BOOK OF ABSTRACTS
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7th Symposium on Medical Radioisotopes

The changing landscape

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Boeretang 200
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Introduction

Dear participants,

The target irradiation for the production of medical radioisotopes is only the first step in a rush against time, involving multiple transports, the separation and purification of the isotopes, the manufacture of generators, the radiolabelling in centralized or hospital radiopharmacies, quality checks and the administration preceding diagnostic imaging or therapy, to finally bring the isotopes to the clinic and the patients. This entire value chain is present in Belgium, which certainly is one of the reasons for our country to be a world leader in the field. It is therefore not a surprise that the only European symposium which addresses the different links in the chain is organised regularly in the country since 2007.

The programme of the symposium reflects key conditions for sustainable innovations in the field: multidisciplinarity and the complementarity between research, implementation and clinical applications. Those ingredients allow the symposium to once again promote the exchange of information about the perspectives of the world production of medical radioisotopes during the next decade; stimulate the discussion on challenges related to the distribution processes including safety, security, transparency and prompt delivery; present breakthroughs of research in radiopharmacy, medical imaging and nuclear medicine; and finally to describe new Belgian industrial and research initiatives.

From this edition on, the symposium is organised by the non-profit organisation ISMERAD ASBL (International Symposium on MEdical RADioisotopes - BE718.605.791). This will allow ISMERAD to be fully compliant with the legal and administrative obligations for all its future events.

On behalf of the Organising and Scientific Committee, I thank all authors, chairs and participants for their valuable contributions and presence. Also, very sincere thanks to our generous sponsors for supporting the organisation of this symposium, thereby allowing students to attend free of charge.

Prof. em. Frank Deconinck
Chair of the Organising Committee

Programme

08:45 – 09:15 **Registration and welcome coffee**

09:15 – 09:30 Opening | Frank Deconinck, PC Chair - Short welcome and introductory address

09:30 – 10:30 **Session 1: Radioisotope production | *Chairs: Bernard Ponsard, SCK•CEN and Lucia Popescu, SCK•CEN***

Lecture 1: Which (new) supply sources for Mo-99/Tc-99m ? | JM Geets, Co-chairman of the AIPES Innovation Working Group and IBA RadioPharma Solutions.

Lecture 2: PET and targeted radionuclide therapy isotopes production in Belgium: the Ge-68 (PET), Lu-177 (beta) and Ac-225 (alpha) theragnostic trio | Dennis Elema, SCK•CEN, and Jean Bonnet, IRE & IRE-ELiT

Lecture 3: MINERVA – first phase of MYRRHA and potential contribution to medical radioisotopes | Hamid Aït Abderrahim, SCK•CEN

10:30 – 11:00 Coffee break and poster session

11:00 – 12:00 **Session 2: Radioisotope Transport and Good Distribution Practice | *Chairs: Kristel Vermeersch, EITA & KVS & Partners – Dangerous Goods Consulting, and Yvan Bruynseraede, KULeuven***

Lecture 4: Perspectives in Integrated Supply Chains Performance Management | Alassane B. Ndiaye, ULB

Lecture 5: The changing European landscape in the isotope transport sector | Pierre Dejonckheere, Transrad & Chairman of the AIPES Working Group Transport

Lecture 6: Lessons learned since the new transport regulations came into effect | Rony Dresselaers, FANC/AFCN

12:00 – 12:20 **Crisis Communication | *Chair: Michel Giot, UCLouvain***

Lecture 7: A crisis resilient nuclear organisation | Wim Uyttenhove, The Binding Energy and PM Risk-Crisis-Change

12:20 – 14:00 Lunch and poster session

14:00 – 15:00 **Session 3: Radiopharmaceuticals | *Chairs: André Luxen, ULiège and Vicky Caveliers, VUB***

Lecture 8: The Brussels RadioTheranostics Platform | Zéna Wimana, IJBordet, and Tony Lahoutte, VUB

Lecture 9: Cold kits for radiopharmaceuticals - beyond SPECT | Sam Voccia, ANMI

Lecture 10: EU Regulations: practical impacts for radiopharmaceuticals | Joël Aerts, Luxembourg Hospital Center

15:00 – 16:00 **Session 4: Medical Radioisotope Applications | *Chairs: Nadia Withofs, ULiège and Thierry Vander Borght, UCLouvain***

Lecture 11: The safety, feasibility and optimization of multiple prolonged breath-holds (> 5 minutes) in radiotherapy | Michael Parkes, University of Birmingham

Lecture 12: Total body PET - from mice to man | Stefaan Vandenberghe, UGent

Lecture 13: Impact of nuclear medicine on personalised patient management | Kristoff Muylle, UZ Brussel

16:00 – 16:15 **Poster prize ceremony**
Traditionally 3 prizes are given for the best posters, respectively 500, 350 and 150 €

16:15 – 16:30 **Conclusions and closure**
Isotopes in medical imaging: past, present and future? | Pieter De Bondt, President of BelNuc

16:30 – 17:30 Reception

Biographies & abstracts

Frank Deconinck

Professor Emeritus

Conference Chair

Frank Deconinck (°18-04-1945) obtained his PhD in Medical Physics from the Vrije Universiteit Brussel (VUB). He was research associate at the University of California (UCSF) and research collaborator at Brookhaven National Laboratory. He is professor emeritus of medical physics at VUB.

In the nuclear field, he is honorary chairman of the board of governors of the Belgian Nuclear Research Centre (SCK•CEN), former vice-president of Belgonucléaire NV, member of the French Commission Nationale d'Evaluation (CNE2), former president of the Belgian Hadron Therapy Consortium foundation and honorary president of the European Nuclear Society. He coordinates Rad4Med.be, the Belgian network for radiation applications in healthcare.

In the socio-cultural field he organised, together with Mrs. Deconinck-De Ries, the exhibition "Tactile Graphic Art", selected in 1989 by UNESCO for the U.N. World decade for cultural development. Exhibitions were held in Belgium, Paris (UNESCO), Köln, Taijou, Osaka, Tokyo,...; he co-organised the International Very Special Arts Festival in Brussels, 1994.

He is author, co-author or editor of 6 books, ≥ 100 articles, ≥ 200 communications and ≥ 200 invited talks, mainly on medical imaging. He received the Hewlett Packard prize for medical informatics in 1984, the Familie Bruers-Colbert and daughter prize for his work on X-ray fluorescence in 1987 and the Honorary Tech-art prize for tactile art for blind people in 1988.

Bernard Ponsard

Radioisotopes Project Manager, SCK•CEN – BR2 Reactor

Bernard Ponsard (Master in Physics, Université Catholique de Louvain, UCL, Belgium, 1983; Master of Science "Nuclear Energy", Université Catholique de Louvain, UCL, Belgium, 1985) joined the 'Belgian Nuclear Research Centre' (SCK•CEN) in Mol in 1985 as reactor physicist at the BR2 High-Flux Material Testing Reactor. In charge of the neutronic calculations of the BR2 reactor core and the interpretation of the related nuclear measurements for 30 years, he developed actively BR2's commercial productions of radioisotopes and NTD-silicon.

He is currently Stakeholder Manager for Radioisotopes and NTD-Silicon Production at the BR2 reactor and in charge of the strategic development of new medical radioisotopes for nuclear medicine and of new products for the semiconductor industry within SCK's Institute for Nuclear Materials Science (NMS).

He is also Deputy-Chairman of the "AIPES Security of Supply Working Group", strongly involved in securing global supply of medical radioisotopes as Mo-99/Tc-99m, Chairman of the "AIPES Emergency Response Team" (ERT) and Co-Chairman of the "European Observatory on the Supply of Medical Radioisotopes".

Lucia Popescu

Head of the Proton Target Research Unit, SCK•CEN

Lucia Popescu graduated from the Faculty of Physics at Bucharest University, Romania. In 2005, she obtained a PhD in physics at Ghent university in Belgium. Her doctoral studies have been focused on the nuclear structure of several isotopes of Co, Ni and Cu. After a short post-doc in Groningen the Netherlands, Lucia returned to Belgium in 2007, as researcher at SCK•CEN, in Mol. Since 2010, she is in charge with ISOL@MYRRHA: a part of the MYRRHA project dedicated to the production of mass-separated radioisotopes extracted on-line.

