexation was complete after 60 minutes. The hydrolysed complex resonance is observed in the mass spectrum at m/z 561.1081 (theoretical mass calculated for C16H25N4O8 [M+H]+: 561.0999). Radioactive tests were performed using 161Tb that was produced and purified at SCK·CEN (production in the BR-2 reactor: 160Gd(n, ɣ)161Gd -> 161Tb). In these tests, 1.3 MBq 161TbCl3 was added to 0.1, 1, 5 or 10 µM DOTA-NHS in a total volume of 1 mL and incubated at 25 or 40℃. Radiochemical yields were determined at different time points using instant thin layer chromatography (iTLC) eluted with acetonitrile;water (75:25 *v/v*) which were counted in a gamma counter. At 25 ℃, 161Tb was easily complexed using 5 µM of DOTA-NHS resulting in near-quantitative yields (96%) after 60 min. At 40 ℃, near-quantitative yields (97%) were obtained using 1 µM of DOTA-NHS after 60 minutes.

Conclusion: DOTA-NHS is a suitable candidate for future radiolabelling studies of heat-sensitive biomolecules. Other chelators of interest will be evaluated and in vitro and in vivo stability of the Terbium-complexes will be assessed.

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Session Classification: Ovarian cancer (PART I)

Track Classification: Preclinical research and development of new radiopharmaceuticals

Contribution ID: **41** Type: **MEDICIS-Promed ESRs**

A Novel Fluorescent Fatty Acid Probe for Non-invasive Imaging of Tumors in Living Animals

Wednesday 1 May 2019 10:35 (20 minutes)

Molecular imaging affords valuable information about biological processes at the molecular and cellular levels within complex living organisms and can help in earlier diagnostics of various diseases. Optical imaging modalities such as fluorescence imaging play a key role for preclinical research. Furthermore, new fluorescence imaging tools have a potential for clinical translation.
In this work, a fluorescent fatty acid probe was developed and applied as a tool for in vivo tumor imaging (1). Several tumors such as glioma may be dependent on the uptake of extracellular long-chain fatty acids (2-3). Hence, fatty acids can be envisioned as tumor-targeting ligands for the design of tumor imaging probes. Based on this idea, a near-infrared fluorescent fatty acid probe ICG-FA was developed. The probe comprises a long-chain fatty acid conjugated to an analog of a near-infrared dye indocyanine green (ICG). In vitro studies in cells demonstrated that the ICG-FA probe mimics the uptake of natural fatty acids and exhibits significant accumulation in glioma cells compared to that of the free ICG dye. Next, ICG FA was successfully applied for glioma imaging in living mice, where it showed significant tumor targeting. Moreover, in a proof-of-concept study ICG-FA was tested for intraoperative fluorescence image-guided surgery in a canine patient bearing mastocytoma. The probe enabled intraoperative tumor imaging and afforded a real-time visual guidance for a surgeon during the tumor resection. The results suggest that ICG-FA has a potential as a diagnostic agent for intraoperative imaging of gliomas and other tumors with increased fatty acid uptake.

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Contributions and acknowledgements.
1. Dr. Ksenya Shchors (collaboration on glioma imaging in transgenic mouse models).
2. Dr. Arno Roos, Veterinair Verwijscentrum Gouda, Netherlands (collaboration on mastocytoma imaging in dogs).
3. Prof. Elena Goun, LCBIM, EPFL (the presented results belong to the laboratory of Prof. Goun).
4. Prof. Christian Heinis, LPPT, EPFL.

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Presenter: Dr KARATEEV, Grigory (EPFL)

Session Classification: Ovarian cancer (PARTII)

Track Classification: Preclinical research and development of new radiopharmaceuticals

Contribution ID: **42** Type: **Oral**

Determination of precision nuclear decay data for the decay of 153Gd

Tuesday 30 April 2019 11:40 (20 minutes)

In the case of emerging radiopharmaceuticals, the accuracy and precision of the decay data of the radionuclide is crucially important. These data, particularly particle emission probabilities and the half-life, are necessary for the correct quantification of PET images and for dosimetry considerations of practitioners and patient alike.
Often precise nuclear data is determined through a multi-technique measurement campaign in which an absolute standardisation is achieved and decay parameters such as the absolute intensities of gamma-ray emissions and half-life of the nuclide are then measured.
The techniques employed at the National Physical Laboratory to achieve these relevant measurements are described in the context of an improved decay data measurement of ^{153}Gd, with reference to other relevant work. This isotope of gadolinium is used in medicine as a line source for SPECT imaging [2] and has been proposed as a possible in-vitro interstitial rotating shield brachytherapy (I-RSBT) source [3]. In the work presented, the intensities of six gamma-ray emissions in the ^{153}Eu daughter nucleus were measured by HPGe gamma-ray spectroscopy with improved precision than in previous studies. Furthermore, an absolute stardardisation of the source was performed using 4π(LS)-γ digital coincidence counting from which an absolute intensity was derived for the most intense gamma-ray emission, the 97.4 keV de-excitation, of 30.15 (20) per 100 decays [4]. This value is different to the current recommended value by 4 % [5].

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Presenter: SHEARMAN, Robert (National Physical Laboratory)

Session Classification: Lessons learned from recent targeted radiotherapy treatments

Track Classification: Preclinical research and development of new radiopharmaceuticals

Contribution ID: **43** Type: **Poster**

The isolation of terbium isotopes from matrix and isobaric impurities using extraction chromatography techniques

Thursday 2 May 2019 17:52 (6 minutes)

Four terbium isotopes (149Tb, 152Tb, 155Tb, and 161Tb) have been shown to possess physical and chemical properties suitable for all therapeutic and diagnostic applications in nuclear medicine[1]. If a diagnostic (e.g. 155Tb) and therapeutic (e.g. 161Tb) terbium isotope can be combined, then it would give theranostic pair with identical chemical properties. This is a particularly promising characteristic because it will facilitate the development of personalised medicine.

