Calibration of HPGe–HPGe coincidence spectrometer through performing standardisation of $^{125}\text{I}$ activity by X-ray-gamma coincidence spectrometry using two HPGe detectors

An X-ray-gamma coincidence measurement method for efficiency calibration of a HPGe–HPGe system, using the methodology for activity standardisation of $^{125}\text{I}$, has been developed. By taking one list-mode time-stamped measurement of the $^{125}\text{I}$ source, six spectra were generated in post-processing: total spectra, coincidence spectra and energy gated coincidence spectra for each of the two detectors. The method provides enough observables for source activity to be determined without a prior knowledge of the detector efficiencies. In addition, once the source is calibrated in this way the same spectra can also be used to perform efficiency calibration of the individual detectors in the low energy range. This new methodology for source activity determination is an alternative to the already established X-ray-(X-ray, gamma) coincidence counting method; with two NaI(Tl) detectors and the sum-peak method using a single HPGe detector. When compared to the coincidence counting method using two NaI(Tl) detectors, the newly developed method displays improved energy resolution of HPGe detectors combined with measurement of only full peak areas, without the need for total efficiency determination. This enables activity determination even in presence of other gamma emitters in the sample. Standard coincidence counting with NaI(Tl) detectors provides lower uncertainties. The method has been used for calibration of a coincidence HPGe spectrometer in the low energy range of $^{125}\text{I}$ and fine adjustments of a Monte Carlo model of the coincidence system.
Challenges associated with the behaviour of radioactive particles in the environment

A series of different nuclear sources associated with the nuclear weapon and fuel cycles have contributed to the release of radioactive particles to the environment. Following nuclear weapon tests, safety tests, conventional destruction of weapons, reactor explosions and fires, a major fraction of released refractory radionuclides such as uranium (U) and plutonium (Pu) were present as entities ranging from sub microns to fragments. Furthermore, radioactive particles and colloids have been released from reprocessing facilities and civil reactors, from radioactive waste dumped at sea, and from NORM sites. Thus, whenever refractory radionuclides are released to the environment following nuclear events, radioactive particles should be expected. Results from many years of research have shown that particle characteristics such as elemental composition depend on the source, while characteristics such as particle size distribution, structure, and oxidation state influencing ecosystem transfer depend also on the release scenarios. When radioactive particles are deposited in the environment, weathering processes occur and associated radionuclides are subsequently mobilized, changing the apparent Kd. Thus, particles retained in soils or sediments are unevenly distributed, and dissolution of radionuclides from particles may be partial. For areas affected by particle contamination, the inventories can therefore be underestimated, and impact and risk assessments may suffer from unacceptable large uncertainties if radioactive particles are ignored. To integrate radioactive particles into environmental impact assessments, key challenges include the linking of particle characteristics to specific sources, to ecosystem transfer, and to uptake and retention in biological systems. To elucidate these issues, the EC-funded COMET and RATE projects and the IAEA Coordinated Research Program on particles have revisited selected contaminated sites and archive samples. This COMET position paper summarizes new knowledge on key sources that have contributed to particle releases, including particle characteristics based on advanced techniques, with emphasis on particle weathering processes as well as on heterogeneities in biological samples to evaluate potential uptake and retention of radioactive particles.

General information
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Organisations: Center for Nuclear Technologies, The Hevesy Laboratory, Radioecology and Tracer Studies, Norwegian University of Life Sciences, Australian Nuclear Science and Technology Organisation, University of Seville, Centro de Investigaciones Energeticas, Medioambientales y Tecnologicas
Authors: Salbu, B. (Ekstern), Kashparov, V. (Ekstern), Lind, O. C. (Ekstern), Garcia-Tenorio, R. (Ekstern), Johansen, M. P. (Ekstern), Child, D. P. (Ekstern), Roos, P. (Intern), Sancho, C. (Ekstern)
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Scopus rating (2016): CiteScore 2.39 SJR 0.956 SNIP 1.488
Web of Science (2016): Impact factor 2.31
Web of Science (2016): Indexed yes
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Scopus rating (2015): SJR 1.147 SNIP 1.555 CiteScore 2.62
Characterisation of an ultra low-background point contact HPGe well-detector for an underground laboratory

Since a few years there are well-type HPGe-detectors with a small, point-like, anode contacts available commercially. This paper describes the characterisation of the first ultra low-background, so-called, SAGe™ well detector with regards to resolution and background performance. Inside a passive lead/copper shield in the underground laboratory HADES a background count rate of $690 \pm 6$ d$^{-1}$ ($268 \pm 3$ d$^{-1}$ per kg Ge) was recorded 19 months after taking it underground.

General information

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Organisations: Center for Nuclear Technologies, The Hevesy Laboratory, Radioecology and Tracer Studies, European Commission Joint Research Centre Institute
Authors: Hult, M. (Ekstern), Marissens, G. (Ekstern), Stroh, H. (Ekstern), Lutter, G. (Ekstern), Tzika, F. (Ekstern), Markovic, N. (Intern)
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Web of Science (2017): Indexed yes
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Web of Science (2016): Indexed yes
BFI (2015): BFI-level 1
Scopus rating (2015): SJR 0.547 SNIP 0.999 CiteScore 1.15
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ISI indexed (2013): ISI indexed yes
Web of Science (2013): Indexed yes
BFI (2012): BFI-level 1
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ISI indexed (2012): ISI indexed yes
Web of Science (2012): Indexed yes
BFI (2011): BFI-level 1
Scopus rating (2011): SJR 0.644 SNIP 1.137 CiteScore 1.21
Web of Science (2011): Impact factor 1.172
ISI indexed (2011): ISI indexed yes
Web of Science (2011): Indexed yes
BFI (2010): BFI-level 1
Scopus rating (2010): SJR 0.715 SNIP 1.098
Web of Science (2010): Impact factor 0.999
Coincidence methods in gamma-ray spectrometry for radioecological applications

Gamma spectrometry is one of the most powerful radiometric techniques available. The nondestructive method enables both quantitative determination and identification of the majority of radioisotopes. Compared to other radiometric techniques, it has a great advantage in being able to detect minor isotopes, even in the presence of a large background from a multitude of other radioactive elements without any need for separating the isotopes. This has enabled the technique to be used as the standard tool in nearly all disciplines where radioisotopes are analyzed.

The technique plays an important role in environmental radioactivity, nuclear safety and reactor monitoring, nuclear medicine, isotope geology… Gamma spectrometric analysis of artificial radioisotopes in man (whole body counting) has improved the understanding of human metabolism, while the analysis of the very same radioisotopes in sea water has shed light on Arctic Ocean water circulation.

All of this is thanks to a deliberate and continuous effort to improve the technique over the years. With improvements in energy resolution, detector size and performance, coupled to better background reduction, studies of new phenomena in environmental radioactivity have become possible. Not seldom have these improvements occurred suddenly though discrete events. The introduction of digital signal processing in gamma spectrometry is definitely one such event, and it will, in the next coming years, revolutionize the way in which we acquire information through environmental gamma spectrometry.

Up till now, gamma spectra were measured in a way that the energy deposited in a detector was measured with an analogue chain (preamplifier, amplifier, ADC), events were saved in computer memory with its energy and arranged into a histogram called spectrum. With digital list-mode systems each event is saved with its energy and time-stamp when the event happened. In simple words, the difference between the standard gamma spectrum and time-stamped list-mode file can be compared to a difference between the long exposition photography and a video.

Coincidence gamma spectrometry exists from the early-days of nuclear research, but the complexity of such systems usually limited its use to large experiments or highly specialized applications. The systems needed delicate tuning for each particular experiment, and once the system was set-up and working, making changes was a cumbersome procedure. Often a change of a single cable (in a fast signal branch) made the system not working. With digital listmode gamma spectrometry, once the acquisition parameters are adjusted and the sample is measured, all the coincidence settings can be tested in post-processing. That means if different coincidence timing or energy gating is needed, it takes only minutes.
to generate a new spectrum, in contrast to ‘standard’ approach where the new measurement needed to be done (often a long time measurement if we’re dealing with low activity levels). That significantly simplified the process of setting up coincidence experiment. Widespread use of the field-programmable gate array (FPGA) technology led to reduction in size and price. A single digital unit replaced a whole set of special analogue units (like CFD, TAC, Coincidence unit, delay unit, shaper...). Small physical size enables integration of coincidence system to mobile (or hand-held) instruments. All that will make changes to gamma spectrometry in coming years, which cannot even be foreseen. Even now some producers are completely stopping the manufacturing of standard analogue NIM bin modules, although the use of time-stamping is still at its start. Developments of IEC standard for list-mode data acquisition will certainly speed-up the things by making the implementation of the new technology into laboratory even easier. The standard will make the implementation easy, enabling universal coincidence acquisition and analysis software, in contrast to current approach where the most groups are developing its own software.

This thesis reveals some promising aspects of digital-list mode acquisition systems when applied to gamma spectrometry, from low-level measurements, where it can be used with veto detectors or multiple HPGe detectors for background reduction and efficiency enhancement, to measurements of high activity levels where, in some cases, coincidence signals with narrow energy gating, enable extraction of weaker signal hidden in high activity matrix. The use of a sum-coincidence mode resulted in 17% efficiency increase. Summing of coincident events energies reconstructed the full energy of a photon Compton scattered between two detectors. Applying anticoincidence setting enables better sensitivity for 210Pb determination by reducing background continuum for ~15%. The two abovementioned methods can be applied also for low or ultra low-level measurements. For high activity samples, narrow energy window gates combined with coincidence gating resulted in almost complete background reduction, revealing the 605 keV 134Cs peak under high 137Cs background. This approach seems promising for determination of impurities in radiopharmaceuticals or characterization of decommissioning samples.

Application of digital systems in activity standardization measurements with liquid scintillation counting (LSC) has become a standard, but its introduction to photon-photon coincidence techniques is still pending full recognition. The last chapter gives some reasoning on possible ways how it could be done. Primary standardization method for 125I using two NaI(Tl) detectors has been set-up at the Radioecology Section. New standardization method for 125I based on two HPGe detectors has been developed. The method, although inferior in precision compared to NaI(Tl) method, has an advantage of not relying on total count rate measurement allowing 125I activity standardization in the presence of impurities. Review of 60Co standardization method is presented with a theoretical solution for extension to 134Cs gamma-gamma standardization.

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State: Published
Organisations: Center for Nuclear Technologies, The Hevesy Laboratory, Radioecology and Tracer Studies
Authors: Markovic, N. (Intern)
Number of pages: 110
Publication date: 2018

Comparison of experimental and calculated shielding factors for modular buildings in a radioactive fallout scenario
Experimentally and theoretically determined shielding factors for a common light construction dwelling type were obtained and compared. Sources of the gamma-emitting radionuclides 60Co and 137Cs were positioned around and on top of a modular building to represent homogeneous fallout. The modular building used was a standard prefabricated structure obtained from a commercial manufacturer. Four reference positions for the gamma radiation detectors were used inside the building. Theoretical dose rate calculations were performed using the Monte Carlo code MCNP6, and additional calculations were performed that compared the shielding factor for 137Cs and 134Cs. This work demonstrated the applicability of using MCNP6 for theoretical calculations of radioactive fallout scenarios. Furthermore, the work showed that the shielding effect for modular buildings is almost the same for 134Cs as for 137Cs.

General information
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Organisations: Center for Nuclear Technologies, The Hevesy Laboratory, Radioecology and Tracer Studies, Lund University
Authors: Hinrichsen, Y. (Intern), Finck, R. (Ekstern), Östlund, K. (Ekstern), Rääf, C. (Ekstern), Andersson, K. G. (Intern)
Deconvolution of $^{238,239,240}$Pu conversion electron spectra measured with a silicon drift detector

Internal conversion electron (ICE) spectra of thin $^{238,239,240}$Pu sources, measured with a windowless Peltier-cooled silicon drift detector (SDD), were deconvoluted and relative ICE intensities were derived from the fitted peak areas. Corrections were made for energy dependence of the full-energy-peak counting efficiency, based on Monte Carlo simulations. A good agreement was found with the theoretically expected internal conversion coefficient (ICC) values calculated from the Bricc database.