JM Geets

Co-chairman of the AIPES Innovation Working Group
IBA RadioPharma Solutions
Integralab Business Developer – IBA Fellow

Jean-Michel Geets holds a Master degree in electrical engineering from U Liege. After being involved since 2002 in cyclotron project management for IBA (Ion Beam Application), he moved to IBA Radio Pharma Solutions in 2005 as product manager dealing with cyclotron and target development in PET and SPECT applications. He has authored various publications in the development of cyclotrons and targets and holds few patents in this field. He is now managing the IntegraLab team and business development; providing complete radiopharmaceutical solutions to the end-Users.
He is an IBA Honorary Fellow in recognition of major innovative contribution to IBA.

Abstract

The talk will review the current status and development of the new sources of Mo 99 and Tc99m with an overview of the production system (accelerators, chemistry, generators).

Dennis Elema

IRE & IRE Elit

Research & innovation manager NURA project

Dennis Ringkjøbing Elema obtained a PhD degree in experimental high-spin nuclear structure physics in 2003 from the University of Copenhagen, The Niels Bohr Institute, Denmark. From 2004 to 2013 he worked as a nuclear physicist at the Hevesy Laboratory - a radiopharmaceutical research and GMP (good manufacturing practice) production facility at DTU Nutech, Technical University of Denmark. Here his main focus was on the production of radioisotopes for technical and medical applications using research reactors and cyclotrons as well as GMP manufacturing of radiopharmaceuticals. His research was centered around a broad spectrum of areas related to the development of new radiopharmaceuticals involving radiochemistry and pre-clinical studies. In 2013 he took the position as head of Division of the Hevesy Laboratory until 2017 where he moved to SCK•CEN, the Belgian Nuclear Research Centre, for a position as research and innovation manager for the NURA project – a dedicated initiative at SCK•CEN focusing on setting up a new organization for radiopharmaceutical research and manufacturing of therapeutic radioisotopes and radiopharmaceuticals.

Jean Bonnet

IRE & IRE Elit

Head of Strategy, Sales and Marketing

Jean Bonnet is a MD with specialty in metabolic biochemistry from the University Hospital of Lyon. He also took a MBA from the HEC School of Management in Paris.

After more than 3 years as research associate in INSERM (U.189), he crossed over to the biotech business and worked almost 2 years for the French start-up IMMUNOTECH, developing its activities in the Italian market.

He took his MBA in 1993, immediately before joining Boehringer Ingelheim. He spent 5 years in France in marketing department, and started a period of international assignments, firstly as regional business manager at Corporate Office of Boehringer Ingelheim.

Then he moved to Greece as head of commercial operations for prescription medicines, before taking the role of Country Manager in Poland, where he served at the board of INFARMA, the polish pharmaceutical industry association.

In 2010, Jean moved back to France to take over a VP position as Area Manager for Southern Europe in the imaging division of Covidien. After the spin-off of Mallinckrodt Pharmaceuticals, he served as VP Strategic Execution and Business Excellence.

In parallel, he also served as General Secretary of AIPES, the European association of medical imaging and equipment supply industry.

More recently, he built up two subsidiaries of the pharmaceuticals company Exeltis in France and Belgium.

Early 2019 he moved back to nuclear medicine as Head of Strategy, Sales and Marketing for IRE and IRE Elit.

Abstract

PET and targeted radionuclide therapy isotopes production in Belgium: the Ge-68 (PET), Lu-177 (beta) and Ac-225 (alpha) theragnostic trio

Ga-68 : First member of the theranostic trio (Dr J BONNET)
Ga-68 quickly took the lead of the radioisotope group eligible for PET diagnostic procedures. As the prospective of development of new tracers continues to grow, for pathology with significant impact on public health. Moreover, the development of internal vectorized radiotherapy coming along with follow-up procedures further increased the need to develop Ga-68 generators offering simpler, faster and more efficient use for larger group of users. IRE ELiT took over the challenge to bring to the nuclear medicine community a product allowing them to perform highly sensitive and specific diagnostic and help patients to access to new therapeutic options. The presentation will review some critical aspects of production of Ga-68 generators.

Lu-177 and Ac-225: The two therapeutic members of the theranostic trio (Dr D Elema)
Targeted RadioNuclide Therapy (TRNT) is presently one of the most promising developing treatments of cancer within nuclear medicine. The therapeutic radioisotope Lu-177 has in combination with the diagnostic partner Ga-68 already proven their success as a powerful theranostic duo in clinical applications. This theranostic duo is at the moment about to develop into an even more powerful trio with the introduction of the alpha emitter, Ac-225, also used for TRNT showing remarkable results.

Sustainable supply and production of these important therapeutic radioisotopes are key elements when it comes to ensuring development and a successful implementation of the next generation of therapeutic radiopharmaceuticals for the benefit of cancer patients.

SCK•CEN and IRE ELit are therefore currently closely collaborating on bringing *non-carrier added* (*nca*) Lu-177 to the market to support the on-going positive developments within the field of theranostics. Furthermore, as an integrated part of the newly established NURA project, SCK•CEN has recently entered a partnership with Global Morpho Pharma – a network of manufacturers and distributors of Lu-177 and Ac-225.

The presentation will focus the new initiatives of SCK•CEN on the production of Lu-177 and Ac-225 and introduce the common plan of SCK•CEN and IRE EliT to become suppliers of GMP (good manufacturing practice) quality *nca* Lu-177.

Hamid Aït Abderrahim

Professor at Institut de Mécanique, Matériaux et Génie Civil – iMMC (UCL)

Deputy Director General for International Affairs of SCK•CEN & Director MYRRHA project

Chairman of SNETP - Sustainable Nuclear Energy Technology Platform

Prof. Dr. Hamid Aït Abderrahim is the Deputy Director General of SCK•CEN, the Belgian nuclear research centre. He is also professor of reactor physics and nuclear engineering at the "Université Catholique de Louvain" (UCL) at the mechanical engineering department of the "Ecole Polytechnique de Louvain (EPL)".

His fields of specialisation are Reactor Physics, Reactor Dosimetry, Nuclear Fuel Cycle, Partitioning and transmutation of high level nuclear waste and Nuclear Reactor Technology.

Since 1998 he is the director of the MYRRHA project: an accelerator driven system coupling a sub-critical Pb-Bi cooled reactor and a high power proton accelerator through a spallation target.

He is partner and/or coordinator of various projects of the European Commission framework programme related to advanced nuclear systems or to partitioning and transmutation of high level nuclear waste management. He chaired the Strategic Research Agenda (SRA) working group of the European Sustainable Nuclear Energy Technology Platform (SNETP) from September 2007 to December 2011. Since 2015 he is the chairman of the Governing Board of SNETP.

He is the representative of Belgium in the Governing Board of the project JHR (Jules Horowitz Reactor, a MTR under construction in Cadarache, France).

He is author of more than 100 scientific publications in publications in peer review journals and international conferences. He directed many PhD and masters theses in the various fields of nuclear technology.

Last but not least in April 2014, he has been honoured by the King of Belgium by nominating him as “Grand Officer in the Crown Order” for his contributions in progressing science and knowledge in the field of nuclear engineering of innovative systems for High Level Waste management.

On February 15, 2016 he received the title of Doctor Honoris Causa to the Kaunas University of Technology for his personal achievements and long term collaboration with Kaunas University, especially with the Baršauskas Ultrasound Research Institute.

Abstract

Realisation of a New Research Infrastructure in Belgium: MYRRHA | Presentation of the Phase 1 MINERVA and its opportunities for medical RI

Since 1998 SCK•CEN is developing the MYRRHA project as an accelerator driven system based on the lead-bismuth eutectic as a coolant of the reactor and a material for its spallation target. The nominal design power of the MYRRHA reactor is 100 MWth. It is driven in sub-critical mode (keff = 0.95) by a high power proton accelerator based on LINAC technology delivering a proton beam in Continuous Wave (CW) mode of 600 MeV proton energy and 4 mA intensity. The choice of LINAC technology is dictated by the unprecedented reliability level required by the ADS application. In the MYRRHA requirements the proton beam delivery should be guaranteed with a number of beam

trips lasting more than 3 seconds limited to maximum 10 for a period of 3 months corresponding to the operating cycle of the MYRRHA facility. Since 2015, SCK•CEN and Belgium government decided to implement the MYRRHA facility in three phases to minimize the technical risks associated to the needed accelerator reliability.