Currently, 149Tb, 152Tb, and 155Tb can only be produced in sufficient quantities for (pre)-clinical studies by the proton-induced spallation reaction on a tantalum target and subsequent mass separation, as is the case at CERN-MEDICIS. Alternative cyclotron-based production has been investigated; primarily, the proton irradiation of enriched gadolinium targets[2,3]. Terbium-161 can be produced by neutron irradiation of an enriched 160Gd target (i.e. 160Gd(n,γ)161Gd -> 161Tb + β-)[4]. The presence of isobaric (e.g. 152Dy in a 152Tb source) and pseudo-isobaric (e.g. 139Ce16O in a 155Tb source) impurities after the mass separation of 149Tb, 152Tb and 155Tb sources necessitates effective radiochemical separation procedures to achieve a high purity and specific activity prior to subsequent (pre)-clinical studies. The isolation of 161Tb from the target material, 160Gd, is also required to achieve the same.

The isolation of terbium from neighbouring lanthanide elements has been studied from nitric acid solutions on LN resin (Triskem International), an extraction chromatography resin based on the liquid extractant, HDEHP. Stable element standards were used for method development and measured by inductively coupled plasma mass spectrometry (ICP-MS) to quantify the quality of the separation. Both batch and column studies were conducted to identify the optimal separation conditions.

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[4]Lehenberger et al. Nucl. Med. Bio. 2011; 38: 917-924

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Session Classification: Posters Session

Track Classification: Methods for production of novel radioisotopes theranostics

Contribution ID: **44** Type: **Invited**

Integrated Remote Handling System Development for MEDICIS

Friday 3 May 2019 14:00 (30 minutes)

The Medicis isotope production process relies on a sequence of remote handling operations involving several different devices which have been integrated to work together. The handling sequence starts with the introduction of a new target in the Medicis facility for irradiation in Isolde and ends with the transfer of the collected isotopes into a fume cupboard in the Medicis laboratory area. The different handling devices making up the whole system include a monorail shuttle system, seven-axis robot, motorised shielding doors, a remotely operated isotope collection point, and a purpose-built shielded isotope transfer system.
The presentation will describe the sequence of operations and the elements making up the integrated handling system along with some of the remote handling design principles applied, development history and lessons learned.

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Session Classification: Devices and Engineering for Radioisotopes Handling

Track Classification: Devices and Engineering for Radioisotope Handling

Contribution ID: **45** Type: **Invited**

Targeting ovarian cancer with anti-MISR2 radiolabelled antibodies

Tuesday 30 April 2019 14:00 (30 minutes)

Ovarian cancer is the most lethal gynecologic malignancy and it has high rate of recurrence justifying the development of new therapeutic tools. Our project aims at developing new radiopharmaceuticals and innovative route of administration to target the small volume residual disease after complete cytoreductive surgery of peritoneal carcinomatosis on preclinical models. We use internalising murine monoclonal antibody (16F12) specific of the anti-müllerian hormone type 2 receptor (AMHR2/MISR2), overexpressed in ovarian cancer and gynaecologic malignancies. Antibodies are radiolabelled with Lutecium-177, a beta minus emitter, and Bismuth-213, an alpha emitter, to perform radioimmunotherapy. Radiolabelled antibodies are injected intraperitoneally but also after Brief IntraPeritoneal RadioImmunoTherapy (BIP-RIT), a technique delivering high activities in the peritoneal cavity for a short time before washing, like Hyperthermic IntraPEritoneal Chemotherapy (HIPEC). We studied biodistribution, dosimetry, toxicity and therapeutic efficacy on various models and combinaison of radionuclides and route of administration. BIP-RIT appears to be always favourable in term of biodistribution and dosimetry (especially for the tumour-over-blood ratio) whatever the radionuclide used. Bismuth-213 is particularly adapted for radioimmunotherapy of small residual tumours, showing therapeutic efficacy with no toxicity. PET/CT imaging of radiolabelled antibodies with Zirconium-89 was performed and may be used as a theranostic tool for (radio)immunotherapy with anti-AMHR2 antibodies. This work may lead to realistic theranostic options in ovarian cancer in clinic.

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Session Classification: Ovarian cancer (PART I)

Track Classification: Preclinical research and development of new radiopharmaceuticals

Contribution ID: **46** Type: **Oral**

Beams of the "lightest radionuclide useful for hadron therapy": neutron beams for BNCT

Thursday 2 May 2019 09:30 (20 minutes)

Formally the neutron is the lightest radionuclide on the bottom left corner of the chart of nuclides. However, in the present context their radioactive decay is not of concern but their interaction with biological tissue. In contrast to the charged particle beams used for hadron therapy, neutrons as neutral particles are not directly ionizing. However, neutron beams can be used for boron neutron capture therapy (BNCT), where the capture of slow neutrons on boron-10 emits an alpha and a lithium-7 ion in an exothermic reaction. These secondary charged particles are highly ionizing and deposit their energy very locally, within less than one cell diameter. Thus the radiobiology of BNCT presents synergies with alpha emitters used in targeted alpha therapy.
We will review the principle and challenges of BNCT and present radiobiological research performed with slow neutron beams at Institut Laue-Langevin in Grenoble.