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Organisations: Center for Nuclear Technologies, The Hevesy Laboratory, Radioecology and Tracer Studies, University of Helsinki, European Commission Joint Research Centre Institute
Authors: Pommé, S. (Ekstern), Marouli, M. (Ekstern), Paepen, J. (Ekstern), Marković, N. (Intern), Pöllänen, R. (Ekstern)
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BFI (2015): BFI-level 1
Scopus rating (2015): SJR 0.547 SNIP 0.999 CiteScore 1.15
Web of Science (2015): Impact factor 1.136
BFI (2014): BFI-level 1
Scopus rating (2014): SJR 0.574 SNIP 1.203 CiteScore 1.27
Web of Science (2014): Impact factor 1.231
Web of Science (2014): Indexed yes
Determination of $^{129}$I in environmental solid samples using pyrolysis separation and accelerator mass spectrometry measurement

An optimized pyrolysis method was presented for release of iodine from environmental solid samples with almost quantitative recovery of iodine. The released iodine trapped in alkali solution was separated using a simple and reliable AgI precipitation method, which was directly used for determination of I-129 using accelerator mass spectrometry (AMS). The mechanism of iodine released in pyrolysis was explored. Surface soil samples collected from the Northwest China
were successfully analyzed for $^{129}$I, showing that $^{129}$I in this area falls to the background level of North Hemisphere.

**General information**

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Organisations: Center for Nuclear Technologies, The Hevesy Laboratory, Radioecology and Tracer Studies, Chinese Academy of Sciences
Authors: Hou, X. (Intern), Zhang, D. (Ekstern)
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Web of Science (2017): Indexed yes
BFI (2016): BFI-level 1
Scopus rating (2016): CiteScore 1.24 SJR 0.521 SNIP 0.831
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BFI (2015): BFI-level 1
Scopus rating (2015): SJR 0.454 SNIP 0.719 CiteScore 0.99
Web of Science (2015): Impact factor 0.983
BFI (2014): BFI-level 1
Scopus rating (2014): SJR 0.453 SNIP 0.826 CiteScore 1.09
Web of Science (2014): Impact factor 1.034
Web of Science (2014): Indexed yes
BFI (2013): BFI-level 1
Scopus rating (2013): SJR 0.502 SNIP 1.152 CiteScore 1.44
Web of Science (2013): Impact factor 1.415
ISI indexed (2013): ISI indexed yes
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BFI (2012): BFI-level 1
Scopus rating (2012): SJR 0.542 SNIP 0.899 CiteScore 1.26
Web of Science (2012): Impact factor 1.467
ISI indexed (2012): ISI indexed yes
BFI (2011): BFI-level 1
Scopus rating (2011): SJR 0.526 SNIP 0.867 CiteScore 1.32
Web of Science (2011): Impact factor 1.52
ISI indexed (2011): ISI indexed yes
Web of Science (2011): Indexed yes
BFI (2010): BFI-level 1
Scopus rating (2010): SJR 0.493 SNIP 0.667
Web of Science (2010): Impact factor 0.777
Web of Science (2010): Indexed yes
BFI (2009): BFI-level 1
Scopus rating (2009): SJR 0.385 SNIP 0.723
Web of Science (2009): Indexed yes
BFI (2008): BFI-level 1
Determination of ultra-low level plutonium isotopes (239Pu, 240Pu) in environmental samples with high uranium

In order to measure trace plutonium and its isotopes ratio (240Pu/239Pu) in environmental samples with a high uranium, an analytical method was developed using radiochemical separation for separation of plutonium from matrix and interfering elements including most of uranium and ICP-MS for measurement of plutonium isotopes. A novel measurement method was established for extensively removing the isobaric interference from uranium (238U/H and 238U/H2 +) and tailing of 238U, but significantly improving the measurement sensitivity of plutonium isotopes by employing NH3/He as collision/reaction cell gases and MS/MS system in the triple quadrupole ICP-MS instrument. The results show that removal efficiency of uranium interference was improved by more than 15 times, and the sensitivity of plutonium isotopes was increased by a factor of more than 3 compared to the conventional ICP-MS. The mechanism on the effective suppress of 238U interference for 239Pu measurement using NH3-He reaction gases was explored to be the formation of UNH+ and UNH2 + in the reactions of UH+ and U+ with NH3, while no reaction between NH3 and Pu+. The detection limits of this method were estimated to be 0.55 fg mL−1 for 239Pu, 0.09 fg mL−1 for 240Pu. The analytical precision and accuracy of the method for Pu isotopes concentration and 240Pu/239Pu atomic ratio were evaluated by analysis of sediment reference materials (IAEA-385 and IAEA-412) with different levels of plutonium and uranium. The developed method were successfully applied to determine 239Pu and 240Pu concentrations and 240Pu/239Pu atomic ratios in soil samples collected in coastal areas of eastern China.

General information
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Organisations: Center for Nuclear Technologies, The Hevesy Laboratory, Radioecology and Tracer Studies, Chinese Academy of Sciences
Authors: Xing, S. (Ekstern), Zhang, W. (Ekstern), Qiao, J. (Intern), Hou, X. (Intern)
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BFI (2017): BFI-level 1
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Web of Science (2017): Impact factor 4.244
Web of Science (2017): Indexed yes
BFI (2016): BFI-level 1
Scopus rating (2016): CiteScore 4.19 SJR 1.168 SNIP 1.276
Web of Science (2016): Impact factor 4.162
Web of Science (2016): Indexed yes
BFI (2015): BFI-level 1
Scopus rating (2015): SJR 1.173 SNIP 1.316 CiteScore 3.99
Web of Science (2015): Impact factor 4.035
Web of Science (2015): Indexed yes
BFI (2014): BFI-level 1
Scopus rating (2014): SJR 1.192 SNIP 1.284 CiteScore 3.71
Web of Science (2014): Impact factor 3.545
Web of Science (2014): Indexed yes
BFI (2013): BFI-level 1
Scopus rating (2013): SJR 1.2 SNIP 1.385 CiteScore 3.74
Web of Science (2013): Impact factor 3.511
ISI indexed (2013): ISI indexed yes
BFI (2012): BFI-level 1
Scopus rating (2012): SJR 1.417 SNIP 1.451 CiteScore 3.74
Web of Science (2012): Impact factor 3.498
ISI indexed (2012): ISI indexed yes
Web of Science (2012): Indexed yes
BFI (2011): BFI-level 1
Scopus rating (2011): SJR 1.432 SNIP 1.507 CiteScore 3.91
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ISI indexed (2011): ISI indexed yes
Web of Science (2011): Indexed yes
BFI (2010): BFI-level 1
Scopus rating (2010): SJR 1.466 SNIP 1.368
Web of Science (2010): Indexed yes
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Scopus rating (2008): SJR 1.35 SNIP 1.304
Scopus rating (2007): SJR 1.439 SNIP 1.483
Web of Science (2007): Indexed yes
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Web of Science (2005): Indexed yes
Scopus rating (2004): SJR 1.169 SNIP 1.514
Web of Science (2004): Indexed yes
Scopus rating (2003): SJR 0.989 SNIP 1.337
Scopus rating (2002): SJR 0.859 SNIP 1.252
Web of Science (2002): Indexed yes
Scopus rating (2001): SJR 0.925 SNIP 1.148
Web of Science (2001): Indexed yes
Scopus rating (2000): SJR 0.817 SNIP 1.181
Web of Science (2000): Indexed yes
Scopus rating (1999): SJR 0.907 SNIP 1.089
Direct measurement of uranium in seawater by inductively coupled plasma mass spectrometry

A simple method for direct measurement of uranium (\(^{238}\)U) in seawater using triple quadrupole inductively coupled plasma mass spectrometry (ICP-MS) was established. The method provides a good analytical performance with respect to detection limit, accuracy, precision and sample throughput. During the method development and application, several interesting facts were observed: 1) Comparison results for reference material using different quantitation approaches indicate that isotope dilution (using \(^{233}\)U) is the most reliable to achieve accurate \(^{238}\)U measurement. The results obtained for direct \(^{238}\)U measurement in 50-fold diluted seawater samples (n = 112) also underline the difference between isotope dilution and internal (or external) standardization. 2) Appropriate dilution of seawater is important to minimize the matrix effect on the ICP-MS measurement and 20-50 dilution is recommended for natural seawater samples. 3) The sensitivity of ICP-MS was observed to increase in the beginning of sample measurement, and then decrease with the continuous injection of samples, which is believed as a consequence of matrix effect from the seawater to the ionization efficiency in the plasma. 4) When measuring samples taken from large volume of seawater stored in immovable containers for relatively long period (i.e., several months), the uranium concentration and salinity data showed slightly increasing trends with the increase of water depth in the container. Therefore, cautions need to be paid in sampling representativeness when performing \(^{238}\)U measurement for such long-term stored large volume samples.

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Web of Science (2017): Indexed yes
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Scopus rating (2016): CiteScore 4.19 SJR 1.168 SNIP 1.276
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Web of Science (2016): Indexed yes
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Scopus rating (2015): SJR 1.173 SNIP 1.316 CiteScore 3.99
Web of Science (2015): Impact factor 4.035
Web of Science (2015): Indexed yes
BFI (2014): BFI-level 1
Scopus rating (2014): SJR 1.192 SNIP 1.284 CiteScore 3.71
Web of Science (2014): Impact factor 3.545
Web of Science (2014): Indexed yes
BFI (2013): BFI-level 1
Scopus rating (2013): SJR 1.2 SNIP 1.385 CiteScore 3.74
Web of Science (2013): Impact factor 3.511
Dual Nicotinic Acetylcholine Receptor α4β2 Antagonists/α7 Agonists: Synthesis, Docking Studies, and Pharmacological Evaluation of Tetrahydroisoquinolines and Tetrahydroisoquinolinium Salts

We describe the synthesis of tetrahydroisoquinolines and tetrahydroisoquinolinium salts together with their pharmacological properties at various nicotinic acetylcholine receptors. In general, the compounds were α4β2 nAChR antagonists, with the tetrahydroisoquinolinium salts being more potent than the parent tetrahydroisoquinoline derivatives. The most potent α4β2 antagonist, 6c, exhibited submicromolar binding Ki and functional IC50 values and high selectivity for this receptor over the α4β4 and α3β4 nAChRs. Whereas the (S)-6c enantiomer was essentially inactive at α4β2, (R)-6c was a slightly more potent α4β2 antagonist than the reference β2-nAChR antagonist DHβE. The observation that the α4β2 activity resided exclusively in the (R)-enantiomer was in full agreement with docking studies. Several of tetrahydroisoquinolinium salts also displayed agonist activity at the α7 nAChR. Preliminary in vivo evaluation revealed antidepressant-like effects of both (R)-5c and (R)-6c in the mouse forced swim test, supporting the therapeutic potential of α4β2 nAChR antagonists for this indication.

General information
Evaluation of gross-α and gross-β activities in groundwater of the Haihe River Plain, China
The investigation provides the first data of gross-α and gross-β activities in groundwater of the Haihe River Plain, China. Ranges of gross-alpha and gross-beta activities vary from 17 to 362 mBq/L and from 18 to 779 mBq/L, respectively. These values are below the permissible limits given by the WHO for drinking water, but they do not include possible additional dose that may emanate from gaseous phases. Comparison of gross-alpha and gross-beta activities with data from groundwater in other parts of China and globally suggests that precipitation rate has strong control on natural radioactivity in groundwater, particularly of shallow aquifers.