MYRRHA is conceived as a flexible fast-spectrum pool-type research irradiation facility cooled by Lead Bismuth Eutectic (LBE), and was identified by SNETP (www.snetp.eu) as the European Technology Pilot Plant for the Lead-cooled Fast Reactor. MYRRHA is proposed to the international community of nuclear energy and nuclear physics as a pan-European large research infrastructure to serve as a multipurpose fast spectrum irradiation facility for various fields of research such as; transmutation of High Level Waste (HLW), material and fuel research for Gen.IV reactors, material for fusion energy, innovative radioisotopes development and production and for fundamental physics. As such MYRRHA is since 2010 on the high priority list of the ESFRI roadmap (https://www.esfri.eu/).

On September 7, 2018 the Belgian federal government decided to build this large research infrastructure. In this decision there is a realization of MINERVA coupling the first stage of the MYRRHA accelerator up to 100 MeV that will be coupled to a Proton Target Facility comprising the ISOL@MYRRHA. In this lecture we will summarize the status of the project today and we will stress the realization of MINERVA in the Phase 1 and its contribution to production of medical radioisotopes.

Kristel Vermeersch

Kristel Vermeersch founded KVS & Partners bvba - Dangerous Goods Consulting (Belgium) in 2002.
Her company is an accredited IATA training school and provides the following services:

- *Dangerous Goods courses for road & air transport, including radioactive substances, infectious and biological substance;*
- *Consultancy on the transport of Lithium Batteries by air, road and sea;*
- *Regulatory compliance advise on dangerous goods issues*
- *Acting as Safety Adviser for transport of dangerous goods by road*
- *Advise and support on classification, packaging and documentation for the transport of dangerous goods*
- *Advise on all packaging issues in cooperation with the Belgian Packaging Institute*
- *Auditor ISO 17025*
- *Secretary General of the European Isotopes Transport Association*

From 2002 to 2012 Kristel was an external dangerous goods expert to the Belgian Civil Aviation Authority and a member of the International Civil Aviation Organisation Dangerous goods Panel (ICAO DGP). Currently she is adviser to the ICAO DGP and to the United Nations Sub-Committee on the transport of Dangerous Goods.

As an expert, trainer and speaker on dangerous goods she attends regularly national and international conferences and meetings related to the transport of dangerous goods, including those organised by the European Biological Safety Organisation (EBSA), the European Isotopes Transport Association (EITA), IATA and ICAO.

She acts also as dangerous consultant to a number of national and international chemical, pharmaceutical and transport companies.

Prior to KVS & Partners, Kristel worked for 15 years at Sabena Cargo Airlines, Belgium, where she was responsible for all Dangerous Goods activities and special cargoes, regulatory compliance and interactions with Civil Aviation Authorities. During that period she was also member of the IATA Dangerous Goods Board.

Kristel obtained a Master in Chemistry and Biochemistry at the Catholic University of Leuven (Belgium) and has completed several specialised courses on radioprotection.

Kristel Vermeersch
KVS & Partners bvba
Dangerous Goods Consulting
Belgium

Yvan Bruynseraede

Professor Emeritus, KU Leuven

Session Chair

Yvan Bruynseraede is Professor Emeritus at the University of Leuven (KU Leuven, Belgium) where he received his doctoral degree in physics in 1967. He was a research fellow and associate at CERN (Geneva), started his academic career in 1971 at KU Leuven, and was until 2003 head of the Laboratory of Solid-State Physics and Magnetism.

His main research activities are in the domain of experimental solid state physics, particularly the study of mesoscopic and nanoscopic magnetic and superconducting structures measured at very low temperatures and at high pulsed magnetic fields. His work has been internationally recognized and resulted in more than 450 publications, numerous invited talks, and active collaboration with scientists all over the world. He is together with Ivan Schuller (UCSD) the recipient of the prestigious 2007 IUMRS SOMIYA Award, which recognizes outstanding research conducted by teams from at least two continents. In the nuclear research field he was a member of the Board of Governors of the Belgian Nuclear Research Center (SCK•CEN), and chairman of the Scientific Advisory Committee. He was chairman or member of National and International Advisory and Reviewing Science Committees, Research Foundations and Councils. Currently he is active as member of the SAC at IMDEA (Madrid) and at INL (Braga).

He is member and Past-President of the Royal Flemish Academy of Belgium for Science and the Arts , member of the Royal Society of Arts and Sciences in Göteborg, the European Academy in Vienna, and is Fellow of the American Physical Society (APS). He was member of the Board of Trustees and the University Association Council at KU Leuven, and is a member and past chairman (2016) of the Forum on Outreach & Engaging the Public of the APS.

Alassane B. Ndiaye

Prof. Dr. Ir. Alassane B. NDIAYE, Civil Engineer, MSc, MBA and PhD is a Professor of Transport Systems & Logistics at the Universite Libre de Bruxelles, founder and Director of Qalinca-Labs Logistics & Transport Systems R&D laboratory and Visiting Scientist at the University of California at Berkeley. Educated in Logistics and Supply Chain Management at Stanford University and at the MIT, Dr. Ndiaye is a guest Professor in 10+ universities in Africa, South America and South East Asia and Chairman of the World Conference Series on Logistics & Supply Chain Management.

Among his achievements is a strong track record of 300+ large industrial and R&D projects delivered worldwide; 150+ PhD and Master Theses mentored worldwide and a 15 excellence and capacity building centers in transport & logistics in Indonesia, Tunisia, Ecuador, Senegal, Vietnam, South Africa, Brazil, Cambodia.

Former Expert Counsellor to the Vice-President and Minister of Transport & Energy; Former Executive Director of the Belgian Interuniversity Center for Mobility, Transport & Logistics; Professor Ndiaye is an Expert Adviser of many national and international bodies such as the Board of the Belgian Federal College of Transport Operators, the EU Horizon2020 High Level Advisory Group for Transport, the EU Joint Research Center, the Horizon 2020 High Level Advisory Group for International Cooperation, the Norwegian Research Council, the Belgian Federal Government, the Board of the Cluster Transport & Logistics of the Walloon Government, the EU Urban Joint Programming Initiative, The Netherlands Research Council, The World Bank.

Certified Performance Management Professional, co-owner of a patented methodology for integrated strategic decision making, co-founder of two R&D start-up companies, Professor Ndiaye's skills are currently particularly oriented towards the innovative ways of integrating ideas from latest research with best practices for the identification, implementation and replication of value creative knowledge solutions; those enablers capable of driving transport, mobility and supply chains systems to a high level of excellence.

Dr. Ir. Milena JANJEVIC, a Polytechnical Engineer, holds a a Ph.D in Transport and Logistics Engineering and is a Senior Research Adviser and Lecturer at Qalinca-Labs, Université Libre de Bruxelles and Postdoctoral fellow at the MIT Megacity Logistics Lab (Boston). She is an invited Lecturer at Ecole des Mines (Paris) and a visiting scholar at the MIT Megacity Logistics Lab (Boston) and at the the Center of Excellence for Sustainable Urban Freight Systems at Rensselaer Polytechnic Institute (New-York). Her field of research and expertise which has been proven in a large number of local, regional, European and international projects include supply chain optimisation, intermodal transport/logistics and urban freight logistics with a particular focus on the modeling of innovative concepts/strategies and the use of new technologies.

MSc Haingo RABARIJAONA is a Master of Economics, Master of Management, Master of Transport and Logistics Science and PhD candidate at Qalinca-Labs, Universite Libre de Bruxelles. She is conducting advanced researches on freight logistics and more particularly in the design and management of medical radioisotopes supply chains.

Abstract

Perspectives in integrated supply chains performance management

A.-B. Ndiaye, M. Janjevic, H. Rabarijaona

Transport systems modelling and supply chain management, become important tools to streamline isotope transport. This talk presents key characteristics of radioisotopes supply chains as well as the critical challenges linked to the definition and management of its key performance indicators (KPI).
It aims at presenting some of the main challenges, trends and best practices with regards to the efficiency and the reliability of the delivery. By highlighting the performance dimensions and the numerous typical constraints, it sheds some light on the challenges laying ahead and research opportunities in the field to the optimization of the medical radioisotopes supply chains.