Authors: PEDROSA, Maria (Institut Laue Langevin); PORRAS, Ignacio (Universidad de Granada); PRAENA, Javier (Universidad de Granada); RUIZ-MAGAÑA, M. José (Universidad de Granada); RUIZ-RUIZ, M. Carmen (Universidad de Granada); FORSYTH, Trevor (Institut Laue Langevin); Dr KÖSTER, Ulli (Institut Laue Langevin)

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Session Classification: Radioisotope beams in hadron therapy

Track Classification: Radioisotope beams in hadron therapy

Contribution ID: **47** Type: **Invited**

Preclinical development with Nanobodies with a focus on ovarian cancer

Wednesday 1 May 2019 09:30 (30 minutes)

Approximately, 10-30% of ovarian cancers have an amplification of the human epidermal growth factor receptor type 2 (HER2) gene or overexpression of its protein product, while it is present at low levels in normal tissues. HER2 is a 185 kDa transmembrane protein that belongs to the HER family of tyrosine kinase receptors. Although controversial, recent studies have confirmed that HER2 overexpression in ovarian cancer is associated with worse patient outcome, implicating HER2 may be a potential prognostic biomarker for ovarian cancer patients.

With the aim of diagnostic imaging of HER2, specifically targeting anti-HER2 Nanobodies have been developed and preclinically validated in SKOV-3 ovarian cancer mouse models. Nanobodies are camelid derived single-domain antibody fragments that are ten times smaller than classic antibodies. These vector molecules reach their in vivo target very rapidly while unbound Nanobody is cleared from the body. This allows for fast high contrast imaging compared to imaging with monoclonal antibodies. This also implicates that short-lived radionuclides such as 68Ga, 18F and 99mTc can be used for radiolabeling. The 68Ga-anti HER2 Nanobody has been succesfully translated to a Phase I clinical trial in breast cancer patients.

Alternatively, the anti-HER2 Nanobody has been fluorescently labeled with the near-infrared IRDye800CW to use as a tool for real-time visualization of tumor lesions during fluorescence-guided surgery. As debulking surgery is still the most effective treatment for advanced ovarian cancer, the efficiency of surgery is of utmost importance. Significantly reduced residual tumor was observed with Nanobody image guidance as compared to conventional surgery.

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Session Classification: Ovarian cancer (PARTII)

Track Classification: Preclinical research and development of new radiopharmaceuticals

Contribution ID: **48** Type: **Oral**

High resolution preclinical and humanTotal body molecular imaging as companion tools for theranostics

Tuesday 30 April 2019 11:20 (20 minutes)

Molecular imaging systems (PET, SPECT) have been improved over the last 20 years using small changes in either reconstruction methods, collimator or detector. The availability of highy sampled Silicon multipliers and advanced positioning algorithms (Maximum Likelihood, Deep learning,..) lead to scintillation detectors with sub mm transverse resolution (at competitive cost with older PMT based detectors). This enables a redesign of PET and SPECT imaging systems. In PET the solid angle can be increased with factor 4-5 for the same amount of detector material as the new detectors have intrinsic depth-of-interaction and can operate very close to the subject. This has led to so-called preclinical Total body PET systems, one of these being developed, tested and commercialised at Molecubes and Innovative Molecular Imaging and Therapy dept (Ghent, Belgium). This is now further optimised for time-of-flight PET so it can used for a clinical Total body PET (PET2020) with very high sensitivity (20 x higher than state of the art Clinical PET-CT) and superior resolution (below 2 mm). This will enable accurate dosimetry, imaging at multiple halflives (eg. Zr-86 up to a month) and imaging of new PET isotopes with even small positron abundances (e.g. Y-90). For SPECT imaging the higher intrinsic resolution enables the use of smaller detectors and collimators with minimal magnification (or even magnification) and leads to more compact systems (fitting on a desktop for preclinical imaging). High energy collimators are now easier to construct (additive manufacturing) and enable imaging of energies up to (or even beyond) 511 keV.

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Presenter: VANDENBERGHE, Stefaan (Ghent university, Belgium)

Session Classification: Lessons learned from recent targeted radiotherapy treatments

Track Classification: Preclinical research and development of new radiopharmaceuticals

Contribution ID: **49** Type: **Invited**

Use of radioactive ions in therapy

Thursday 2 May 2019 09:00 (30 minutes)

The relativistic high-energy heavy-ion beam gives the good localized dose distribution and the large relative biological effectiveness, thus twelve heavy-ion radiotherapy (HIRT) facilities are under operation and six are under commissioning or construction worldwide. HIRT awakens worldwide interest. It is expected that clinical results will be improved through the more concentrated dose distribution on tumour with the smallest margin on normal tissues. In order to verify the real dose distribution and to obtain more accurate treatment planning, the radioactive nuclear beam (RNB) was developed. The position of implanted particles can be measured, since a short-lived positron emitted nuclei such as 11C or 19Ne can be detected its position with a positron camera or a positron emission tomography (PET).
The application of RNB was originally studied at BEVALAC of the Lawrence Berkeley Laboratory in 1980's. Although their early results showed useful data on the error of the stopping power in the treatment planning causes from the difference between the X-ray CT numbers and the actual stopping power, unfortunately, BEVALAC was shut down before the full completion of the RNB application. A 12C beam is used for cancer therapy at the Heavy Ion Medical Accelerator in Chiba (HIMAC) since 1994. Preclinical studies of RNB have been continued at HIMAC. The biological and chemical process of the metabolism is an important parameter for the precise measurement. The biological lifetimes in animals have been observed. An efficient detector system and an intense RNB production system have been developed too.