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Organisations: Center for Nuclear Technologies, The Hevesy Laboratory, Radioecology and Tracer Studies, Hohai University, United Arab Emirates University
Authors: Yi, P. (Ekstern), Gong, M. (Ekstern), Zhang, W. (Ekstern), Hou, X. L. (Intern), Aldahan, A. (Ekstern), Yang, J. (Ekstern), Chen, P. (Ekstern)
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Web of Science (2017): Indexed yes
BFI (2016): BFI-level 1
Scopus rating (2016): CiteScore 1.24 SJR 0.521 SNIP 0.831
Web of Science (2016): Impact factor 1.282
Web of Science (2016): Indexed yes
BFI (2015): BFI-level 1
Scopus rating (2015): SJR 0.454 SNIP 0.719 CiteScore 0.99
Web of Science (2015): Impact factor 0.983
BFI (2014): BFI-level 1
Scopus rating (2014): SJR 0.453 SNIP 0.826 CiteScore 1.09
The half-lives of $^{132}$La and $^{135}$La were determined via serial gamma spectroscopy, and the half-life of $^{135}$La was further determined by a high-precision ionization-chamber measurement. The results are 18.9(2) hr for $^{132}$La and 4.59(4) hr for $^{135}$La compared with the previously compiled values of 19.5(2) hr and 4.8(2) hr, respectively. These lanthanum isotopes comprise a medically interesting system with positron emitter $^{132}$La and Auger-electron emitter $^{135}$La forming a theranostic pair for internal diagnostics and therapeutics. The precise half-lives are necessary for proper evaluation of their value in medicine and for a more representative tabulation of nuclear data.
Impact of North Korean nuclear weapons test on 3 September, 2017 on inland China traced by $^{14}$C and $^{129}$I

Environmental impact of North Korea nuclear weapons testing on 3 Sept, 2017, is of key concern. In order to investigate whether there is radioactive leakage and whether it can be transported to inland China, $^{14}$C and $^{129}$I are determined in aerosol samples collected in a Chinese inland city before and after the test. Aerosol $\Delta^{14}$C values before and after the test do not show any significant difference. In contrast, a four-fold increase of $^{129}$I/$^{127}$I ratios was found after the test. The possible sources of $^{129}$I in these atmospheric samples and the impact of the North Korea nuclear test are discussed.

General information
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Organisations: Center for Nuclear Technologies, The Hevesy Laboratory, Radioecology and Tracer Studies, Chinese Academy of Sciences
Authors: Zhang, L. (Ekstern), Hou, X. (Intern), Cheng, P. (Ekstern), Chen, N. (Ekstern), Fan, Y. (Ekstern), Liu, Q. (Ekstern)
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Web of Science (2016): Indexed yes
BFI (2015): BFI-level 1
Scopus rating (2015): SJR 0.454 SNIP 0.719 CiteScore 0.99
Web of Science (2015): Impact factor 0.983
BFI (2014): BFI-level 1
Scopus rating (2014): SJR 0.453 SNIP 0.826 CiteScore 1.09
Web of Science (2014): Impact factor 1.034
Web of Science (2014): Indexed yes
BFI (2013): BFI-level 1
Scopus rating (2013): SJR 0.502 SNIP 1.152 CiteScore 1.44
We have developed a 125I-radiolabeled injectable fiducial tissue marker with the potential to replace current methods used for surgical guidance of non-palpable breast tumors. Methods in routine clinical use today such as radioactive seed localization, radio-guided occult lesion localization and wire-guided localization suffers from limitations that this injectable fiducial tissue marker offers solutions to. The developed 125I-radiolabeled injectable fiducial tissue marker is based on highly viscous sucrose acetate isobutyrate. The marker was readily inserted in NMRI mice and proved to be spatially well-defined and stable over a seven day period with excellent CT contrast (>1500 HU), enabling fluoroscopic visualization of markers during placement. The radioactivity remains strongly associated with the marker during the implantation period, which limits exposure to healthy tissue. Biodistribution studies show that there is negligible radioactivity in all non-tumor tissues sampled, with the exception of the thyroid gland, where limited accumulation was observed (0.06% of injected dose after 7 days). Based on the excellent performance of the marker and the fact that it can be delivered through thin hypodermic needles (≥27G), the marker holds great promise for clinical application, since patient discomfort is reduced
significantly compared to current methods. Statement of Significance. A new type of tissue marker for local administration to non-palpable breast tumors has been developed. The surgical guidance marker is based on derivatives of the biomaterial sucrose acetate isobutyrate and unlike currently used markers it is injectable in the tissue using thin needles, reducing the discomfort to the patients significantly. The marker confers CT contrast and has radioactive properties, meaning it also could find use in brachytherapy. The design of the iodine-125 labeled fiducial tissue marker enables control of dosimetry as well as a choice of iodine isotope used. The marker is anticipated to be clinical applicable due to its contrast performance in mice and its potential for enhanced flexibility in surgical procedures, compared to current methods.

General information
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Organisations: Department of Chemistry, Center for Nuclear Technologies, The Hevesy Laboratory, Department of Micro- and Nanotechnology, Colloids and Biological Interfaces, Organic Chemistry, University of Copenhagen
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Web of Science (2017): Impact factor 6.383
Web of Science (2017): Indexed yes
BFI (2016): BFI-level 2
Scopus rating (2016): CiteScore 6.66 SJR 1.856 SNIP 1.947
Web of Science (2016): Impact factor 6.319
Web of Science (2016): Indexed yes
BFI (2015): BFI-level 2
Scopus rating (2015): SJR 2.02 SNIP 1.963 CiteScore 6.58
Web of Science (2015): Indexed yes
BFI (2014): BFI-level 2
Scopus rating (2014): SJR 1.835 SNIP 2.28 CiteScore 6.53
Web of Science (2014): Indexed yes
BFI (2013): BFI-level 2
Scopus rating (2013): SJR 1.988 SNIP 2.24 CiteScore 6.41
Web of Science (2013): Impact factor 5.684
ISI indexed (2013): ISI indexed yes
Web of Science (2013): Indexed yes
BFI (2012): BFI-level 2
Scopus rating (2012): SJR 1.904 SNIP 2.108 CiteScore 5.51
Web of Science (2012): Impact factor 5.093
ISI indexed (2012): ISI indexed yes
Scopus rating (2011): SJR 1.831 SNIP 1.893 CiteScore 5.15
Web of Science (2011): Impact factor 4.865
ISI indexed (2011): ISI indexed yes
Scopus rating (2010): SJR 1.805 SNIP 1.955
Web of Science (2010): Impact factor 4.824
Web of Science (2010): Indexed yes
Scopus rating (2009): SJR 1.404 SNIP 1.657
Introducing the concept of the isodose for optimisation of decontamination activities in a radioactive fallout scenario: Paper

In the recovery phase after a radioactive release incident, it is important to be able to focus decontamination operations on the areas that contribute most to the radiation dose. Monte Carlo simulations were applied to determine the shielding effect of a building against radiation from various directions, also giving information on the dose contributions at various locations inside the building from specific areas outside. The concept of the isodose was developed to optimise decontamination activities, and was applied as isodose lines to define the smallest areas that lead to a certain dose reduction through decontamination of areas surrounding the building. The shape and position of the isodose lines depend on the building's geometry, wall thickness, and material, and on the observation point inside the building. Calculations have been made with a surface resolution of 1 m² for four observation points in a modular building, assuming depositions of 137Cs and 60Co on the ground surface and on the roof, as well as 1 cm below the ground surface to represent ground penetration. For example, a ten times as large area would have to be decontaminated to increase the dose reduction from 10% to 30%, if it is assumed that all the contamination is located at a depth of 1 cm.

General information

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Organisations: Center for Nuclear Technologies, The Hevesy Laboratory, Radioecology and Tracer Studies, Lund University
Authors: Hinrichsen, Y. (Intern), Finck, R. (Ekstern), Rääf, C. (Ekstern), Andersson, K. G. (Intern)
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Web of Science (2018): Indexed yes
BFI (2017): BFI-level 1
Scopus rating (2017): CiteScore 1.11 SJR 0.848 SNIP 0.898
Web of Science (2017): Impact factor 1.274
Web of Science (2017): Indexed yes
BFI (2016): BFI-level 1
Scopus rating (2016): SJR 0.706 SNIP 1.075 CiteScore 1.3
Web of Science (2016): Impact factor 1.657
BFI (2015): BFI-level 1
Scopus rating (2015): SJR 0.777 SNIP 1.089 CiteScore 1.33
Web of Science (2015): Impact factor 1.581
BFI (2014): BFI-level 1
Scopus rating (2014): SJR 0.565 SNIP 1.104 CiteScore 1.24
Web of Science (2014): Impact factor 1.702
BFI (2013): BFI-level 1
Scopus rating (2013): SJR 0.405 SNIP 0.817 CiteScore 0.86
Web of Science (2013): Impact factor 1.319
BFI (2012): BFI-level 1
Iodine isotopes ($^{129}$I and $^{127}$I) in the hydrosphere of Qinghai-Tibet region and South China Sea

The radioactive isotope $^{129}$I, with a half-life of $1.57 \times 10^7$ years, is widely used as a tracer to assess nuclear safety, to track environmental and geological events and to figure out the details of the stable iodine geochemical cycle. This work investigated the $^{129}$I and $^{127}$I distribution in water samples collected from the terrestrial (rivers, lakes and springs) and marine water systems (estuary and sea) in China. The measured $^{129}$I concentrations of $(1–51) \times 10^6$ atoms/L and $^{129}$I/$^{127}$I ratios of $(0.03–21) \times 10^{-10}$ shows the variability of $^{129}$I level in the water systems. The local permafrost and seasonal frozen environment play a key role in groundwater recharge in the Qinghai-Tibet region, which is reflected in the $^{129}$I distribution in surface water. The depth distribution of $^{129}$I in the water column of the South China Sea reflects the effluence of different currents. The results also indicate that the hydrosphere of China contains one to three orders of magnitude less $^{129}$I compared to those reported in Europe. Despite the large distance, the European nuclear fuel reprocessing facilities represent the major source of $^{129}$I in the hydrosphere of China through atmospheric transport. The contribution of the Fukushima nuclear accident to $^{129}$I levels in the hydrosphere of China was negligible.

**General information**

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Organisations: Center for Nuclear Technologies, The Hevesy Laboratory, Radioecology and Tracer Studies, Hohai University, United Arab Emirates University
Authors: Yi, P. (Ekstern), Chen, X. (Ekstern), Wang, Z. (Ekstern), Aldahan, A. (Ekstern), Hou, X. (Intern), Yu, Z. (Ekstern)
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Joint Nordic nuclear research to strengthen nuclear emergency preparedness after the Fukushima accident

Contrary to most areas of Europe, the Nordic countries (Denmark, Finland, Iceland, Norway, Sweden, and the Faroe Islands) have for many years shared a regional research and development program on nuclear reactor safety and emergency preparedness - NKS. In spite of its project results having received great recognition and having been integrated in state-of-the-art emergency preparedness tools over the world, NKS as an organization does not seem well known outside the Nordic countries. Although the Fukushima accident had no health impact at all in Nordic areas, it taught a number of lessons of generic nature with respect to new R&D tasks that could further strengthen and secure future maintenance of the Nordic region's capability to effectively respond to such events. For broader inspiration, this paper briefly introduces the Nordic nuclear emergency preparedness cooperation channels and outlines the related NKS R&D project initiatives launched after the Fukushima accident, many of which should be of general interest also far outside the region. The paper is intended as an introduction to NKS with an invitation to explore its results. All project results are available cost-free on the NKS website.
Liposome accumulation in irradiated tumors display important tumor and dose dependent differences

Radiation therapy may affect several important parameters in the tumor microenvironment and thereby influence the accumulation of liposomes by the enhanced permeability and retention (EPR)-effect. Here we investigate the effect of single dose radiation therapy on liposome tumor accumulation by PET/CT imaging using radiolabeled liposomes. Head and neck cancer xenografts (FaDu) and syngenic colorectal (CT26) cancer models were investigated. Radiotherapy displayed opposite effects in the two models. FaDu tumors displayed increased mean accumulation of liposomes for radiation doses up to 10 Gy, whereas CT26 tumors displayed a tendency for decreased accumulation. Tumor hypoxia was found negatively correlated to microregional distribution of liposomes. However, liposome distribution in relation to hypoxia...
was improved at lower radiation doses. The study reveals that the heterogeneity in liposome tumor accumulation between tumors and different radiation protocols are important factors that need to be taken into consideration to achieve optimal effect of liposome based radio-sensitizer therapy.