Pierre Dejonckheere

General Manager of TRANSRAD
Chairman of the AIPES Working Group Transport

Pierre Dejonckheere is graduated from the University of Brussels, Belgium, where he obtained his degree of electro-mechanical civil engineer in 1988. From 1989 until 2016, he assumed several operational and corporate positions within Engie, an international utilities company, in the field of the thermal power generation. He spent 5 years in Italy as responsible of the construction of a combined cycle plant (CCGT) and 3 years at the headquarter in Paris as performance engineer. From 2012 until 2016, he was member of the executive committee of the Business Unit Generation in charge of the performance of the power generation assets in Europe.
Since October 2016, he is the General Manager of TRANSRAD, Fleurus, Belgium. TRANSRAD is a transport company specialized in the class 7 goods, radioactive as well as nuclear. Since January 2019, he is the chairman of the AIPES Working Group Transport.

Abstract

The changing European landscape in the isotope transport sector

Rony Dresselaers

Director Security and Transport, FANC

Rony Dresselaers was awarded a Master's degree in industrial sciences, nuclear technology and radiochemistry from XIOS Hasselt in 1987. He is also holder of a post graduate in operations management of the University of Leuven.

From 1989 to 2007 he worked for FBFC International, a subsidiary of Areva producing UO2 and Mox fuel assemblies for nuclear reactors. At FBFC he held various positions in process engineering, project management and operations management. In his last position at FBFC International he was the manager for the uranium productions and member of the direction of the facility.

In 2008 he joined the Federal Agency for Nuclear Control as Director for the department of Nuclear Security and Transport. Within the FANC, the Security & Transport department is organised in 2 services. The nuclear security service is in charge of the nuclear security and the physical protection of radioactive materials including nuclear materials. The service has also responsibilities in the frame of safeguards and nuclear non - proliferation by ensuring the interface between the operators and the IAEA and Euratom inspectorates. The Import and Transport service is in charge of issuing the import and transport licences, package approvals certificates, ADR training and regulations.

At international level he is member of the International Steering Committee on denials of shipment and he is also nominated as a member of the Nuclear Security Guidance Committee both at the IAEA.

He is also an active member of the European Association for the Competent Authorities for the transport of radioactive materials.

In 2014 he was the chairman for the European Nuclear Security Regulators Association.

Abstract

Lessons learned since the new transport regulations came into effect

Michel Giot

Since 2006, **Michel Giot** is emeritus professor at the UCLouvain (Université catholique de Louvain, Louvain-la-Neuve, Belgium), where he got his doctoral degree in 1970. During his career as researcher, he was active in the field of multiphase phase flow and heat transfer with applications to nuclear safety (e.g. choked flow, fast transients) and the process industries (e.g. leak detection in pipes, pumping of manganese nodules). As teacher, among his contributions to engineering education, the course on nuclear thermal-hydraulics for the postgraduate students of the Belgian nuclear interuniversity programme was one of his a major achievements.

He was elected Dean of Engineering at UCLouvain from 1989 to 1994.

To-day, Michel GIOT is member of the Board of Governors of the Belgian Nuclear Research Centre (SCK•CEN), and active in several scientific advisory bodies like the Scientific Council of CEA/DEN (France), the Visiting Committee of IRSN (France), the Research Committee of PSI/NES (Switzerland), and the Scientific Council of Ionizing Radiation (FANC, Belgium). He also chairs the Scientific Committee of the International conferences on Advancements in Nuclear Instrumentation, Measurement Methods and their Applications (ANIMMA).

Wim Uyttenhove

PhD

Founder & Consulting Engineer, The Binding Energy

Senior Advisor, PM Risk-Crisis-Change

Dr. **Wim Uyttenhove** holds a PhD in nuclear engineering (TU Delft – The Netherlands), and a master in nuclear and mechanical engineering (Ghent University - Belgium). He has 15 years of experience in nuclear expert consultancy, project management, licensing, training, risk engineering and crisis resilience.

Wim launched in 2015 The Binding Energy, a start-up in strategical engineering and communication. The Binding Energy focuses on expert nuclear engineering and radiation protection consultancy, safety analyses and crisis resilience, trainings and business development. Their clients are dealing with complex technological risks, mainly active the nuclear and chemical industry.

Based on their common vision on risk and crisis management, The Binding Energy has a fruitful collaboration with PM Risk-Crisis-Change. PM is the Belgian reference in crisis management and communication. Since 15 years, they provide innovative consultancy, training, advice and support in all stages of the crisis timeline: before, during and after.

The collaboration with PM focuses on the implementation of a risk engineering and crisis resilient management system in companies dealing with complex technological risks.

Abstract

A crisis resilient nuclear organisation

Nuclear technology is a complex technology. Risk and crisis management should therefore be tightly coupled. Too many interdependencies exist to rely on conventional risk management techniques only to make your organisation crisis resilient.

An efficient crisis resilient management strategy is based on (daily) working principles, rather than on heavy procedures. A performant crisis team is flexible and scalable. It can be active on operational, management and communication level. Working principles are applicable on different types of crises.

In particular in a society with a polarised nuclear debate, communication efforts are essential before, during and after a crisis. Communication is always too late, but essential, as nuclear risks go far beyond the border of the organisation's premises.

André Luxen
Prof. Uliège, head of the GIGA Cyclotron Research Centre

Vicky Caveliers

Prof **Vicky Caveliers** is Head of the Radiopharmacy Unit at the University Hospital UZ Brussel and Professor at the In vivo Cellular and Molecular Imaging Laboratory (ICMI) at the Faculty of Medicine and Pharmacy of the VUB.
She is responsible for the preparation and quality control of PET and SPECT radiopharmaceuticals for routine patient administration. She is the coordinator of the Brussels Imaging Pharmacy (*BIP*) project, a centralized GMP-PET radiopharmacy within the Brussels region.

The research focus of the ICMI laboratory is on the development of new radiopharmaceuticals based on camelid single domain antibody fragments (also called VHH or Nanobodies) for diagnosis and radionuclide therapy applications. The main goal of the research is translation of these preclinically validated radiopharmaceuticals to early phase clinical trials, including fulfilling all regulatory requirements.

Zéna Wimana

Nuclear Medicine/Radiopharmacy, Institut Jules Bordet, ULB

Zéna Wimana obtained her PhD in Biomedical and Pharmaceutical sciences from the Université Libre de Bruxelles (ULB), where she currently teaches radiopharmacy. She became the coordinator of the radiopharmacy of the Jules Bordet Institute and contributed to the introduction of several radiopharmaceuticals in the clinic as premier in Belgium (eg. ^{177}Lu-DOTATATE, ^{68}Ga-PSMA,...). She is also a board member in different scientific and professional associations, including the Belgian Association of Radiopharmaceutical Reasearch (BARR) under the umbrella of the of the Belgian nuclear medicine society (BelNuc).

Tony Lahoutte

UZ Brussel, Head of department Nuclear Medicine

VUB, Head of the Molecular Imagang Research Unit

Prof Dr Tony Lahoutte is head of the department of nuclear medicine at UZ Brussel and head of the molecular imaging research unit at the Vrije Universiteit Brussel (VUB) in Belgium. In 2014 he co-founded the company Camel-IDS NV that is developing a pipeline of radio-immuno therapeutics where he is CSO. He obtained his medical degree in 1998 and started his research activities in combination with a residency program in nuclear medicine. His current research is focused on the development and clinical translation of molecular imaging probes and targeted radionuclide therapies for the detection and treatment of cancer.

Abstract

The Brussels RhadioTheranostics Platform

Personalized medicine has become the core paradigm in modern oncology, with a shift from one size fits all chemotherapy to a therapy that is tailored to the individual patient. Nuclear Medicine offers a unique opportunity for tailoring therapy, namely the radiotheranostic approach. In this approach the same molecule targeting a specific molecular biomarker of the tumor is used for both imaging and molecular radionuclide therapy. These radiotheranostics have shown great potential with improved outcomes for patients receiving the radiotheranostic compared to the standard treatments (eg. Netter-1).