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Presenter: Dr KITAGAWA, Atsushi (National Institutes for Quantum and Radiological Science and Technology)

Session Classification: Radioisotope beams in hadron therapy

Track Classification: Radioisotope beams in hadron therapy

Contribution ID: **50** Type: **Invited**

Preclinical development of folate receptor-targeted radiopharmaceuticals for ovarian cancer

Wednesday 1 May 2019 09:00 (30 minutes)

Ovarian cancer represents the most common cause of gynecological cancer death with a 5-year relative survival rate of 29% for patients diagnosed at a metastasized stage (1). The development of new treatment options is urgently needed to treat patients with refractory disease and platinum-resistance (1).
The folate receptor (FR) is overexpressed on the cell surface of a variety of tumors including ovarian cancer (>80%), being therefore a promising target for radiotheragnostics (2). The vitamin folic acid has been chemically derivatized for the delivery of radionuclides to FRpositive tumors. The overexpression of FR in the kidneys has been, however, the main obstacle towards the development of effective and safe radiofolates for therapeutic applications.
Different strategies have been used to increase the accumulation of radioactivity in the tumor and dicrease the kidney uptake (3). At PSI, a radiofolate was functionalized with an albumin-binding entity (AB) for the first time, which resulted in a reduced glomerular filtration of the radioligand and, consequently, a 6-fold higher tumor-to-kidney ratio, enabling the first therapy study in mice with a 177Lu-AB-folate. Further modification in the linker part led to even superior pharmacokinetic properties. The developed radiofolates were radiolabeled also with 47Sc and 44Sc as well as with 161Tb and 155Tb, potentially enabling the realization of the radiotheragnostic principle.
Based on the results reached so far, further pharmacokinetic optimization is necessary and studies are ongoing at PSI to develop safe and effective radiofolates for the management of ovarian cancer patients.

References:

1. Lhereux S et al., Lancet. 2019;393:1240-1253.
2. Low PS et al., Curr Opin Chem Biol. 2009;13:256-262.
3. Siwowska K et al., Q J Nucl Med Mol Imaging. 2015;59:269-286.

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Session Classification: Ovarian cancer (PARTII)

Contribution ID: **51** Type: **MEDICIS-Promed ESRs**

Charge breeding investigations for a future 11C treatment facility

Thursday 2 May 2019 11:20 (20 minutes)

In this contribution, the possibilities of using a charge breeding scheme based on an Electron Beam Ion Source for beam preparation of a radioactive 11C beam for hadron therapy are discussed. Test measurements under extreme operating conditions were conducted at the REX-ISOLDE facility to explore the limitations of the charge breeder for high-intensity, low-repetition-rate, molecular CO+ beams. Based on the findings, different possible scenarios of coupling a charge breeder with either a medical synchrotron or linear accelerator are evaluated.

References: CERN-ACC-NOTE-2018-0078

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Session Classification: Radioisotope beams in hadron therapy

Track Classification: Radioisotope beams in hadron therapy

Contribution ID: **52** Type: **Invited**

Isotope Harvesting at FRIB

Thursday 2 May 2019 14:00 (30 minutes)

Much like at ISOLDE, the unused primary beam at the Facility for Rare Isotope Beams (FRIB) will retain a majority of its isotope-producing capability even after passing through the main target. In the spirit of MEDICIS, we are planning to make use of that unused capacity to access valuable radioisotopes for applications such as theranostics. This secondary isotope production will occur mainly in a water-filled beamdump, and the induced radioisotopes will be "harvested"chemically via the beamdump's water and gas cooling streams. Owing to the relative isotopic impurity of harvested elements, generator schemes will be used to achieve high specific activity and high radionuclidic purity. Preliminary testing of harvesting techniques are underway at the National Superconducting Cyclotron Laboratory (NSCL), where the theranostic 47Sc has been isolated cleanly from its parent 47Ca, which was produced during 48Ca bombardment of a low-power prototype beamdump. The results are promising so far, but the complexity is sure to increase as FRIB is commissioned and ramps up to full power over the coming years.

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Session Classification: Methods for production of novel radioisotopes for theranostics

Track Classification: Methods for production of novel radioisotopes theranostics

Contribution ID: **53** Type: **Oral**

Ba-131 derived Cs-131 in evaluation of the radiobiological effects of internalized Auger-electron emitters.

Wednesday 1 May 2019 10:55 (20 minutes)

Auger electron emitters are promising candidates for targeted radionuclide therapy. They decay by internal conversion or electron capture, resulting in Auger cascades with the emission of several low energy (eV-keV) electrons. The multiplicity of electrons combined with their short range (nm-µm) results in a high local energy deposition density near the decay site. Decays happening close to the DNA therefore have high radiotoxicity while decays happening outside the cell have low radiotoxicity. Several Auger electrons emitters (e.g. I-125, In-111, Tc-99m) have been intensely studied in order to understand the underlying radiobiology and quantify their radiotoxicity in the form of RBE-values. However, the already complex dosimetry is further complicated by the non-trivial intracellular organometallic chemistry of these radionuclides. The resulting absorbed dose calculations are therefore subject to high uncertainties.
We have developed the use of a "new"radionuclide, Cs-131, for investigating the radiotoxicity of Auger electrons. Cs-131 itself is not suitable for radionuclide therapy, but has several characteristics that makes it an ideal "model"isotope. Cs-131 can be formed from reactor produced Ba-131, using a "solution generator"principle. Cs-131 decays by electron capture (100 %) with a half-life of 9.69 days. It emits on average 10 electrons per decay, with an average energy of 613 eV1. Most importantly, its alkali chemistry result in a homogenous intracellular distribution. This allowed us to make simple but robust absorbed dose calculations, without the inherent uncertainties. Using this setup, we investigated the radiotoxicity of intracellular Cs-131 decays. Preliminary results show an RBE-value of approximately 4.2