**General information**

State: Published

Organisations: Department of Micro- and Nanotechnology, Colloids and Biological Interfaces, Center for Nuclear Technologies, The Hevesy Laboratory, Radioecology and Tracer Studies, Technical University of Denmark, University of Copenhagen


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- Web of Science (2017): Impact factor 6.5
- Web of Science (2017): Indexed yes
- BFI (2016): BFI-level 1
- Scopus rating (2016): CiteScore 6.22 SJR 1.687 SNIP 1.367
- Web of Science (2016): Impact factor 5.72
- Web of Science (2016): Indexed yes
- BFI (2015): BFI-level 1
- Scopus rating (2015): SJR 1.857 SNIP 1.686 CiteScore 6.65
- Web of Science (2015): Impact factor 5.671
- Web of Science (2015): Indexed yes
- BFI (2014): BFI-level 1
- Scopus rating (2014): SJR 1.876 SNIP 1.795 CiteScore 6.8
- Web of Science (2014): Impact factor 6.155
- BFI (2013): BFI-level 1
- Scopus rating (2013): SJR 2.179 SNIP 1.965 CiteScore 7.49
- Web of Science (2013): Impact factor 5.978
- ISI indexed (2013): ISI indexed yes
- Web of Science (2013): Indexed yes
- Scopus rating (2012): SJR 2.379 SNIP 2.089 CiteScore 7.45
- Web of Science (2012): Impact factor 6.93
- ISI indexed (2012): ISI indexed yes
- Scopus rating (2011): SJR 2.013 SNIP 1.723 CiteScore 6.68
- ISI indexed (2011): ISI indexed no
- Scopus rating (2010): SJR 1.768 SNIP 1.628
- Scopus rating (2009): SJR 1.612 SNIP 1.415
- Web of Science (2009): Indexed yes
- Scopus rating (2008): SJR 1.025 SNIP 0.941
- Scopus rating (2007): SJR 0.709 SNIP 0.662
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Liposome, PET, Radiotherapy, Radio-sensitizer, Hypoxia

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Manganese-52: applications in cell radiolabelling and liposomal nanomedicine PET imaging using oxine (8-hydroxyquinoline) as an ionophore

The ionophore 8-hydroxyquinoline (oxine) has been used to radiolabel cells and liposomal medicines with 111In and, more recently, 89Zr, for medical nuclear imaging applications. Oxine has also shown promising ionophore activity for the positron-emitting radionuclide 52Mn that should allow imaging of labelled cells and nanomedicines for long periods of time (>14 days). However, to date, the radiometal complex formed and its full labelling capabilities have not been fully characterised. Here, we provide supporting evidence of the formation of [52Mn]Mn(oxinate)2 as the metastable complex responsible for its ionophore activity. The cell labelling properties of [52Mn]Mn(oxinate)2 were investigated with various cell lines. The liposomal nanomedicine, DOXIL® (Caelyx) was also labelled with [52Mn]Mn(oxinate)2 and imaged in vivo using PET imaging. [52Mn]Mn(oxinate)2 was able to label various cell lines with moderate efficiency (15-53%), however low cellular retention of 52Mn (21-25% after 24 h) was observed which was shown not to be due to cell death. PET imaging of [52Mn]Mn-DOXIL at 1 h and 24 h post-injection showed the expected pharmacokinetics and biodistribution of this stealth liposome, but at 72 h post-injection showed a profile matching that of free 52Mn, consistent with drug release. We conclude that oxine is an effective ionophore for 52Mn, but high cellular efflux of the isotope limits its use for prolonged cell tracking. [52Mn]Mn(oxinate)2 is effective for labelling and tracking DOXIL in vivo. The release of free radionuclide after liposome extravasation could provide a non-invasive method to monitor drug release in vivo.

General information

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Organisations: Center for Nuclear Technologies, The Hevesy Laboratory, King’s College London, GlaxoSmithKline, Hebrew University of Jerusalem, Imperial College London
Authors: Gawne, P. (Ekstern), Man, F. (Ekstern), Fonslet, J. (Intern), Radia, R. (Ekstern), Bordoloi, J. (Ekstern), Cleveland, M. (Ekstern), Jimenez-Royo, P. (Ekstern), Gabizon, A. (Ekstern), Blower, P. J. (Ekstern), Long, N. (Ekstern), de Rosales, R. T. (Ekstern)
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Scopus rating (2017): CiteScore 3.93 SJR 1.306 SNIP 0.904
Web of Science (2017): Impact factor 4.099
Web of Science (2017): Indexed yes
BFI (2016): BFI-level 2
Scopus rating (2016): CiteScore 3.85 SJR 1.229 SNIP 0.918
Web of Science (2016): Impact factor 4.029
Web of Science (2016): Indexed yes
BFI (2015): BFI-level 2
Scopus rating (2015): SJR 1.302 SNIP 1.064 CiteScore 4.1
Web of Science (2015): Impact factor 4.177
Web of Science (2015): Indexed yes
BFI (2014): BFI-level 2
Scopus rating (2014): SJR 1.389 SNIP 1.064 CiteScore 4.06
Web of Science (2014): Impact factor 4.197
Web of Science (2014): Indexed yes
BFI (2013): BFI-level 1
Methods for studying the action of low-energy electron emissions on single cells

New approaches are needed for studying the radiobiological effects of low-energy electrons on living cells. This thesis describes the development, the validation, and the use of two new tools, called COOLER (COmputation Of Local Electron Release) and CoCoNut (Colony Counter developed by the Nutech department at the Technical University of Denmark). COOLER is a general purpose absorbed dose calculation method that has been entrusted to a novel software program of the same name. It uses Monte Carlo simulations of monoenergetic point dose kernels as a base for finding analytical solutions to cellular dosimetry problems. The COOLER approach is applicable to a wide range of cellular geometries and the software handles electron energies up to 50 keV.

Electron ranges are calculated and compared to MIRD (Medical Internal Radiation Dose) predictions, whose results appear to be overestimated above 20 keV. Cellular S-values are obtained for dierent activity distribution scenarios and compared to MIRD predictions and Monte Carlo simulations. We prove that COOLER can successfully reproduce Monte Carlo results using an analytical approach. By comparing COOLER to MIRD results, we show that the largest
discrepancies between the two methods can be expected for electrons between 25 and 30 keV for a V79 cellular model. For those energies, S-values disagree from 50 to 100%, depending on the activity distribution. MIRD predictions fail the most when the activity is modeled on the cell surface.

Description of COOLER is contained in the publication: Siragusa et al. The COOLER code: a novel analytical approach to calculate subcellular energy deposition by internal electron emitters. Radiat Res. 2017;188(2):204-220.

COOLER has been successfully employed to calculate absorbed dose values of free floating and attached V79 cells contaminated with tritiated water (HTO). In order to use HTO as a model for investigating the biological effects of low-energy electrons, experiments have been carried out avoiding tritium incorporation into precursor biomolecules. In this thesis, we compare low-energy electron cell-killing efficacy to that of external photon irradiation using RBE (Relative Biological Effectiveness) values obtained from clonogenic cell survival experiments. RBEs are calculated at the 10% survival fraction and are based on the ratio of COOLER-calculated absorbed doses.

Irrespective of the cell geometry, RBE results for floating and adherent cells are always 2. Results confirm that low-energy electrons contribute significantly more to the radiation damage than could be expected for such electrons. Moreover, COOLER shows that the change in the cell culture growth condition is relevant as suspended V79 cells tend to quickly form small cell clusters, which are responsible for an increased radiation resistance of the cells. The role of the dose rate of the reference radiation for RBE-calculations is also investigated. In our experiments, RBEs range from 1.6 to 2.0 for adherent V79 cells, when compared respectively to acute exposures or to similar dose rates of external g-rays.

Results on HTO experiments have been published: Siragusa et al. Radiobiological effects of tritiated water short-term exposure on V79 clonogenic cell survival. Int J Radiat Biol. 2018;94(2):157-165. All radiobiological results contained in the previously mentioned article have been obtained counting many cell clones in a number of clonogenic cell survival experiments. In this thesis, I describe the development of a combined software/hardware tool, called CoCoNut, that automates the otherwise slow counting process. CoCoNut consists of an open source ImageJ macro and a 3D-printable photographic light-box, engineered to work together. The full method is tested against V79 cell survival in cell culture flasks and Petri dishes. It proves able to identify cell clones with unconventional morphology, to successfully distinguish between single and merged colonies, and to identify colonies bordering on flask edges.


Finally, COOLER is used to compute accurate absorbed dose calculations for the novel Auger electron emitter $^{135}$La, as reported in the publication: Fonslet et al. $^{135}$La as an Auger-electron emitter for targeted internal radiotherapy. Phys Med Biol. 2017;63(1):015026. In that article, COOLER-derived cellular S-values are compared to MIRD results for a spherical V79 cellular model. S-value contributions to the cell nucleus from different source regions are determined. When compared to MIRD, COOLER S-value results show an increased dose for the combinations N Cy (38%) and N CS (89%), while the N N case shows a 5% decrease. Being N the cell Nucleus, Cy the Cytoplasm, and CS the Cell Surface. Our results make clear that MIRD calculations may underestimate absorbed dose values for tumor treatment plannings based on $^{135}$La.

COOLER and CoCoNut have succeeded in giving meticulous and prompt radiobiological results for our experiments. Therefore, their combination is suitable for future research projects aimed at assessing the role of low-energy electrons in, for example, therapeutic applications and radiation protection scenarios.

General information
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Organisations: Center for Nuclear Technologies, The Hevesy Laboratory
Authors: Siragusa, M. (Intern)
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Relations
Projects:
Methods for studying the action of low-energy electron emissions on single cells
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Microbeam evolution: From single cell irradiation to preclinical studies
Purpose: This review follows the development of microbeam technology from the early days of single cell irradiations, to investigations of specific cellular mechanisms and to the development of new treatment modalities in vivo. A number of microbeam applications are discussed with a focus on preclinical modalities and translation towards clinical application.
Conclusions: The development of radiation microbeams has been a valuable tool for the exploration of fundamental radiobiological response mechanisms. The strength of micro-irradiation techniques lies in their ability to deliver precise doses of radiation to selected individual cells in vitro or even to target subcellular organelles. These abilities have led to the development of a range of microbeam facilities around the world allowing the delivery of precisely defined beams of charged particles, X-rays, or electrons.

In addition, microbeams have acted as mechanistic probes to dissect the underlying molecular events of the DNA damage response following highly localised dose deposition. Further advances in very precise beam delivery have also enabled the transition towards new and exciting therapeutic modalities developed at synchrotrons to deliver radiotherapy using plane parallel microbeams, in Microbeam Radiotherapy (MRT).