In Belgium, the Institut Jules Bordet has been a major protagonist in the development and clinical introduction of radiotheranostics. On the other hand, the Vrije Universiteit Brussel has been at the forefront of innovative vectors based on single domain fragments (sdAbs).
Consequently, we decided to bring expertise and infrastructure together to create the Brussels RadioTheranostics Platform or 'BRTP'. The objectives of the BRTP are to (1) generate a wide range of innovative radiotheranostics as well as (2) explore the fundamental and applied aspects of radiobiology. The BRTP will lead to a network of scientist and clinicians in the Brussels region and foster exchange between academia and industry.
The combined forces and the new infrastructure will put the BRTP in a premier position with the ultimate goal of bringing the field of radiotheranostics to the forefront of oncology research.

Sam Voccia

PhD

Chief Scientific Officer, ANMI

Vice President Research & Developments Europe, Telix Pharmaceuticals

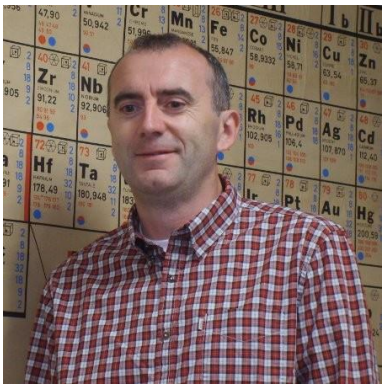
Sam has over 15 years' experience in the nuclear medicine industry and more particularly strong expertise in research and development, IP and project management. Former R&D manager in Trasis. He co-founded ANMI in 2015 where he acted as Chief Scientific Officer. He holds a PhD in Chemistry, Polymer and Material Sciences from the University of Liège

Abstract

Cold kits for radiopharmaceuticals - beyond SPECT

Cold kits are used for decades for the preparation of SPECT radiopharmaceuticals, being involved in more than 75% of the nuclear medicine procedure worldwide. With the recent availability of Ga-68 (from generator or cyclotrons), our field is at the dawn of a new era for PET, with a lot of remaining challenges. What are cold kits? Why are they attractive? How can they modify PET landscape and beyond? What are the main challenges ahead? These are a few interrogations that will be considered.

Joël Aerts



Joël Aerts studied chemistry and pharmacy in Liège University Belgium and got his PhD in 2008 in the field of PET tracers development. He has worked from 1998 as industrial pharmacist and radiopharmacist at Cyclotron Research Center of Liège, implementing GMPs and producing PET tracers with marketing authorization or for clinical trials. From 2013, he was Associate Professor at Paris-Diderot University/ INSERM U1148/ Bichat Hospital Paris. By the end of 2017, he joined the Luxembourg Hospital Center for the implementation of good pratices in radiopharmacy. He is belgian expert at EDQM.

Abstract

EU Regulations: practical impacts for radiopharmaceuticals

The radioactive products used in nuclear medicine are pharmaceuticals. The pharmaceutical regulations must thus be applied for the manufacture, the preparation and the use of radiopharmaceuticals. The purpose of this talk will be to rapidly review the most important authorities, regulations and quality referentials that have an impact in the practice of radiopharmacy by different actors (industries and hospitals).

Nadia Withofs

Dr **Nadia Withofs**, MD, PhD, received her medical degree from the University of Liege.
She did her residency in nuclear medicine in the division of nuclear nedicine and oncological imaging, department of medical physics at the University hospital of Liege.
She was research Scholar in the Pr. Sam S. Gambhir's laboratory in the Molecular Imaging Program at Stanford, USA.
She holds a PhD in medical sciences and investigated [18F]FPRGD2 PET/CT inaging of integrins.
She works in the division of nuclear nedicine the CHU of Liege and has a particular interest in imaging myeloma, prostate cancer and osteoarthritis.
She is currently the general secretary of the Belgian Society of Nuclear Medicine (BELNUC).

Thierry Vander Borght

Dr **Thierry Vander Borght** is head of the department of nuclear medicine at CHU UCL Namur, Godinne site, full professor at the Université catholique de Louvain (UCL) and invited professor at the Université de Namur (UNamur). He obtained his medical degree in 1986 and started his research project on the development of [2-11C]thymidine for measuring cellular proliferation during his residency program in nuclear medicine. Thanks to this work, he became doctor of biomedical sciences and received the Marie Curie award of the European Society of Nuclear Medicine. After spending one year in neurology, he spent more than 2 years at the University of Michigan to develop vesicular monoamine transporter (VMAT2) ligands for measuring dopamine neuron integrity. Back to Belgium at UCL, he defended his PhD degree and started research projects in both neurology and oncology. These two fields remain his major research interests.

Michael Parkes

Michael Parkes is a physiologist whose research and teaching has covered a wide range of expertise in physiology. His research on breath-holding and its breakpoint (Parkes, 2006;Parkes, 2012), and the technique he developed to enable unmedicated and conscious subjects to be mechanically ventilated (Cooper *et al.*, 2003;Cooper *et al.*, 2004) is now being applied to revolutionize radiotherapy treatment and medical imaging. This is to use a mechanical ventilator to regularize breathing during treatment (Parkes *et al.*, 2016c;West *et al.*, 2018) and to enable patients to perform single prolonged breath-holds safely for >5 minutes (Parkes *et al.*, 2014;Lens *et al.*, 2016;Parkes *et al.*, 2016a;Parkes *et al.*, 2016b).

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***Parkes**, M.J., Green, S., Stevens, A., Parveen, S., Stephens, R., & Clutton-Brock, T. (2016c). Reducing the within-patient variability of breathing for radiotherapy delivery in conscious, unsedated cancer patients using a mechanical ventilator. Br J Radiol 89, 20150741*

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Abstract

The safety, feasibility and optimization of multiple prolonged breath-holds (> 5 minutes) in radiotherapy

Parkes, [1, 2, 3] Michael John., Green[3], Stuart., Kilby, Warren[4], Cashmore, Jason[3]. Ghafoor, Qamar[3]., Clutton-Brock, Thomas Henry.[2, 5]

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Movement of thoracic and abdominal tumours with breathing remains a substantial problem in radiotherapy. One strategy to mitigate this is the use of multiple (10 or more?), short (about 20 seconds?) breath holds. Clinically this is increasingly successful (Boda-Heggemann *et al.*, 2016).

The physiology of breath-holding and its breakpoint (Parkes, 2006) is not normally taught in medical schools, because until now it had no clinical application. So there is no widespread clinical awareness of what breath-holding features are safe and feasible for patients.

We have previously demonstrated that 37 to 74 year old patients with breast cancer, and healthy volunteers, can safely perform single prolonged breath-holds of over 5 minutes (Parkes *et al.*, 2014;Parkes *et al.*, 2016a)). This is easily achieved using pre-oxygenation and hypocapnia (breathing 60% oxygen, with hypocapnia induced via a facemask and mechanical ventilator).

We now demonstrate that healthy volunteers can safely perform up 9 multiple prolonged breath-holds, each of 4.3 ±2 minutes mean duration, in a single session (Parkes *et al.*, 2019). The mean recovery time between breath-holds is 3.1 ±0.2 minutes. Furthermore, the 9th breath-hold is as easy (as long, 6.0 ±0.3 minutes) as their original single prolonged breath-hold (mean duration 6.1 ±0.3 minutes).

In other words, we can safely offer 41 minutes of radiotherapy treatment time (breath-holding) in one 65 minute treatment session.

I will discuss how easy it is to train patients how to do this. There is a further advantage for radiotherapy delivery of our mechanical ventilation technique. This is that it results in patients breathing in an almost perfectly regular breathing pattern (over a wide range of imposed frequencies or inflation volumes) for periods of up to 1 hour (Parkes *et al.*, 2016b). This too has important implications for mitigating respiratory movement during breath-holding.