Reference:
1. Personal communication with Lee QB. Based on Monte Carlo calculations as described in ref: Lee BQ, Nikjoo H, Ekman J, Jönsson P, Stuchbery AE, Kibédi T. A stochastic cascade model for Auger-electron emitting radionuclides. Int J Radiat Biol 2016;3002:1–13.
2. Fredericia PM. 2017. Quantification of Radiation -Induced DNA Damage Following Intracellular Auger-Cascades [dissertation]. Technical University of Denmark, DK

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Session Classification: Ovarian cancer (PARTII)

Track Classification: Preclinical research and development of new radiopharmaceuticals

Contribution ID: **54** Type: **Poster**

ACCRA : Automatisme & Contrôle Commande Radiochimie, a software for an automated radiometals separation.

Thursday 2 May 2019 17:10 (10 minutes)

Our developments on production of 165Er and 52Mn [1] for bimodal sensor MRI/PET or SPECT turn to be necessary an automatisation of separation process especially in case of 52Mn in terms of radiation protection. For that, a homemade system has been developed for purification of radiometal target especially for separation step with homemade software, ACCRA to remote control all operations. The system has 22 input-output switches controlled by Siemens automate in state 0 or 1. Then radiochemist define application for each switch, create a sketch in a paint file, and create a word file to coordinate real command of switch with its position on sketch. Finally, he creates a second word file to define for all step state of switch. Easy use and versatility of ACCRA has been demonstrated [2]. Nevertheless, repeatability was not satisfactory [3]. An evolution of system with introduction of more sensors and actuators on line is necessary to develop.

Reference :
[1] P. K. Malikidogo et al. , Chem. Commun., 2018, 54, 7597-7600 [2] K. Djanashvili et al. , (in press)
[3] J. Vaudon et al. Instruments 2018, 2, 15.
Acknowledgments: I. Da Silva thanks Triskem Society and particularly Aude Bombard for technical discussions on separation process, Louis Frealle for design of automation of process, Patrice Rifard and William Hate for electronics developments and ACCRA conception.

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Session Classification: Posters Session

Track Classification: Devices and Engineering for Radioisotope Handling

Contribution ID: **55** Type: **Poster**

CiSCoTe : Cible Solide Irradiée Contrôlée en Température (Solid Target irradiated under control temperature by thermocouple and pyrometer)

Thursday 2 May 2019 18:04 (6 minutes)

In a context of development of radiometals (165Er, 52Mn or 89Zr) for imaging applications at Orleans'cyclotron, more regular and higher activities are necessary. For that, a new targetry was developed for solid target using a known cooling system [1] where target was in a shuttle. In this targetry, two measurements of temperature have been integrated: one by thermocouple on the backside of the target [2] and a second in its front side without contact by pyrometric measurement. For these experiments, targetry has been evaluated with irradiation of holmium solid target by protons (16MeV) and 17.5MeV (deuterons) [3] for 165Er, Cr target (14MeV) for 52Mn and Y target (12MeV) for 89Zr. First results demonstrated difficulties to direct measurements of lanthanides, certainly due to its excitation. Using a foil of Aluminum, measurements have been obtained from 1 to 20µA with a flow limited at 3.6L/min but reproducibility of results was not possible. Explanations why were in progress and some new experiments must be realized to more clarify these points.

Reference :
[1] G. Goin et al., Proc. 9th Int. Conf. on Cyclotrons and their Applications, 1981, p. 133-135.
[2] S. Chan et al., Proc. 15th International Workshop Targetry and Target Chemistry, 2016, 27-30
[3] J. Vaudon et al. Instruments 2018, 2, 15.
Acknowledgments: I. Da Silva thanks the financial support of AAP - Défi 2017 "Instrumentation aux limites "project "CiSCOTe": Cible Solide Irradiée Contrôlée en temperature and the French National Research Agency (grant ANR-13-JS07- 0007) for financial support. I. Da Silva thanks too especially Sun Chan, cyclotron engineer manager at Sir Charles Gairdner Hospital in Perth (Australia) and J. Comor, targetry and irradiation engineer for cyclotron, manager of ELEX Commerce (Servia), for all exchanges about this project and technical information.

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Session Classification: Posters Session

Track Classification: Accelerator techniques for medical isotope production

Contribution ID: **56** Type: **MEDICIS-Promed ESRs**

The chemical vapour deposition (CVD) of graphene

Thursday 2 May 2019 16:40 (20 minutes)

The chemical vapour deposition (CVD) of graphene is the most promising route for the production of large-area graphene films. In this work, the growth of graphene on transition metals via CVD was investigated. The mechanisms of graphene formation on metals with different carbon solubility and therefore different affinity to carbon were observed and discussed.
In this work, three transition metals were subjected as the growth substrate for graphene deposition –copper, tantalum, and rhenium. The last two metals are the object of interest for further investigation with the collaboration group in CERN within the MEDICIS project. The copper foil was chosen as a test metal since all growth graphene pattern mechanisms were "well-studied" and reported.
Alongside with the general consistency of obtained results regarding the copper foil, there was found poorly studied phenomena while studying the growth of graphene on copper, namely - the growth of a multilayer of graphene, the mechanism which possibly differs from surface mediated. Also, in this work, the application of CVD grown graphene on copper, including the formation of graphene from liquid precursor was studied.
The growth of graphene on tantalum was investigated using the isothermal - isobar approach. In the case of rhenium, it was found that there is an effective window of growth conditions for graphene formation. Tantalum and rhenium being both refractory metals have low and great affinity to carbon, correspondingly. The mechanism of graphene formation on these two metals, thus differ significantly.
The growth conditions, possible mechanisms of graphene formation on studied metals as well as the protective properties of graphene in terms of aggressive chemical media were investigated and reported.