General information
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Organisations: Center for Nuclear Technologies, The Hevesy Laboratory, Queen's University Belfast, University of Bern, National Physical Laboratory, European Synchrotron Radiation Facility
Authors: Ghita, M. (Ekstern), Fernandez-Palomo, C. (Ekstern), Fukunaga, H. (Ekstern), Fredericia, P. M. (Intern), Schettino, G. (Ekstern), Bräuer-Krisch, E. (Ekstern), Butterworth, K. T. (Ekstern), McMahon, S. J. (Ekstern), Prise, K. M. (Ekstern)
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BFI (2017): BFI-level 1
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Web of Science (2017): Impact factor 1.97
Web of Science (2017): Indexed yes
BFI (2016): BFI-level 1
Scopus rating (2016): CiteScore 1.84 SJR 0.72 SNIP 0.757
Web of Science (2016): Impact factor 1.992
BFI (2015): BFI-level 1
Scopus rating (2015): SJR 0.74 SNIP 0.771 CiteScore 1.89
Web of Science (2015): Impact factor 1.779
BFI (2014): BFI-level 1
Scopus rating (2014): SJR 0.588 SNIP 0.808 CiteScore 1.78
Web of Science (2014): Impact factor 1.687
BFI (2013): BFI-level 1
Scopus rating (2013): SJR 0.71 SNIP 0.716 CiteScore 1.91
Web of Science (2013): Impact factor 1.837
ISI indexed (2013): ISI indexed yes
BFI (2012): BFI-level 1
Scopus rating (2012): SJR 0.866 SNIP 0.914 CiteScore 2.12
Web of Science (2012): Impact factor 1.895
ISI indexed (2012): ISI indexed yes
BFI (2011): BFI-level 1
Scopus rating (2011): SJR 0.729 SNIP 0.984 CiteScore 2.11
Web of Science (2011): Impact factor 2.275
ISI indexed (2011): ISI indexed yes
BFI (2010): BFI-level 1
Scopus rating (2010): SJR 0.782 SNIP 0.736
Inductively coupled plasma mass spectrometry (ICP-MS) techniques are widely used for determination of long-lived radionuclides and their isotopic ratios in the nuclear fields. Uranium (U) and Pu (Pu) isotopes have been determined by many researchers with ICP-MS due to its relatively high sensitivity and short measurement time. In this work, an inter-laboratory comparison exercise among the Nordic countries was performed, focusing on the measurement of U and Pu isotopes in certified reference materials by ICP-MS. The performance and characters of different ICP-MS instruments are evaluated and discussed in this paper.

General information
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Organisations: Center for Nuclear Technologies, The Hevesy Laboratory, Radioecology and Tracer Studies, Swedish Defence Research Agency, ALS Scandinavia, University of Helsinki, Norwegian University of Science and Technology, Norwegian University of Life Sciences, Geological Survey of Finland
Authors: Qiao, J. (Intern), Lagerkvist, P. (Ekstern), Rodushkin, I. (Ekstern), Salminen-Paatero, S. (Ekstern), Roos, P. (Intern), Lierhagen, S. (Ekstern), Jensen, K. A. (Ekstern), Engstrom, E. (Ekstern), Lahaye, Y. (Ekstern), Skipperud, L. (Ekstern)
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Main Research Area: Technical/natural sciences

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BFI (2017): BFI-level 1
Scopus rating (2017): CiteScore 1.14 SJR 0.47 SNIP 0.738
Web of Science (2017): Impact factor 1.181
Web of Science (2017): Indexed yes
BFI (2016): BFI-level 1
Scopus rating (2016): CiteScore 1.24 SJR 0.521 SNIP 0.831
Web of Science (2016): Impact factor 1.282
Web of Science (2016): Indexed yes
Pacific Proving Grounds radioisotope imprint in the Philippine Sea sediments

Radionuclide concentrations were studied in sediment cores taken at the continental slope of the Philippine Sea off Mindanao Island in the equatorial Western Pacific. High resolution deposition records of anthropogenic radionuclides were collected at this site. Excess 210Pb together with excess 228Th and anthropogenic radionuclides provided information about accumulation rates. Concentrations of Am and Pu isotopes were detected by gamma spectrometry, alpha spectrometry and ICP-MS. The Pu ratios indicate a high portion (minimum of 60%) of Pu from the Pacific Proving Grounds (PPG). This implies that the transport of PPG derived plutonium with the Mindanao Current southward is similarly effective as the previously known transport towards the north with the Kuroshio Current. The record is compared to other studies from northwest Pacific marginal seas and Lombok basin in the Indonesian Archipelago. The sediment core top was found to contain a 6 cm thick layer dominated by terrestrial organic matter, which was interpreted as a result of the 2012 Typhoon Pablo-related fast deposition.

General information
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Organisations: Center for Nuclear Technologies, The Hevesy Laboratory, Radioecology and Tracer Studies, University of Bremen, Alfred Wegener Institute
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Main Research Area: Technical/natural sciences

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Web of Science (2018): Indexed yes
BFI (2017): BFI-level 1
Scopus rating (2017): CiteScore 2.26 SJR 0.989 SNIP 1.377
Web of Science (2017): Impact factor 2.263
Web of Science (2017): Indexed yes
BFI (2016): BFI-level 1
Scopus rating (2016): CiteScore 2.39 SJR 0.956 SNIP 1.488
Web of Science (2016): Impact factor 2.31
Web of Science (2016): Indexed yes
BFI (2015): BFI-level 1
Scopus rating (2015): SJR 1.147 SNIP 1.555 CiteScore 2.62
Web of Science (2015): Impact factor 2.047
Web of Science (2015): Indexed yes
BFI (2014): BFI-level 1
Scopus rating (2014): SJR 1.061 SNIP 1.72 CiteScore 2.54
Web of Science (2014): Impact factor 2.483
BFI (2013): BFI-level 1
Scopus rating (2013): SJR 1.613 SNIP 2.059 CiteScore 2.97
Web of Science (2013): Impact factor 3.571
ISI indexed (2013): ISI indexed yes
Web of Science (2013): Indexed yes
BFI (2012): BFI-level 1
Scopus rating (2012): SJR 1.082 SNIP 1.71 CiteScore 1.95
Web of Science (2012): Impact factor 2.119
ISI indexed (2012): ISI indexed yes
Web of Science (2012): Indexed yes
BFI (2011): BFI-level 1
Scopus rating (2011): SJR 1.106 SNIP 1.638 CiteScore 1.61
Radiobiological effects of tritiated water short-term exposure on V79 clonogenic cell survival

We set out to improve the accuracy of absorbed dose calculations for in-vitro measurements of the Relative Biological Effectiveness (RBE) of tritiated water (HTO) for the clonogenic cell survival assay, also considering the influence of the end-of-track Linear Energy Transfer (LET) of low-energy electrons. The COmputation Of Local Electron Release (COOLER) program was adopted to investigate the cell geometry and the tritium full beta-decay spectrum impact on the S-values and subsequently on the RBE of HTO for clonogenic cell survival at similar high dose rates. S-values for cells growing in suspension are usually comparable to those for adherent cells. RBEs calculated at the 10% survival fraction through the use of the average energy are almost similar to those obtained with the beta-spectrum. For adherent cells, an RBE of 1.6 was found when HTO cell survival curves were compared to acute γ-ray exposures. Irrespective of the geometrical configuration, the RBE was 2.0 when the comparison was made with similar dose rates. These results underline the importance of irradiating at equal dose rates and cell culture conditions when measuring in-vitro RBE-values.

General information

State: Accepted/In press
Organisations: Center for Nuclear Technologies, The Hevesy Laboratory
Authors: Siragusa, M. (Intern), Fredericia, N. P. M. (Intern), Jensen, M. (Intern), Groesser, T. (Intern)
Number of pages: 28
Pages: 1-28
Publication date: 2018
Main Research Area: Technical/natural sciences
Remote loading of liposomes with a 124I-radioiodinated compound and their in vivo evaluation by PET/CT in a murine tumor model

Long circulating liposomes entrapping iodinated and radioiodinated compounds offer a highly versatile theranostic platform. Here we report a new methodology for efficient and high-yielding loading of such compounds into liposomes, enabling CT/SPECT/PET imaging and 131I-radiotherapy. Methods: The CT contrast agent diatrizoate was synthetically functionalized with a primary amine, which enabled its remote loading into PEGylated liposomes by either an ammonium sulfate or a citrate based pH transmembrane gradient. Further, the amino-diatrizoate was radiolabeled with either 124I (t1/2 = 4.18 days) for PET or 125I (t1/2 = 59.5 days) for SPECT, through an aromatic Finkelstein reaction. Results: Quantitative loading efficiencies (>99%) were achieved at optimized conditions. The 124I-labeled compound was remote-loaded into liposomes, with an overall radiolabeling efficiency of 77 ± 1%, and imaged in vivo in a CT26 murine colon cancer tumor model by PET/CT. A prolonged blood circulation half-life of 19.5 h was observed for the radiolabeled liposomes, whereas injections of the free compound were rapidly cleared. Lower accumulation was observed in the spleen, liver, kidney and tumor than what is usually seen for long-circulating liposomes. Conclusion: The lower accumulation was interpreted as release of the tracer from the liposomes within these organs after accumulation. These results may guide the design of systems for controlled release of remote loadable drugs from liposomes.

General information
State: Accepted/In press
Organisations: Department of Chemistry, Organic Chemistry, Department of Micro- and Nanotechnology, Colloids and Biological Interfaces, Center for Nuclear Technologies, The Hevesy Laboratory, Technical University of Denmark, University of Copenhagen
Number of pages: 23
Publication date: 2018
Main Research Area: Technical/natural sciences

Publication information
Journal: Theranostics
ISSN (Print): 1838-7640
Ratings:
BFI (2018): BFI-level 2
Web of Science (2018): Indexed yes
BFI (2017): BFI-level 1
Scopus rating (2017): CiteScore 8.7 SNIP 1.791 SJR 2.515
Web of Science (2017): Impact factor 8.537
Web of Science (2017): Indexed yes
BFI (2016): BFI-level 1
Scopus rating (2016): CiteScore 9.07 SNIP 2.015 SJR 2.375
Web of Science (2016): Impact factor 8.766
BFI (2015): BFI-level 1
Scopus rating (2015): CiteScore 8.77 SNIP 2.003 SJR 2.586
BFI (2014): BFI-level 1
Scopus rating (2014): CiteScore 7.41 SNIP 1.918 SJR 1.955
Web of Science (2014): Impact factor 8.022
BFI (2013): BFI-level 1
Scopus rating (2013): CiteScore 7.17 SNIP 1.416 SJR 1.56
Web of Science (2013): Impact factor 7.827
Web of Science (2012): Impact factor 7.806
Web of Science (2011): Impact factor
Original language: English
Remote loading, pH-gradient liposomes, Transmembrane ammonium sulfate, Iodinated imaging agents, PET imaging, I-124
Electronic versions:
I_124_compress_31Aug2018.pdf
Publication: Research - peer-review › Journal article – Annual report year: 2018
Remote-loading of liposomes with manganese-52 and in vivo evaluation of the stabilities of $^{52}$Mn-DOTA and $^{64}$Cu-DOTA using radiolabelled liposomes and PET imaging

Liposomes are nanoparticles used in drug delivery that distribute over several days in humans and larger animals. Radiolabeling with long-lived positron emission tomography (PET) radionuclides, such as manganese-52 ($^{52}$Mn, $T_\frac{1}{2}=5.6$ days), allow the imaging of this biodistribution. We report optimized protocols for radiolabeling liposomes with $^{52}$Mn, through both remote-loading and surface labeling. For comparison, liposomes were also remote-loaded and surface labeled with copper-64 ($^{64}$Cu, $T_\frac{1}{2}=12.7$ h) through conventional means. The chelator DOTA was used in all cases. The in vivo stability of radiometal chelates is widely debated but studies that mimic a realistic in vivo setting are lacking. Therefore, we employed these four radiolabeled liposome types as platforms to demonstrate a new concept for such in vivo evaluation, here of the chelates $^{52}$Mn-DOTA and $^{64}$Cu-DOTA. This was done by comparing "shielded" remote-loaded with "exposed" surface labeled variants in a CT26 tumor-bearing mouse model. Remote loading (90 min at 55°C) and surface labeling (55°C for 2 h) of $^{52}$Mn gave excellent radiolabeling efficiencies of 97-100% and 98-100% respectively, and the liposome biodistribution was imaged by PET for up to 8 days. Liposomes with surface-conjugated $^{52}$Mn-DOTA exhibited a significantly shorter plasma half-life ($T_\frac{1}{2}=14.4$ h) when compared to the remote-loaded counterpart ($T_\frac{1}{2}=21.3$ h), whereas surface-conjugated $^{64}$Cu-DOTA cleared only slightly faster and non-significantly, when compared to remote-loaded (17.2±2.9 h versus 20.3±1.2 h). From our data, we conclude the successful remote-loading of liposomes with $^{52}$Mn, and furthermore that $^{52}$Mn-DOTA may be unstable in vivo whereas $^{64}$Cu-DOTA appears suitable for quantitative imaging.