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Stefaan Vandenberghe

Prof. Dr. **Stefaan Vandenberghe** obtained his MSc in Physics in 1996 and an additional degree in Biomedical Engineering in 1997 from KU Leuven. After working in the nuclear medicine department of the University Hospital Ghent (1997-1999) he started a Ph.D. in the MEDISIP group on the optimal configuration of gamma cameras for PET imaging and on list-mode reconstruction techniques for PET systems. He received a Ph.D. (Engineering) from this university in 2002. During his FWO postdoctoral research (BAEF) he worked on rotating slat systems (with solid state detectors) Monte Carlo simulations and natural pixel reconstruction. In 2004 he joined Philips Research USA (Briarcliff) to work as a Senior Scientist in the Clinical Site Program at the University of Pennsylvania (Dr. Joel Karp) in Philadelphia to work on simulations, reconstructions and measurements for Time-Of- Flight PET systems (LaBr3 and LYSO). At the end of 2005 he returned to Belgium to work on Monte Carlo simulations, rotating slat SPECT, Time-of-Flight PET, PET-MRI and quantification for radionuclide dosimetry. He has been appointed as full time research professor (BOF-ZAP) at UGent since October 2007 and leads the MEDISIP research group since 2008. He has co-authored about 100 scientific A1 journal papers and four patents. He was Associate Editor of IEEE Transactions on Nuclear Science (till 2017) and involved in conferences and workshop on PET-MR and SPECT-MR. During the last years his research was onattenuation correction and PET system design simulations for PET-MR in two EU-FP7 projects Hyperimage and Sublima. Together with Christian Vanhove he leads the small animal molecular imaging facility (Infinity) of Ugent. The detector technology and micro SPECT and PET prototypes of the MEDISIP research group have led to the creation of the spinoff company Molecubes. Since 2017 he is also the editor-in-chief of EJNMMI Physics and coordinates together with the Nuclear medicine unit the Innovative Imaging and Therapy Consortium of Ghent university and its hospital (Imitghent.be). He received the EANM 2007 Marie Curie Young investigator award and the Barco scientific award in 2003 for his PhD.

Abstract

Total body PET – from mice to man

The idea of a very sensitive Positron emission tomography (PET) system covering a large portion of the body of a patient already dates back to the early 90s. In the period 1990-2010 only some prototypes have been built, which never resulted in systems used for clinical research. One of the reasons were the limitations in the available detector technology, which did not yet have sufficient energy resolution, timing resolution or countrate capabilities for fully exploiting the benefits of a long axial FOV design. Total body PET is an old theoretical concept but has recently been realised for humans or other subjects of this size. In 2016 the development of total body PET system with a 2 m long axial FOV at UCDavis (California) and a 1,4 m long axial FOV at UPENN (Philadelphia) has been initiated. Both are based on similar detector technology as existing clinical scanners. Each of these US projects is focusing on one specific aspect. UC Davis is developing the longest system (push highest sensitivity and axial FOV), UPenn is developing the system with the best timing resolution (push limits of TOF with ~220 ps). UGent has started a project for building clinical PET technology for the best spatial resolution of about ~2mm with Depth-of-Interaction (DOI).

This presentation gives an overview of the recent developments with regards to PET scanners with a long axial Field of view covering at least the majority of the body (so called Total Body PET systems). After explaining the benefits and challenges of total body PET systems, the different total body PET system designs proposed for clinical imaging are described in detail. The axial length is one of the major factors determining the total cost of the system but there are also other options in detector technology, design and processing for reducing the cost these systems. The limitations and advantages of different designs for research and clinical use are discussed taking into account potential applications and the increased cost of these systems.

Kristoff Muylle

University Hospital Brussels (UZ Brussel)

After completion of his medical studies in 1999 and his training in Nuclear Medicine in 2004 at the Free University of Brussels (VUB), **Kristoff Muylle** started his professional career at the Jules Bordet Cancer Institute in Brussels, where his work mainly focused on clinical and research activities related to nuclear medicine procedures in (hemato-)oncology with a specific interest in radioimmunotherapy and immuno-PET. In 2015, he joined the clinical staff of the nuclear medicine department at the University Hospital of Brussels (UZ Brussel) and combines this activity with a position as nuclear medicine physician at AZ Delta in Roeselare since July 2018.

Kristoff Muylle was President of the Belgian Society of Nuclear Medicine from 4/2014 until 4/2016. He joined the Board of the European Association of Nuclear Medicine (EANM) as President-Elect in 2015 and served as EANM President in 2017 and 2018.

Abstract

Impact of nuclear medicine on personalised patient management

Patient selection by molecular characterization of disease subtype in an individual patient becomes increasingly important to avoid unnecessary toxicity, improve patient outcome and reduce the costs for clinical trials. Biomarkers are objectively measured indicators of biological and pathogenic processes and can be used to predict patient outcome (regardless of therapy), to predict response to specific therapies and for response assessment (monitoring). The advantages of imaging biomarkers over those that require a biopsy sample include non-invasiveness, the ability to quantify cellular targets for the entire disease burden, and thereby to avoid the sampling error that can occur with heterogeneous receptor expression and the potential for serial studies of the in vivo effects of a drug on the target.
The scope of this presentation is to highlight the potential of nuclear medicine for image guided patient-tailored therapy and to illustrate its impact by examples in the management of breast cancer patients.

Pieter De Bondt

Isotopes in medical imaging: past, present and future

Serge Goossens

Serge Goossens has an extended experience in transport and logistic of medical isotopes in Europe and the US. Prior joining MEDraysintell as co-author and advisor, he was the CEO, until September 2017, of Isotopes Services International, a company he founded in 1988 in Belgium. He also co-founded ISOVital in France; both companies are active in the international distribution of radioactive isotopes for the pharmaceutical market. Serge was also the president of EITA (European Isotopes Transport Association) until March 2018, a non-profit association focusing on transport and handling of radioactive isotopes, which he co-founded in 1998. He co-organized the Symposiums on Medical Isotopes (Belgium) and was an active member of AIPES (Association of Imaging Producers & Equipment Suppliers) transport working group until 2018.

Abstracts posters

Digestion Mechanism of UAlx Fuel in Alkaline Solution for Isotope Production

Authors

Andrew Cea[1,2], Ann Leenaers[1], Sven Van den Berghe[1], Thomas Pardoen[2]

Affiliations

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[2] Université catholique de Louvain, Institute of Mechanics, Materials and Civil Engineering, Belgium

Abstract

ROMOL-99 is a well-known process to recover medical isotopes from irradiated UAlx fuel. An alkaline solution is used to digest UAlx dispersion targets to convert the fuel into sodium diuranate (NaDU), releasing the isotopes into the solution. Despite its crucial role in isotope production, little is known about the fuel digestion or corrosion kinetics and mechanism. To study the evolution of digested fuel, experiments were performed on ground UAl_2, UAl_3, and mixed fuel. Digestions were preformed in 4M and 8M of NaOH for two hours at 95°C. The conversion of UAlx to NaDU was interrupted at various digestion times by aliquoting the digestion solution from the digestion vessel. The samples were immediately cold quenched to 4°C and neutralized to arrest the reaction. The quenched samples were embedded, cut, and polished to expose how digestion or corrosion proceeded throughout the material and was examined by scanning electron microscopy (SEM), energy dispersive spectroscopy (EDX), and X-ray powder diffraction (XRD). The SEM/EDX cross-sections of digested fuel particles revealed three distinct stages of digestion for pure UAL_3 fuel particles: 1) Surface Corrosion was found to occur during the first 10 minutes of digestion. A corrosion layer formed only a few micrometers in thickness before the surface was passivated. 2) Corrosion at grain boundary triple junctions (TJs) occurred after 15 minutes. Corrosion of TJs occurred deep in the fuel particles and were indiscriminate on TJ type. 3) Intergranular corrosion along grain boundaries (GBs). GB corrosion connected the corroded TJs to form a percolation network and proceeded until the fuel particle was completely digested. Total corrosion of large UAl_3 particles (D>100µm) was observed in 8M NaOH solution for 2hrs. In contrast, only surface corrosion of UAl_2 was visible in the same conditions with no noticeable TJ or GB corrosion. Results presented here demonstrate the importance of microstructure on digestion rates and the optimal conditions for the complete digestion of UAl_3.