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Session Classification: Methods for production of novel radioisotopes for theranostics

Track Classification: Methods for production of novel radioisotopes theranostics

Contribution ID: **57** Type: **MEDICIS-Promed ESRs**

COST-EFFECTIVE DESIGN STRATEGIES FOR A TYPE B CONTAINER BASED ON NUMERICAL CALCULATIONS: THE COLIBRI-30

Friday 3 May 2019 15:10 (20 minutes)

Type B packages are required for the transport of radionuclides with activity higher than the limits described by the current European Regulation1, named A1 and A2. The homologation for a Type B container can be obtained only after having proved, via strict tests described by the International Atomic Energy Agency (IAEA), the radioprotection and the mechanical resistance in normal and accidental conditions. An adequate number of tests carried on directly with several prototypes is prohibitive especially when the article is costly and considering the high price of the tests. In the drawing phase it is possible to simulate thanks to numerical tools the damages of the package in the exact test conditions, reducing the incidence of mechanical failures and saving time and budget. In the design process, the first step consists in the specification of the radionuclides to be transported and their radioprotection constraints, in term of dimensions and material for the shielding. The second phase is a virtual cut-and-try testing procedure. Once a primary design is chosen, a 3D Finite Element Analysis Software is used to carry out transient thermal analysis and evaluate deformations and stress due to the accidental impacts. Depending on the results, the design is adjusted at each step and the simulations repeated until the good compromise is reached. This process leaded to the design of a container named ColiBRI (Colis Type B pour RadioIsotopes). Two prototypes have been manufactured and will be tested soon.

References: 1. Regulations for the Safe Transport of Radioactive Material, 2012 Edition - Specific Safety Requirement No. SSR-6, IAEA.

Acknowledgments: This project has received founding from the European Union's EU Horizon 2020 Research and Innovation program under grant agreement No. 642889.

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Session Classification: Devices and Engineering for Radioisotopes Handling

Track Classification: Devices and Engineering for Radioisotope Handling

Contribution ID: **58** Type: **Poster**

Isotope Production at European Spallation Source –A potential new access to neutrons

Thursday 2 May 2019 18:10 (6 minutes)

The medical use of radioactive isotopes for diagnosis and treatment is a publicly accepted and well supported success history. The rapid growth of molecular imaging, PET scanning and radionuclide therapy of cancer has increased the demand for isotope production across the globe. Unfortunately, we are also witnessing the decreased availability of large nuclear facilities due to aging facilities and changes in research priority. The need for special isotopes is however still there. It is an obvious possibility to augment the ESS installation with irradiation facilities to enable production and extraction of medically important, otherwise unavailable isotopes.

Here we present a potential location to place isotope production targets in the vicinity of the spallation target as well as initial calculations on available neutron quality, spectrum and flux there. The proposal is based on current ESS design parameters, a 2.0 GeV proton beam on the solid tungsten target at 5 MW beam power.

Two equally important source terms can be identified. These are direct neutron activation in small targets located in points of high thermal neutron flux close to the water moderator and fast neutron activation using unmoderated spallation neutrons.

We propose the formation of an EU funded consortium of research institutions to work out detailed plans for necessary infrastructure at ESS and a feasibility list of worthy, feasible radioisotopes together with their calculated yields. A future facility of this kind may benefit from close collaboration with facilities for electromagnetic isotope separation of radioisotopes, increasing radio-nuclidic purity and specific activity.

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Presenter: LEE, Yongjoong (Target Division, European Spallation Source (ESS) ERIC, Sweden)

Session Classification: Posters Session

Contribution ID: **59** Type: **Invited**

Small molecule inhibitors for tumor imaging and therapy

Tuesday 30 April 2019 09:30 (30 minutes)

Technological advances in molecular biology and biotechnology are increasingly used for the development of new tumor targeting tracers. In oncology, major progress has recently been achieved with peptidic and small molecule compounds. This relies on the identification and validation of new target structures in close conjunction with the application of new techniques for the development of new biocompatible molecules. These are based on either rational design or highthroughput methods. Their further evaluation and optimization consists in the characterization of the structure-function relationships and subsequent improvement with respect to binding, internalization and biodistribution of corresponding analogues. The concept will be shown for two the fibroblast activation protein (FAP).

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Session Classification: Lessons learned from recent targeted radiotherapy treatments

Track Classification: Preclinical research and development of new radiopharmaceuticals

Contribution ID: **60** Type: **Invited**

Augmented and individualized radionuclide treatment (advances in PRRT / PRLT with a clinical focus on PSMA targeted radioligand therapy)

Tuesday 30 April 2019 10:30 (30 minutes)

With translation of new radioligands into clinical theragnostic practice, the therapeutic branch of nuclear medicine has gained fundamental momentum. The agonist-to-antagonist change in paradigm for different peptide receptor targeting systems is another current issue of major relevance. PSMA-targeted approaches are being discussed as role model treatment approach. Understanding the mechanism and specific issues of PSMA-targeted PRLT, as well as potential risk factors for unfavorable course of disease under therapy, is helpful to escalate PRLT when needed. Indications for PRLT and arguments for earlier application will be covered, as well as contraindications and pseudo-contraindications. Augmentation methods for PRLT including comedication and potential maintenance therapy in PRLT responders are matters of clinical concern. Also toxicity issues of Lu177 and Ac225 based PSMA-targeted PRLT, covering the subject of tandem vs single isotope approach.