General information
State: Published
Organisations: Center for Nuclear Technologies, The Hevesy Laboratory, Department of Micro- and Nanotechnology, Colloids and Biological Interfaces, Department of Chemistry, University of Copenhagen
Pages: 100-109
Publication date: 2018
Main Research Area: Technical/natural sciences
Så meget radioaktivitet kan man måle i danskerne

General information
State: Published
Organisations: Center for Nuclear Technologies, The Hevesy Laboratory, Radioecology and Tracer Studies
Authors: Nielsen, S. P. (Intern)
Publication date: 2018
Main Research Area: Technical/natural sciences

Publication information
Journal: Videnskab.dk
Volume: 2018
Issue number: april
ISSN (Print): 1903-301X
Original language: English
Links:
https://videnskab.dk/naturvidenskab/saa-meget-radioaktivitet-kan-man-maale-i-danskerne

Sedimentary record of plutonium in the North Yellow Sea and the response to catchment environmental changes of inflow rivers
Plutonium (Pu) isotopes were first determined in surface and core sediment samples collected from the northern North Yellow Sea (NYS) to elucidate their source terms and deposition process as well as the response to catchment environmental changes of inflow rivers. $^{240}$Pu/$^{239}$Pu atom ratios in all sediments showed the typical global fallout value
of ∼0.18 without any influences from the nuclear weapons tests conducted recently in the North Korea or early in the Pacific Proving Ground. The large variation of 239+240Pu activities (0.022±0.515 mBq/g) observed in surface sediments should be mainly attributed to the re-suspension and transportation of fine sediments influenced by the Liaonan Costal Current. Based on the two 239+249Pu depth profiles with easily observed onset fallout levels (1952) and global fallout peaks (1963), 239+240Pu served as a valid time mark in the coastal sedimentary system. Riverine input Pu contributed only 15±27% to the total global fallout inventory (92.5±108.8 Bq/m2) in the northern NYS, much lower than that in the Yangtze River estuary (77±80%), indicating a better soil conservation in the northeast China due to higher forest coverage compared to the Yangtze River's drainage basin. The increase of riverine input Pu after 1980s reflected the more intense soil erosion degree caused by the land use and cover change due to the increment of human activities in the northeast China at the same period. Our results demonstrated that plutonium is a good indicator for studying sedimentary process and its response to the environment in the coastal area.

General information
State: Published
Organisations: Radioecology and Tracer Studies, Center for Nuclear Technologies, The Hevesy Laboratory, Nanjing University, Ministry of Environmental Protection
Authors: Xu, Y. (Ekstern), Pan, S. (Ekstern), Gao, J. (Ekstern), Hou, X. (Intern), Ma, Y. (Ekstern), Hao, Y. (Ekstern)
Number of pages: 9
Pages: 130-138
Publication date: 2018
Main Research Area: Technical/natural sciences

Publication Information
Journal: Chemosphere
Volume: 207
ISSN (Print): 0045-6535
Ratings:
BFI (2018): BFI-level 2
Web of Science (2018): Indexed yes
BFI (2017): BFI-level 2
Scopus rating (2017): CiteScore 4.62 SJR 1.435 SNIP 1.448
Web of Science (2017): Impact factor 4.427
Web of Science (2017): Indexed yes
BFI (2016): BFI-level 2
Scopus rating (2016): CiteScore 4.39 SJR 1.447 SNIP 1.625
Web of Science (2016): Impact factor 4.208
Web of Science (2016): Indexed yes
BFI (2015): BFI-level 2
Scopus rating (2015): SJR 1.497 SNIP 1.567 CiteScore 4.04
Web of Science (2015): Impact factor 3.698
Web of Science (2015): Indexed yes
BFI (2014): BFI-level 2
Scopus rating (2014): SJR 1.59 SNIP 1.639 CiteScore 3.76
Web of Science (2014): Impact factor 3.34
Web of Science (2014): Indexed yes
BFI (2013): BFI-level 2
Scopus rating (2013): SJR 1.721 SNIP 1.751 CiteScore 3.92
Web of Science (2013): Impact factor 3.499
ISI indexed (2013): ISI indexed yes
Web of Science (2013): Indexed yes
BFI (2012): BFI-level 2
Scopus rating (2012): SJR 1.794 SNIP 1.618 CiteScore 3.5
Web of Science (2012): Impact factor 3.137
ISI indexed (2012): ISI indexed yes
Web of Science (2012): Indexed yes
BFI (2011): BFI-level 2
Scopus rating (2011): SJR 1.962 SNIP 1.508 CiteScore 3.61
Web of Science (2011): Impact factor 3.206
135La as an auger-electron emitter for targeted internal radiotherapy

Introduction: 135La has favorable nuclear and chemical properties for Auger-based targeted internal radiotherapy. Here we present detailed investigations of the production, emissions, imaging characteristics, and dosimetry related to 135La therapy. Methods and Results: 135La was produced by 16.5 MeV proton irradiation of metallic natBa on a medical cyclotron, and was isolated and purified by trap-and-release on weak cation-exchange resin. The average production rate was 407 ± 19 MBq/µA (saturation activity, n = 3), and the radionuclidic purity was 98% at 20 h post irradiation. Chemical separation recovered > 98 % of the 135La with an effective molar activity of 70 ±20 GBq/µmol. To better assess cellular and organ dosimetry of this nuclide, we have recalculated the X-ray and Auger emission spectra using a Monte Carlo model accounting for effects of multiple vacancies during the Auger cascade. The generated Auger spectrum was used to recalculate cellular S-factors. Conclusion: 135La was produced with high specific activity, reactivity, radionuclidic purity, and yield. The emission spectrum and the dosimetry are favorable for internal radionuclide therapy.

General information
State: Published
Number of pages: 74
Publication date: 2018

Identification and imaging of modern paints using Secondary Ion Mass Spectrometry with MeV ions
Secondary Ion Mass Spectrometry using MeV ion excitation was applied to analyse modern paint materials containing synthetic organic pigments and binders. It was demonstrated that synthetic organic pigments and binder components with molecular masses in the m/z range from 1 to 1200 could be identified in different paint samples with a high efficiency and in a single measurement. Different ways of mounting of mostly insulating paint samples were tested prior to the analysis in order to achieve the highest possible yield of pigment main molecular ions. As Time-of-Flight mass spectrometer for MeV Secondary Ion Mass Spectrometry is attached to the heavy ion microprobe, molecular imaging on cross-sections of small paint fragments was performed using focused ions. Due to the fact that molecules are extracted from the uppermost layer of the sample and to avoid surface contamination, the paint samples were not embedded in the resin as is usually done when imaging of paint samples using different techniques in the field of cultural heritage.

General information
State: Published
Organisations: Center for Nuclear Technologies, The Hevesy Laboratory, Radioecology and Tracer Studies, Ruder Boskovic Institute, Akademie der Bildenden Kunste Wien - Academy of Fine Arts Vienna
Authors: Bogdanović Radović, I. (Ekstern), Siketić, Z. (Ekstern), Jembrih-Simbürger, D. (Ekstern), Marković, N. (Intern), Anghelone, M. (Ekstern), Stoytschew, V. (Ekstern), Jakšić, M. (Ekstern)
Number of pages: 6
Pages: 296-301
Publication date: 1 Sep 2017
Main Research Area: Technical/natural sciences

Publication information
Journal: Nuclear Instruments and Methods in Physics Research, Section B: Beam Interactions with Materials and Atoms
A 60-year record of $^{129}$I in Taal Lake sediments (Philippines): Influence of human nuclear activities at low latitude region

The influence of human nuclear activities on environmental radioactivity is not well known at low latitude region that are distant from nuclear tests sites and nuclear facilities. A sediment core collected from Taal Lake in the central Philippines was analyzed for $^{129}$I and $^{127}$I to investigate this influence in a low-latitude terrestrial system. A baseline of $^{129}$I/$^{127}$I atomic ratios was established at $((2.04–5.14) \times 10^{-12})$ in the pre-nuclear era in this region. Controlled by the northeasterly equatorial trade winds, increased $^{129}$I/$^{127}$I ratios of $(20.1–69.3) \times 10^{-12}$ suggest that atmospheric nuclear weapons tests at the Pacific Proving Grounds in the central Pacific Ocean was the major source of $^{129}$I in the sediment during 1956–1962. The $^{129}$I/$^{127}$I ratios, up to $157.5 \times 10^{-12}$ after 1964, indicate a strong influence by European nuclear fuel reprocessing plants. The East Asian Winter Monsoon is found to be the dominant driving force in the atmospheric dispersion of radioactive iodine ($^{129}$I) from the European nuclear fuel reprocessing plants to Southeast Asia, which is also important for dispersion of other airborne pollutants from the middle-high, to low latitude regions. A significant $^{129}$I/$^{127}$I peak at 42.8 cm in the Taal Lake core appears to be the signal of the Chernobyl accident in 1986. In addition, volcanic activities are reflected in the iodine isotope profiles in the sediment core, suggesting the potential of using iodine isotopes as an indicator of volcanic eruptions.
Ratings:
BFI (2018): BFI-level 2
Web of Science (2018): Indexed yes
BFI (2017): BFI-level 2
Scopus rating (2017): CiteScore 4.62 SJR 1.435 SNIP 1.448
Web of Science (2017): Impact factor 4.427
Web of Science (2017): Indexed yes
BFI (2016): BFI-level 2
Scopus rating (2016): CiteScore 4.39 SJR 1.447 SNIP 1.625
Web of Science (2016): Impact factor 4.208
Web of Science (2016): Indexed yes
BFI (2015): BFI-level 2
Scopus rating (2015): SJR 1.497 SNIP 1.567 CiteScore 4.04
Web of Science (2015): Impact factor 3.698
Web of Science (2015): Indexed yes
BFI (2014): BFI-level 2
Scopus rating (2014): SJR 1.59 SNIP 1.639 CiteScore 3.76
Web of Science (2014): Impact factor 3.34
Web of Science (2014): Indexed yes
BFI (2013): BFI-level 2
Scopus rating (2013): SJR 1.721 SNIP 1.751 CiteScore 3.92
Web of Science (2013): Impact factor 3.499
ISI indexed (2013): ISI indexed yes
Web of Science (2013): Indexed yes
BFI (2012): BFI-level 2
Scopus rating (2012): SJR 1.794 SNIP 1.618 CiteScore 3.5
Web of Science (2012): Impact factor 3.137
ISI indexed (2012): ISI indexed yes
Web of Science (2012): Indexed yes
BFI (2011): BFI-level 2
Scopus rating (2011): SJR 1.962 SNIP 1.508 CiteScore 3.61
Web of Science (2011): Impact factor 3.206
ISI indexed (2011): ISI indexed yes
Web of Science (2011): Indexed yes
BFI (2010): BFI-level 2
Scopus rating (2010): SJR 1.879 SNIP 1.424
Web of Science (2010): Impact factor 3.155
Web of Science (2010): Indexed yes
BFI (2009): BFI-level 2
Scopus rating (2009): SJR 1.842 SNIP 1.572
Web of Science (2009): Indexed yes
BFI (2008): BFI-level 1
Scopus rating (2008): SJR 1.658 SNIP 1.58
Web of Science (2008): Indexed yes
Scopus rating (2007): SJR 1.5 SNIP 1.605
Web of Science (2007): Indexed yes
Scopus rating (2006): SJR 1.418 SNIP 1.673
Web of Science (2006): Indexed yes
Scopus rating (2005): SJR 1.479 SNIP 1.558
Web of Science (2005): Indexed yes
Scopus rating (2004): SJR 1.627 SNIP 1.479
Web of Science (2004): Indexed yes
Scopus rating (2003): SJR 1.321 SNIP 1.323
Anthropogenic $^{236}\text{U}$ in Danish Seawater: Global Fallout versus Reprocessing Discharge