Combining multi-product commercial production in a GMP environment with Clinical & R&D activities

Authors

Gameiro[1], Cristiana; Bormans[2], Guy; Abrunhosa[3], Antero; [4]Luurtsema, G. and Elsinga[4], Philip

Affiliations

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[2] PET Center, University of Leuven/BE;
[3]ICNAS, University of Coimbra/PT;
[4]Medical Imaging Centre, University of Groningen/NL;

Abstract

Radiopharmaceutical facilities mostly provide [^{18}F]FDG and are progressively evolving into multi-product sites to support new developments and R&D programs. In this paper, three successful sites in Europe handling both routine production and R&D activities will be described.

ICNAS is a research unit of the University of Coimbra in Portugal that hosts a GMP-compliant PET production facility, which supports clinical and pre-clinical R&D programs and supplies RPs to nearby hospitals. The unit is in operation for distribution since 2012 and currently has 5 radiopharmaceuticals (RPs) authorized in the market ([^{18}F] FDG, ([^{18}F] FCH, [^{18}F]NaF, and [^{68}Ga]DOTA-NOC and [^{68}Ga]PSMA). All produced with the Synthera® platform, which in total represents over 5000 cycles. An extensive R&D program is in place with production of other tracers based on ^{18}F (F-DOPA), [^{13}N]NH_3, ^{11}C (Methionine, Raclopride, Flumazenil, PK11195, β-CIT and PiB) and ^{6}4Cu -ATSM.

The PET centre of the KU Leuven has been operating for 28 years producing several radiopharmaceuticals for routine use; such as: [^{13}N]NH3, [^{18}F]FDG, [^{18}F]-FET, [^{15}O]H_2O, [^{11}C]methionine, [^{11}C]-PiB. The PET center has a strong cooperation with several pharmaceutical companies (Merck, J&J, UCB among others) supporting their drug development mainly in the CNS area. Recently, the center has built GMP laboratories to meet the evolving strict pharmaceutical regulations. Besides, the non-GMP lab is used for radiochemistry and radiopharmaceutical research and tracer production for non-clinical applications.

The Medical Imaging Center of University of Groningen, in the Netherlands, is one the most active centers in Nuclear Medicine. The center has been producing routinely a wide range of radiopharmaceuticals since 1992; [^{18}F]FDG, [^{18}F]FDOPA (electrophilic), [^{18}F]NaF, [^{18}F]FES and [^{18}F]PSMA, [^{68}Ga]DOTATOC, and also [^{11}C]choline, [^{11}C]methionine, [^{11}C]PiB, and [^{13}N]NH_3. The center combines the routine production with an intense program covering basic research, pre-clinical and clinical research studies in several areas (basic radiochemistry, neurology oncology, and cardiology). The most frequent produced ^{18}F-tracers are [^{18}F]FDG, [^{18}F]NaF, [^{18}F]PSMA and [^{18}F]FEOBV. They are all produced on dedicated Synthera synthesis modules. Currently, [^{18}F]FDOPA (nucleophilic) and [^{18}F]FES are under development using the same type of Synthera platform.

The three centers described have demonstrated that the combination of routine GMP production of multiple radiopharmaceuticals and a busy research program can be successfully achieved.

An overview of SCK•CEN's NURA projects on radioisotope purification and radiopharmaceutical drug development

Authors

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Abstract

In recent years, the Belgian nuclear research centre SCK•CEN has extended its R&D activities into radioisotopes for medical applications. Various projects focusing on different aspects are coordinated by the NURA program, aimed at production and purification of radioisotopes on one hand and development and preclinical testing of new radiopharmaceuticals on the other hand. The abstract attempts to overview the currently on-going PhD research projects on radioisotope purification, radiopharmaceutical development and preclinical testing.

Radioisotopes of interest include alpha emitters Ac-225 and Bi-213 and beta emitters Lu-177, Re-188, Tb-161 and Sm-153. Except for Ac-225, these nuclides emit gamma rays that can be used for diagnostic purposes and real-time imaging of therapeutic treatment follow-up. Radiopharmaceuticals under development all envisage a targeted approach, in which the radionuclide is bound via a chelator molecule to an antibody or small molecule that targets specific receptors on cancer cells. In this way, the potential of precursor drugs for the treatment of various cancer types, such as colorectal cancer, prostate cancer, breast and ovarian cancer and treatment of neuroendocrine tumors is evaluated. Research efforts are directed towards improved radiopharmaceutical performance in various ways: first, in terms of increased radiation dose delivered to the tumor cell, by for example the combined use of Lu-177 and radiosensitizing Au nanoparticles, both bound to an antibody; second, in terms of exploration of the therapeutic value of Tb-161 and Re-188, nuclides which are far less studied than alternative nuclides Lu-177 and Tc-99m with similar half-lifes, respectively. The third focus is on development of new chelators that increase in vivo stability and improve the tumor to kidney uptake ratio through optimization of the radiopharmaceutical design.

Efforts into radiopharmaceutical design must be complemented with establishing ways of reliable production and purification of target nuclides. Alpha emitters Ac-225 and Bi-213 can be obtained in pure fractions by cation exchange chromatography, however, commercially available resins degrade under the high radiation doses of permanently bound Ac-225. We aim to synthesize activated carbon based resins that can be used as an alternative to conventional resins. Radiolanthanides are far more difficult to separate from a neighboring lanthanide in case of high purity demands and large differences in concentrations. Therefore, prior to chromatographic purification, an initial step to either (electro)chemically oxidize (Tb-161) or reduce (Eu-154 impurity in Sm-153) one component of the mixture allows to chromatographically separate both lanthanides from each

other with much larger separation factors, improving efficiency and robustness of the purification method.

Electrochemical Oxidation of Terbium – the future of high purity Tb-161 for medical applications

Authors
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Abstract

Several lanthanide radionuclides show favorable decay properties, energies and half-lives to be used in noninvasive diagnostic or therapeutic purposes in nuclear medicine. Among them, terbium has four clinically interesting isotopes offering complementary decay characteristics making them favorable for α-, β- targeted radionuclide therapy and PET, SPECT diagnosis applications: ^{149}Tb ($T_{1/2}$ 4.16 h, α-decay), ^{152}Tb ($T_{1/2}$ 17.5 h, β^+-decay), ^{155}Tb ($T_{1/2}$ 5.32 d, E.C.), and ^{161}Tb ($T_{1/2}$ 6.89 d, β^--decay) [1]. Currently, carrier free ^{161}Tb can be produced via neutron irradiation of highly enriched ^{160}Gd targets in the Belgian Reactor 2 (BR2) at SCK•CEN. In this process ^{161}Tb is synthesized by β-decay of the short-lived intermediate ^{161}Gd following the ^{160}Gd (n,γ) ^{161}Gd nuclear reaction, and part of the produced ^{161}Tb will decay to the stable ^{161}Dy. Therefore, isolation and purification of ^{161}Tb from the target material and other radiolanthanides is necessary.

The separation process for the neighboring lanthanides is challenging due to their similar chemical properties – having similar ionic radii and a stable trivalent oxidation state in solution. There already exists a well-defined column separation protocol based on ion exchange by using eluent α-HIBA, providing high efficiency in separation of micro amounts ^{161}Tb [2]. Yet, the complete separation cannot be achieved by this method, and implementation to macro amounts results in peak tailing and broadening.

In order to achieve high separation factors, the strategy is to change the chemical properties of terbium by oxidizing Tb(III) to its tetravalent state prior to the separation. Previous works have shown that Tb(III) can be oxidized in aqueous media by chemical or electrochemical methods. Furthermore, Tb(IV) can be stabilized in the solution despite its high redox potential inducing possible back-reduction (E^0:+3.1V vs SHE). To avoid further contamination by redox chemicals that could inhibit radiolabeling protocols, the strategy is to use electrochemical methods in order to oxidize Tb(III) to Tb(IV). Following the electrochemical oxidation a compatible separation method will be developed. The first experimental results on the electrolysis experiments show that Tb(III) can be oxidized to Tb(IV) and stabilized in carbonate and periodate media at alkaline conditions. Preliminary tests on solvent extraction by using ionic liquids as the extractant are also conducted. Further investigation will be conducted to find a suitable extractant with high selectivity towards the Tb tetravalent oxidation state in alkaline media.