Author: Prof. EZZIDDIN , Samer (Saarland University Hospital, Homburg)

Presenter: Prof. EZZIDDIN , Samer (Saarland University Hospital, Homburg)

Session Classification: Lessons learned from recent targeted radiotherapy treatments

Track Classification: Preclinical research and development of new radiopharmaceuticals

Contribution ID: **61** Type: **Invited**

Ovarian cancer: Diagnosis and Systemic Treatment

Tuesday 30 April 2019 13:30 (30 minutes)

Ovarian cancer is the 8th most common cancer in women and the 5th most common reason for cancer death. There is no recognized screening method and ovarian cancer is most often diagnosed at an advanced stage. I will give a short background on epidemiology of epithelial ovarian cancer as well as on its diagnosis and genetic background. Then, we will discuss current standard treatment which consists in surgery followed by platinum containing chemotherapy. And finally, we will also talk about new targeted therapies such as the PARP inhibitors that have brought new interesting treatment options to ovarian cancer patients at early as well as late stages. To conclude, we will also discuss immunotherapy for ovarian cancer.

Author: Dr WOLFER, Anita (CHUV, Lausanne)

Presenter: Dr WOLFER, Anita (CHUV, Lausanne)

Session Classification: Ovarian cancer (PART I)

Track Classification: Preclinical research and development of new radiopharmaceuticals

Contribution ID: **62** Type: **Invited**

How versatile a cyclotron is for isotope production

Thursday 2 May 2019 13:30 (30 minutes)

Radionuclides are used in different fields of medicine like oncology, neurology and cardiology, either for diagnostic or therapy. In most cases, radionuclides must be coupled to a carrier molecule to target the cells of interest. Many radionuclides may be of medical interest due to their emitted radiations (beta / alpha emitters, Auger emitters) and/or their half-lives that can be adapted to the carrier molecule transit time and to the pathology. Recently, the theranostic approach [1] has emerged. It combines imaging information and therapeutic use of radionuclides. This approach shows great promises especially because it may allow personalizing the treatment to each patient. The diagnosis test done prior to the treatment allows to determine patient response and to determine the needed injected dose for the therapeutic agent. After treatment, the imaging agent can be used to follow the patient response to the injected radiopharmaceutical. Finally, this approach allows a better control of the targeting and increases the benefit/toxicity ratio as useless treatments on patients with no response to the diagnosis test are avoided. All these points lead to a renewal interest on radionuclide production and in particular on metals for which chelation can be used to bind radionuclides to the vector molecules.
Radionuclide production is mainly done using neutrons in nuclear reactors and protons in accelerators. However, it is possible to use accelerators on more versatile ways than was done before in order to make available large quantities of radionuclide of interest with high quality and affordable prices.
The purpose of this presentation is to illustrate how versatile accelerator can be for isotope production and how they can help fulfill medical needs.
References
1. SC. Srivastava, JPM 2013 ; 47(1)31-46

Acknowledgements
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Author: Prof. HADDAD, Ferid (GIP Arronax)

Presenter: Prof. HADDAD, Ferid (GIP Arronax)

Session Classification: Methods for production of novel radioisotopes for theranostics

Track Classification: Methods for production of novel radioisotopes theranostics

Contribution ID: **63** Type: **Invited**

The Unites Stated Department of Energy Continues to Play a Key Role in Isotope Production by Making Significant Upgrades to its Facilities and Expanding its Collaborations

Saturday 4 May 2019 09:00 (30 minutes)

Radionuclides play a major role in research applications, in environmental studies and in industrial applications as sources as well as in nuclear medicine imaging and therapy. The United States Department of Energy (DOE) isotope program has a long history of utilizing its unique national laboratory facilities and expertise to develop and supply radionuclides that are in high demand and commercially unavailable. They were the original inventors of the Mo-99/Tc-99m generator and many other radionuclides including I-131, Sr-90/Y-90, C-14, F-18 FDG, Pb-212/Bi-212 just to name a few. It further has increased and strengthened its ties with Universities to enhance the supply of isotopes to stakeholders and is continuing to develop unique collaborations to increase the library of radionuclides available. It has consistently upgraded facilities and capabilities to provide both novel radionuclides for researchers as well as upgrading its quality systems to provide routine reliable quality radioisotopes for medical and commercial applications.

DOE is actively developing novel production and purification methods for radioisotopes for use in a variety of applications. Current efforts have focused on developing methods to produce therapeutic radioisotopes particularly alpha emitters with high purity and thus minimal to no impurities as well as high specific activity theragnostics which can be attached to biomolecules or targeting vectors that selectively distribute within diseased tissues, thus delivering toxic radioactivity to diseased tissue while minimizing or sparing damage to healthy or normal cells.

Furthermore, DOE has upgraded its production facilities and capabilities to meet increased demand and to allow for assessment of novel production methods. While simultaneously increasing its testing facilities and quality programs to meet the regulations required for radioisotopes of use in clinical trials and in approved drug formulations. This presentation will present an overview of the program and its facilities highlighting upgrades it has made at its various facilities to meet the needs of its various stakeholder.