This work focuses on the occurrence of $^{236}\text{U}$ in seawater along Danish coasts, which is the sole water-exchange region between the North Sea-Atlantic Ocean and the Baltic Sea. Seawater collected in 2013 and 2014 were analyzed for $^{236}\text{U}$ (as well as $^{238}\text{U}$ and $^{137}\text{Cs}$). Our results indicate that $^{236}\text{U}$ concentrations in Danish seawater are distributed within a relatively narrow range of $(3.6-8.2) \times 10^7$ atom/L and, to a certain extent, independent of salinity. $^{236}\text{U}/^{238}\text{U}$ atomic ratios in Danish seawater are more than 4 times higher than the estimated global fallout value of $1 \times 10^{-9}$. The levels of $^{236}\text{U}/^{238}\text{U}$ atomic ratios obtained are comparable to those reported for the open North Sea and much higher than several other open oceans worldwide. This indicates that besides the global fallout input, the discharges from the two major European nuclear reprocessing plants are dominating sources of $^{236}\text{U}$ in Danish seawater. However, unexpectedly high $^{236}\text{U}/^{238}\text{U}$ ratios as well as high $^{236}\text{U}$ concentrations were observed at low-salinity locations of the Baltic Sea. While this feature might be interpreted as a clue for another significant $^{236}\text{U}$ input in the Baltic Sea, it may also be caused by the complexity of water currents or slow turnover rate.
Coincidence gamma-ray spectrometry

Gamma-ray spectrometry with high-purity germanium (HPGe) detectors is often the technique of choice in an environmental radioactivity laboratory. When measuring environmental samples associated activities are usually low so an important parameter that describes the performance of the spectrometer for a nuclide of interest is the minimum detectable activity (MDA). There are many ways for lowering the MDAs in gamma spectrometry. Recently, developments of fast and compact digital acquisition systems have led to growing number of multiple HPGe detector spectrometers. In these applications all detected events are recorded in a list mode file with their timestamp and energy, enabling coincidence identification and spectrum manipulation in post-processing. When coincidence gamma-spectrometry is used for cascade emitting nuclides, coincident signals can be extracted thus significantly reducing the background, as random coincidences are unlikely. This is especially evident when there is high activity of other nuclides present in the sample contributing to high Compton background. When the nuclide of interest is a single-gamma emitter, coincidence signal can be subtracted from the total to lower the background. In this work, we present a new coincidence spectrometer operated at the Gamma Laboratory of the Radioecology Section at Center for Nuclear Technologies (Nutech). NUCLeGeS consists of two HPGe detectors equipped with a digital acquisition system enabling timestamped list mode data acquisition with 10 ns time resolution. Post-processing software enables coincidence identification and produces spectra ready for use with GENIE2000 analysis software.

Comparison of the analytical methods used to determine natural and artificial radionuclides from environmental samples by gamma, alpha and beta spectrometry: Final Report from the NKS-B CAMNAR activity

In CAMNAR, an extensive interlaboratory exercise on the analytical methods used to determine several radionuclides present in the environmental samples was organized. Activity concentration of different natural radionuclides, such as Rn-222, Pb-210, Po-210, K-40, Ra-226, Ra-228 and isotopes of uranium, in addition to artificial Cs-137 and Am-241 were analysed from lake sediment samples and drinking water. The measurement techniques were gamma-ray spectrometry, alpha spectrometry, liquid scintillation counting and inductively coupled plasma mass spectrometry. Twenty six laboratories from nine Nordic and European countries participated in the intercomparison. Extraordinary variation between the results reported by different laboratories were revealed for some radionuclides indicating the need of future intercomparisons especially in the case of natural water samples.
Comprehensive radiochemical analysis for nuclear decommissioning and waste management at DTU Nutech

General information
State: Published
Organisations: Center for Nuclear Technologies, The Hevesy Laboratory, Radioecology and Tracer Studies
Authors: Jakobs, G. (Intern)
Number of pages: 1
Publication date: 2017
Event: Abstract from Annual Meeting on Nuclear Technology, .
Main Research Area: Technical/natural sciences
Electronic versions:
Abstract_Comprehensive_radiochemical_analysis_for_nuclear_decommissioning_and_waste_management_at_DTU_Nutech.pdf

Relations
Activities:
Comprehensive radiochemical analysis for nuclear decommissioning and waste management at DTU Nutech, Risø, Denmark
Publication: Research - peer-review › Conference abstract for conference – Annual report year: 2017

Corrigendum to "Large Gliadin Peptides Detected in the Pancreas of NOD and Healthy Mice following Oral Administration*
In the article titled "Large Gliadin Peptides Detected in the Pancreas of NOD and Healthy Mice following Oral Administration" [1], there was an error in the peptide sequences in Section . Gliadin Peptides, which should be corrected as follows:

The sequences H-LQLQPFPQPELPYPQPQPELPYPQPQPELPYP-OHY and H-LGQQPFPQPPQPYQPQPQPF-OHY should be corrected to H-LQLQPFPQPELPYPQPQPELPYPQPQPF-OH and H-LGQQPFPQPPQPYQPQPQPF-OH.

General information
State: Published
Organisations: The Hevesy Laboratory, Rigshospitalet, Statens Serum Institut, Novozymes A/S
Number of pages: 1
Publication date: 2017
Main Research Area: Technical/natural sciences

Publication information
Journal: Journal of Diabetes Research
Volume: 2017
Article number: 9709704
ISSN (Print): 2314-6745
Ratings:
BFI (2018): BFI-level 1
Web of Science (2018): Indexed yes
BFI (2017): BFI-level 1
Scopus rating (2017): SNIP 0.919 SJR 1.116 CiteScore 2.73
Web of Science (2017): Impact factor 2.885
Web of Science (2017): Indexed yes
Determination of radionuclidic impurities in $^{99m}$Tc eluate from $^{99}$Mo/$^{99m}$Tc generator for quality control

Technetium-99m is the principal radioisotope used in medical diagnostics; radionuclidic impurity is the major concern of its quality. This work presents an analytical method for sequential determination of all radionuclidic impurities listed in pharmacopoeia including gamma emitters, alpha emitters, $^{89}$Sr and $^{90}$Sr. Radioactive decay for removal of $^{99m}$Tc, ion exchange and extraction chromatography for removal of $^{99}$Mo and $^{99}$Tc are effective for separation of interferences. Gamma spectrometry, LSC with alpha/beta discrimination, and Cherenkov counting using LSC are sensitive methods for measurement of the impurity radionuclides. The detection limits of this method are well meet the requirement of the quality control according to the limitation of the pharmacopoeia.

General information

State: Published
Organisations: Center for Nuclear Technologies, The Hevesy Laboratory, Radioecology and Tracer Studies
Authors: Hou, X. (Intern)
Pages: 659-668
Publication date: 2017
Main Research Area: Technical/natural sciences
Publication information
Journal: Journal of Radioanalytical and Nuclear Chemistry
Volume: 314
Issue number: 2
ISSN (Print): 0236-5731
Ratings:
BFI (2018): BFI-level 1
Web of Science (2018): Indexed yes
BFI (2017): BFI-level 1
Scopus rating (2017): CiteScore 1.14 SJR 0.47 SNIP 0.738
Web of Science (2017): Impact factor 1.181
Web of Science (2017): Indexed yes
BFI (2016): BFI-level 1
Scopus rating (2016): CiteScore 1.24 SJR 0.521 SNIP 0.831
Web of Science (2016): Impact factor 1.282
Web of Science (2016): Indexed yes
BFI (2015): BFI-level 1
Scopus rating (2015): SJR 0.454 SNIP 0.719 CiteScore 0.99
Web of Science (2015): Impact factor 0.983
BFI (2014): BFI-level 1
Scopus rating (2014): SJR 0.453 SNIP 0.826 CiteScore 1.09
Web of Science (2014): Impact factor 1.034
Web of Science (2014): Indexed yes
BFI (2013): BFI-level 1
Scopus rating (2013): SJR 0.502 SNIP 1.152 CiteScore 1.44
Web of Science (2013): Impact factor 1.415
ISI indexed (2013): ISI indexed yes
Web of Science (2013): Indexed yes
BFI (2012): BFI-level 1
Scopus rating (2012): SJR 0.542 SNIP 0.899 CiteScore 1.26
Web of Science (2012): Impact factor 1.467
ISI indexed (2012): ISI indexed yes
BFI (2011): BFI-level 1
Scopus rating (2011): SJR 0.526 SNIP 0.867 CiteScore 1.32
Web of Science (2011): Impact factor 1.52
ISI indexed (2011): ISI indexed yes
Web of Science (2011): Indexed yes
BFI (2010): BFI-level 1
Scopus rating (2010): SJR 0.493 SNIP 0.667
Web of Science (2010): Impact factor 0.777
Web of Science (2010): Indexed yes
BFI (2009): BFI-level 1
Scopus rating (2009): SJR 0.385 SNIP 0.723
Web of Science (2009): Indexed yes
BFI (2008): BFI-level 1
Scopus rating (2008): SJR 0.442 SNIP 0.804
Web of Science (2008): Indexed yes
Scopus rating (2007): SJR 0.441 SNIP 0.717
Web of Science (2007): Indexed yes
Scopus rating (2006): SJR 0.393 SNIP 0.645
Web of Science (2006): Indexed yes
Scopus rating (2005): SJR 0.397 SNIP 0.667
Scopus rating (2004): SJR 0.451 SNIP 0.656
Web of Science (2004): Indexed yes
Determination of $^{226}$Ra in natural water samples by liquid scintillation counting

General information
State: Published
Organisations: Center for Nuclear Technologies, The Hevesy Laboratory, Radioecology and Tracer Studies, The National Public Health and Medical Officer Service
Authors: Osváth, S. (Intern), Rell, P. (Ekstern), Kónyi, J. K. (Ekstern), Szabó, G. (Ekstern)
Publication date: 2017
Event: Poster session presented at International Conference on Advances in Liquid scintillation Spectrometry 2017, Copenhagen, Denmark.
Main Research Area: Technical/natural sciences
Electronic versions:
226Ra_LSC2017_v10_3_.pdf
Source: PublicationPreSubmission
Source-ID: 141856494
Publication: Research - peer-review › Poster – Annual report year: 2017

Determination of $^{93}$Zr in nuclear power plant wastes
A radioanalytical method (based on separation using UTEVA columns and ICP-MS measurement) has been used for determination of $^{93}$Zr in 37 nuclear power plant samples. As $^{93}$Nb might affect the detection of $^{93}$Zr, Monte Carlo activation model was used to calculate the expected $^{93}$Zr/$^{94}$Zr mass ratio, which was compared to measured ones. It was found, that a decontamination factor of $10^3$ is sufficient to get a measurement uncertainty of less than 10%.

General information
State: Published
Organisations: Center for Nuclear Technologies, The Hevesy Laboratory, Radioecology and Tracer Studies, Hungarian Academy of Sciences, RadAnal Ltd., Budapest University of Technology and Economics, Isotoptech Zrt
Authors: Osváth, S. (Intern), Vajda, N. (Ekstern), Molnar, Z. (Ekstern), Kovacs-Szeles, E. (Ekstern), Braun, M. (Ekstern), Halasz, M. (Ekstern)
Number of pages: 8
Pages: 31-38
Publication date: 2017
Main Research Area: Technical/natural sciences

Publication information
Journal: Journal of Radioanalytical and Nuclear Chemistry
Volume: 314
Issue number: 1
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BFI (2018): BFI-level 1
Web of Science (2018): Indexed yes
BFI (2017): BFI-level 1
Scopus rating (2017): CiteScore 1.14 SJR 0.47 SNIP 0.738
Digital gamma-gamma coincidence HPGe system for environmental analysis

The performance of a new gamma-gamma coincidence spectrometer system for environmental samples analysis at the Center for Nuclear Technologies of the Technical University of Denmark (DTU) is reported. Nutech Coincidence Low Energy Germanium Sandwich (NUCLEGeS) system consists of two HPGe detectors in a surface laboratory with a digital acquisition system used to collect the data in time-stamped list mode with 10. ns time resolution. The spectrometer is used in both anticoincidence and coincidence modes.