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Supported ionic liquid phases for the purification of medical samarium-153

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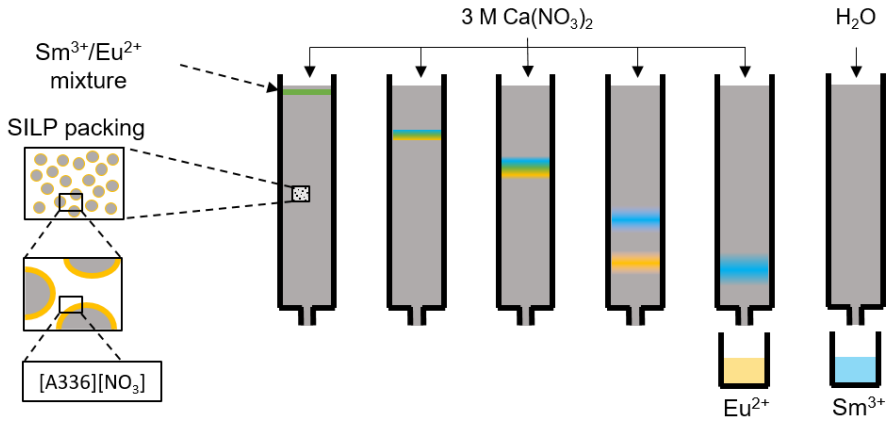
Abstract
Samarium-153 is a medical radionuclide that serves in nuclear medicine for bone pain palliation or imaging of the skeleton, and is produced in a nuclear research reactor by irradiation of an enriched samarium-152 target with a high flux of thermal neutrons. However, long-lived europium-154 impurities are formed concurrently, which restricts the use of the samarium-153 radiopharmaceutical. Previously, a solvent extraction method was developed to separate samarium and europium efficiently by making use of the undiluted ionic liquid [A336][NO_3]. Current research efforts investigated the feasibility to convert the separation method to an extraction chromatography application, taking advantage of solid phase extraction techniques. TEVA particles, where the ionic liquid is immobilized onto a solid support, served as the stationary phase in the column. In a first step, Eu^{3+} is reduced to Eu^{2+} in a concentrated nitrate salt solution prior to the separation step. After loading of the feed solution onto the extraction chromatography column, Eu^{2+} is not retained by the TEVA particles upon elution with a concentrated nitrate salt solution, whereas Sm^{3+} is extracted to the ionic liquid layer. Sm^{3+} can be efficiently removed from the column by elution with water, hence yielding a simple, yet efficient separation method. Using this approach, more than 85% of the initial europium content could be removed from samarium in a single run and a short period of time.



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Radiolabeling of gold nanoparticles with Lu-177 as a platform for cancer theranostics

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Abstract
Cancer is among the leading causes of mortality worldwide. Currently, the conventional therapeutic approaches are surgical removal combined with chemo- and/or radiotherapy. However, despite the recent advances in cancer therapy, a significant number of patients still experience tumor recurrence and have serious side effects due to damage to the healthy tissues. Therefore, there is a need to develop new strategies that allow a more efficient cancer cell killing, while sparing surrounding healthy tissues.
In cancer radiotherapy, gold nanoparticles have emerged as promising radiosensitizers, which accumulate in the tumor and increase the effectiveness of external beam radiotherapy by local production of reactive oxygen species (ROS) and secondary electrons upon irradiation. Five nm gold nanoparticles surrounded by an organic shell of polyallylamine are produced by plasma vapor deposition and are conjugated to anti-EGFR-antibodies (Cetuximab) for active tumor targeting (AuNPs-PAA-Ctxb). In order to increase the therapeutic effect of the AuNPs-PAA-Ctxb, we aim to radiolabel the nanoparticles with 177-Lu. In a first approach, we conjugated Cetuximab to bifunctional chelators (BFC) DOTA and DTPA. MALDI-ToF MS analysis indicated that a 20, 40 and 80 molar excess addition of the bifunctional chelator to the labeling reaction, leads to an increasing BFC:antibody ratio of 2, 3 and 5, respectively. However, a 40 and 80 molar BFC excess profoundly reduced the binding capacity of Cetuximab to EGFR-overexpressing A431 cells. A radiochemical purity of > 95% was achieved after 3h at 50°C for Cetuximab-DOTA-Lu-177 or instantly at room temperature for Cetuximab-DTPA-Lu177. Moreover, both radiolabeled immuno-complexes were stable for at least 3 days in serum at 37°C. In addition, we showed that Cetuximab-DOTA and Cetuximab-DTPA lose their target binding capacity when subsequently conjugated to gold nanoparticles. Therefore, in a second approach, we will link Cetuximab-conjugated gold nanoparticleswith DOTA and DTPA and investigate the binding capacity of this nanoconjugate to A431 cells.
When successful radiolabeling of AuNPs-PAA-Ctxb is achieved and the target binding capacity of the nanoconjugates is preserved, further experiments can be conducted to investigate the specificity of the enhanced cancer cell killing effect on EGFR-overexpressing A431 cells. Furthermore, the biodistribution and the therapeutic effect of the radiolabeled AuNPs-PAA-Ctxb-^{177}Lu could be assessed after injection in tumor-bearing mice.

Investigation of productions of some PET radioisotopes in particle accelerators

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Abstract

We investigated the production of some radioisotopes used in PET via particle accelerators. For this aim, the cross-sections, the activities, yield of products and integral yields of each reaction process were simulated and calculated under certain conditions such as particle beam current of 1 μA, irradiation time of 1 h, in the energy range Eparticle=100→1 MeV. The obtained results compared with experimental data in the literature. Based on these results, the productions of PET radioisotopes in particle accelerator were discussed [1-5].

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In vitro and *in vivo* evaluation of the anti-HER2 nanobody labeling with the α-particle emitter bismuth-213

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Abstract

Introduction: Survival from metastatic breast cancer remains poor, particularly due to the impossibility to penetrate through the whole tumor. The use of nanobodies (Nbs) as vehicles in targeted radionuclide therapy has gained traction due to their excellent in vivo properties, high affinity and fast clearance kinetics. Moreover, Nbs show good (homogeneous) tumor penetration due to their small size and conformational structure. This study investigates a novel targeted radionuclide therapy, which combines the α-emitter bismuth-213 (^{213}Bi) and a HER2-targeting nanobody (Nb) to selectively kill HER2^{pos} metastases in breast cancer. **Methods:** First, a ^{213}Bi-labeled-Nb was developed using p-SCN-Bn-CHX-A''–DTPA as bifunctional chelator for complexing ^{213}Bi and conjugating the complex to the anti-HER2 Nb. *In vitro* saturation binding assay, clonogenic assay, IncuCyte® live cell imaging and double strand break e*x vivo* immunofluorescence staining were performed on HER2^{pos} cells to determine the affinity and cytotoxicity of [^{213}Bi]DTPA-Nb. The biodistribution of [^{213}Bi]DTPA-Nb was analyzed in relevant mouse models. **Results:** Under optimized labeling conditions, [^{213}Bi]DTPA-Nb remained stable up to 100 min with a radiochemical purity ≥95% in PBS at room temperature and 37 °C. *In vitro,* [^{213}Bi]DTPA-Nb bound specifically to the HER2^{pos} SKOV-3 cells with a K_D of 5.06 ± 1.19 nM. High tumor uptake was reached 15 min after injection of [^{213}Bi]DTPA-Nb in HER2^{+} tumor-bearing mice. Extremely low uptake values were observed in normal tissues at all time points. [^{213}Bi]DTPA-Nb was excreted via the kidney into the urine, leading to significant kidney retention of the radioconjugate of 59.9 ± 5.1%ID/g after 60 min. Co-infusion of 150mg/kg gelofusine resulted in a 2-fold reduction in kidney uptake. The injection of unlabeled anti-HER2 Nb 30 min prior to injection of [^{213}Bi]DTPA-Nb reduced the tumor uptake by 50% and a significant decrease in double strand DNA damage was observed compared to the group that did not receive a pre-injection. **Conclusion:** Here we describe for the very first time the successful labeling of an anti-HER2 Nb with an α-emitter, ^{213}Bi, using a DTPA derivative, resulting in high yields with excellent preservation of affinity for its HER2 target, high *in vivo* stability and high

tumor-to-background ratios. This study shows that [^{213}Bi]DTPA-Nb is a promising new radioconjugate for targeted α-particle therapy and supports its further development.