Authors: Ms CUTLER, Cathy (BNL,Collider Accelerator Department); GILLO , Jehanne (US DOE)

Co-authors: GARLAND, Marc (US DOE); JOHN, Kevin (ORNL); COPPING, Roy (ORNL); BOLLE, Rose (ORNL); ROTSCH, Dave (ANL)

Presenter: Ms CUTLER, Cathy (BNL,Collider Accelerator Department)

Session Classification: Devices and Engineering for Radioisotopes Handling

Track Classification: Devices and Engineering for Radioisotope Handling

Contribution ID: **64** Type: **not specified**

Welcome

Tuesday 30 April 2019 16:30 (5 minutes)

Presenter: STORA, Thierry (CERN)

Session Classification: Kick-off Meeting: European Network of Facilities for medical isotopes by mass separation

Contribution ID: **65** Type: **not specified**

Presentation from the European Association of Nuclear Medicine (EANM)

Tuesday 30 April 2019 16:35 (20 minutes)

Presenter: Prof. DECRISTOFORO, Clemens (University of Innsbruk)

Session Classification: Kick-off Meeting: European Network of Facilities for medical isotopes by mass separation

Contribution ID: **66** Type: **not specified**

Presentation from the International Federation of Pharmaceutical Manufacturers & Associations (IFPMA)

Tuesday 30 April 2019 16:55 (20 minutes)

Presenter: Mr GENCOGLU, Mumun (Ifpma)

Session Classification: Kick-off Meeting: European Network of Facilities for medical isotopes by mass separation

Contribution ID: **67** Type: **not specified**

Presentation from the International Atomic Energy Agency (IAEA).

Tuesday 30 April 2019 17:15 (20 minutes)

Presenter: Prof. JALILIAN, Amirrezza (IAEA)

Session Classification: Kick-off Meeting: European Network of Facilities for medical isotopes by mass separation

Contribution ID: **68** Type: **Invited**

Simultaneous cancer treatment and online imaging with radioactive ion beams at FAIR

Wednesday 1 May 2019 11:35 (30 minutes)

Radiotherapy using accelerated heavy ions has the potential to overhaul cancer treatment and replace invasive techniques (surgery, catheter ablation) for selected noncancer diseases. However, particle therapy is hampered by the range uncertainty and requires more precision to fully leverage its physical advantages and expand the applications to noncancer diseases such as heart arrhythmia. The best way to visualize online the beam in vivo would be the use of ⍰+ emitters for treatment. Radioactive ion beams (RIB) with positron emitting isotopes can in fact be visualized by PET. Compared to PET monitoring of stable particles [1], RIB improve the count rate by orders of magnitude, eliminate the shift between the peaks of measured activity and dose, and reduce the impact of washout using short-lived isotopes and acquisition times. The use of RIB as a pre-treatment range probe had been already proposed many years ago, but therapeutic use was hampered by the low intensity achievable at conventional accelerators [2]. The RIB intensity will be increased x10,000 at FAIR compared to the current beams [3]. This means that currents around 107-108 pps will be reached. We will will especially concentrate on isotopes with short half-life t1/2, such as 10C, which have obviously the greatest potential for online beam monitoring. At FAIR, RIB are produced using the in-flight technique and are separated in an electromagnetic separator: the FRS. From SIS18, using the FRS, the beam can be directed to the Cave M, where we can exploit the medical equipment including the online BASTEI PET. We will then perform physical beam dosimetry in a water phantom and biological dosimetry in a cellular phantom to assess the biological effectiveness of the RIB. Finally, the system will be tested in an animal model. The goal of the project is to achieve a resolution <0.3 mm during the treatment.

[1] K. Parodi, Vision 20/20: Positron emission tomography in radiation therapy planning, delivery, and monitoring. Med Phys (2015) 42:7153–7168.
[2] M. Kanazawa et al., Application of an RI-beam for cancer therapy: In-vivo verification of the ion-beam range by means of positron imaging. Nucl Phys A (2002) 701:244–252.
[3] M. Durante et al., Applied nuclear physics at the new high-energy particle accelerator facilities. Phys. Rep. (2019). DOI: 10.1016/j.physrep.2019.01.004

Author: Prof. DURANTE, Marco (1GSI Helmholtzzentrum für Schwerionenforschung, Biophysics Department, Darmstadt, Germany)

Presenter: Prof. DURANTE, Marco (1GSI Helmholtzzentrum für Schwerionenforschung, Biophysics Department, Darmstadt, Germany)

Session Classification: Radioisotope beams in hadron therapy

Track Classification: Radioisotope beams in hadron therapy

Contribution ID: **69** Type: **not specified**

INFRA-2-2020 call: Proposal preparation

Tuesday 30 April 2019 17:35 (20 minutes)

Presenters: LEUFGEN, Kirsten (SCIPROM); STORA, Thierry (CERN)

Session Classification: Kick-off Meeting: European Network of Facilities for medical isotopes by mass separation

Contribution ID: **70** Type: **not specified**

Other Contributions

Tuesday 30 April 2019 17:55 (1h 35m)

Session Classification: Kick-off Meeting: European Network of Facilities for medical isotopes by mass separation

Contribution ID: **71** Type: **Poster**

Production of High Intensity 11C Beams for PET-aided Hadron Therapy

Thursday 2 May 2019 18:16 (10 minutes)

Presenter: STEGEMANN, Simon Thomas (KU Leuven)

Session Classification: Posters Session