General information
State: Published
Organisations: Center for Nuclear Technologies, The Hevesy Laboratory, Radioecology and Tracer Studies
Authors: Markovic, N. (Intern), Roos, P. (Intern), Nielsen, S. P. (Intern)
Number of pages: 3
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Main Research Area: Technical/natural sciences

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Journal: Applied Radiation and Isotopes
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Ratings:
BFI (2018): BFI-level 1
Web of Science (2018): Indexed yes
BFI (2017): BFI-level 1
Scopus rating (2017): CiteScore 1.15 SJR 0.528 SNIP 0.973
Web of Science (2017): Impact factor 1.123
Web of Science (2017): Indexed yes
BFI (2016): BFI-level 1
Scopus rating (2016): CiteScore 1.17 SJR 0.537 SNIP 1.027
Web of Science (2016): Impact factor 1.128
Web of Science (2016): Indexed yes
BFI (2015): BFI-level 1
Scopus rating (2015): SJR 0.547 SNIP 0.999 CiteScore 1.15
Web of Science (2015): Impact factor 1.136
BFI (2014): BFI-level 1
Scopus rating (2014): SJR 0.574 SNIP 1.203 CiteScore 1.27
Web of Science (2014): Impact factor 1.231
Web of Science (2014): Indexed yes
BFI (2013): BFI-level 1
Scopus rating (2013): SJR 0.526 SNIP 0.953 CiteScore 1.24
Web of Science (2013): Impact factor 1.056
ISI indexed (2013): ISI indexed yes
Web of Science (2013): Indexed yes
BFI (2012): BFI-level 1
Scopus rating (2012): SJR 0.671 SNIP 1.151 CiteScore 1.29
Web of Science (2012): Impact factor 1.179
ISI indexed (2012): ISI indexed yes
Web of Science (2012): Indexed yes
BFI (2011): BFI-level 1
Effects of the 2014 major Baltic inflow on methane and nitrous oxide dynamics in the water column of the central Baltic Sea

In late 2014, a large, oxygen-rich salt water inflow entered the Baltic Sea and caused considerable changes in deep water oxygen concentrations. We studied the effects of the inflow on the concentration patterns of two greenhouse gases, methane and nitrous oxide, during the following year (2015) in the water column of the Gotland Basin. In the eastern basin, methane which had previously accumulated in the deep waters was largely removed during the year. Here, volume-weighted mean concentration below 70 m decreased from 108 nM in March to 16.3 nM over a period of 141 days (0.65 nM d(-1)), predominantly due to oxidation (up to 79 %) following turbulent mixing with the oxygen-rich inflow. In contrast nitrous oxide, which was previously absent from deep waters, accumulated in deep waters due to enhanced nitrification following the inflow. Volume-weighted mean concentration of nitrous oxide below 70 m increased from 11.8 nM in March to 24.4 nM in 141 days (0.09 nM d(-1)). A transient extreme accumulation of nitrous oxide (877 nM) was observed in the deep waters of the Eastern Gotland Basin towards the end of 2015, when deep waters turned anoxic again, sedimentary denitrification was induced and methane was reintroduced to the bottom waters. The Western Gotland Basin gas biogeochemistry was not affected by the inflow.

General information
State: Published
Organisations: Center for Nuclear Technologies, The Hevesy Laboratory, Radioecology and Tracer Studies, University of Helsinki, Leibniz Institute for Baltic Sea Research Warnemünde (IOW)
Authors: Myllykangas, J. (Ekstern), Jilbert, T. (Ekstern), Jakobs, G. (Intern), Rehder, G. (Ekstern), Werner, J. (Ekstern), Hietanen, S. (Ekstern)
Environmental radioactivity and tracer studies over the past sixty years in Denmark

Erratum to: Inter-laboratory exercise with an aim to compare methods for $^{90}\text{Sr}$ and $^{239,240}\text{Pu}$ determination in environmental soil samples

In the original article, the LOD assigned to method Sr-B in Table 1 was published incorrectly as 24 Bq/kg, the correct LOD for that method should be 10.4 Bq/kg. As a consequence the range of LODs, as presented in the first sentence of the section Limit of detection should be stated as "It can be seen from Table 1 that, the LODs of $^{90}\text{Sr}$ vary from 0.2 to 10.4 Bq/kg among the four methods used in this work".
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Journal: Journal of Radioanalytical and Nuclear Chemistry
Volume: 314
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Scopus rating (2017): CiteScore 1.14 SJR 0.47 SNIP 0.738
Web of Science (2017): Impact factor 1.181
Web of Science (2017): Indexed yes
BFI (2016): BFI-level 1
Scopus rating (2016): CiteScore 1.24 SJR 0.521 SNIP 0.831
Web of Science (2016): Impact factor 1.282
Web of Science (2016): Indexed yes
BFI (2015): BFI-level 1
Scopus rating (2015): SJR 0.454 SNIP 0.719 CiteScore 0.99
Web of Science (2015): Impact factor 0.983
BFI (2014): BFI-level 1
Scopus rating (2014): SJR 0.453 SNIP 0.826 CiteScore 1.09
Web of Science (2014): Impact factor 1.034
Web of Science (2014): Indexed yes
BFI (2013): BFI-level 1
Scopus rating (2013): SJR 0.502 SNIP 1.152 CiteScore 1.44
Web of Science (2013): Impact factor 1.415
ISI indexed (2013): ISI indexed yes
Web of Science (2013): Indexed yes
BFI (2012): BFI-level 1
Scopus rating (2012): SJR 0.542 SNIP 0.899 CiteScore 1.26
Web of Science (2012): Impact factor 1.467
ISI indexed (2012): ISI indexed yes
BFI (2011): BFI-level 1
Scopus rating (2011): SJR 0.526 SNIP 0.867 CiteScore 1.32
Web of Science (2011): Impact factor 1.52
ISI indexed (2011): ISI indexed yes
Web of Science (2011): Indexed yes
BFI (2010): BFI-level 1
Scopus rating (2010): SJR 0.493 SNIP 0.667
Web of Science (2010): Impact factor 0.777
Web of Science (2010): Indexed yes
BFI (2009): BFI-level 1
Scopus rating (2009): SJR 0.385 SNIP 0.723
Web of Science (2009): Indexed yes
BFI (2008): BFI-level 1
Scopus rating (2008): SJR 0.442 SNIP 0.804
Web of Science (2008): Indexed yes
Scopus rating (2007): SJR 0.441 SNIP 0.717
Web of Science (2007): Indexed yes
Scopus rating (2006): SJR 0.393 SNIP 0.645
Web of Science (2006): Indexed yes
Foreword

General information
State: Published
Organisations: Center for Nuclear Technologies, The Hevesy Laboratory, Radioecology and Tracer Studies
Authors: Hou, X. (Intern)
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Web of Science (2017): Impact factor 1.181
Web of Science (2017): Indexed yes
BFI (2016): BFI-level 1
Scopus rating (2016): CiteScore 1.24 SJR 0.521 SNIP 0.831
Web of Science (2016): Impact factor 1.282
Web of Science (2016): Indexed yes
BFI (2015): BFI-level 1
Scopus rating (2015): SJR 0.454 SNIP 0.719 CiteScore 0.99
Web of Science (2015): Impact factor 0.983
BFI (2014): BFI-level 1
Scopus rating (2014): SJR 0.453 SNIP 0.826 CiteScore 1.09
Web of Science (2014): Impact factor 1.034
Web of Science (2014): Indexed yes
BFI (2013): BFI-level 1
Scopus rating (2013): SJR 0.502 SNIP 1.152 CiteScore 1.44
Web of Science (2013): Impact factor 1.415
ISI indexed (2013): ISI indexed yes
Web of Science (2013): Indexed yes
Historical changes in $^{239}$Pu and $^{240}$Pu sources in sedimentary records in the East China Sea: Implications for provenance and transportation

Concentrations and isotopic compositions of plutonium (Pu) are widely used for its source identification and to determine transport processes of Pu-associated particulate matter and water. We investigated the concentrations of $^{239}$Pu and $^{240}$Pu and their ratios in a number of sediment samples from the East China Sea (ECS) collected in the summer of 2013 (August 6–28). The $^{239}$Pu activity concentrations in surface sediment samples were found to range between 0.048 and 0.492 Bqkg$^{-1}$ and the $^{240}$Pu/$^{239}$Pu atom ratios showed a similar trend as that of the $^{239}$, $^{240}$Pu activities; the Pu atom ratios ranged from 0.158 to 0.297 and were mostly higher than the mean global fallout value of 0.18. The $^{239+240}$Pu inventories in the ECS varied widely, from 2 to 807 Bqm$^{-2}$, with the highest values commonly found in the coastal areas. In the Yangtze Estuary, the mean $^{239+240}$Pu activity concentration is close to the estimated value of the suspended material from the Yangtze River catchment (0.18 Bqkg$^{-1}$), and the $^{240}$Pu/$^{239}$Pu atom ratio was found to be ~0.18, which indicates that the Yangtze River input is the dominant source of Pu for this area. The total annual Yangtze River input of $^{239+240}$Pu was estimated to be $2.4 \times 10^{10}$Bq, which is small compared to the total amount of $^{239+240}$Pu buried, $3.1 \times 10^{10}$Bq in the whole ECS. The Pacific Proving Ground input appears to be the dominant source of Pu to the ECS, accounting for 45%–52% of the total inventory. The fractional amount of $^{239+240}$Pu scavenged from the total $^{239+240}$Pu transported by the Kuroshio Current (KC) and Taiwan Warm Current (TWC) into ECS sediments is estimated to be ~10%. Our study shows that the $^{240}$Pu/$^{239}$Pu atom ratio is useful not only to obtain a better insight of the biogeochemistry
influenced by the KC, but also to trace the long-range transport of other particle-reactive species. Besides, the sedimentation rates obtained based on the penetration depths of 239+240Pu and vertical profiles of excess 210Pb agree within uncertainties, which suggests that 239+240Pu can potentially be used as a chronostratigraphic time marker in the marine environment.

General information
State: Published
Organisations: Center for Nuclear Technologies, The Hevesy Laboratory, Radioecology and Tracer Studies, East China Normal University, Wayne State University
Authors: Wang, J. (Ekstern), Baskaran, M. (Ekstern), Hou, X. (Intern), Du, J. (Ekstern), Zhang, J. (Ekstern)
Pages: 32-42
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Main Research Area: Technical/natural sciences

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BFI (2018): BFI-level 2
Web of Science (2018): Indexed yes
BFI (2017): BFI-level 2
Scopus rating (2017): CiteScore 4.77 SJR 3.166 SNIP 1.616
Web of Science (2017): Impact factor 4.581
Web of Science (2017): Indexed yes
BFI (2016): BFI-level 2
Scopus rating (2016): CiteScore 4.53 SJR 3.156 SNIP 1.554
Web of Science (2016): Impact factor 4.409
Web of Science (2016): Indexed yes
BFI (2015): BFI-level 2
Scopus rating (2015): SJR 3.499 SNIP 1.569 CiteScore 4.61
Web of Science (2015): Indexed yes
BFI (2014): BFI-level 2
Scopus rating (2014): SJR 3.369 SNIP 1.79 CiteScore 4.84
Web of Science (2014): Impact factor 4.734
Web of Science (2014): Indexed yes
BFI (2013): BFI-level 2
Scopus rating (2013): SJR 3.613 SNIP 1.741 CiteScore 4.94
Web of Science (2013): Impact factor 4.724
ISI indexed (2013): ISI indexed yes
Web of Science (2013): Indexed yes
BFI (2012): BFI-level 2
Scopus rating (2012): SJR 3.537 SNIP 1.712 CiteScore 4.35
Web of Science (2012): Impact factor 4.349
ISI indexed (2012): ISI indexed yes
Web of Science (2012): Indexed yes
BFI (2011): BFI-level 2
Scopus rating (2011): SJR 3.944 SNIP 1.627 CiteScore 4.25
Web of Science (2011): Impact factor 4.18
ISI indexed (2011): ISI indexed yes
BFI (2010): BFI-level 2
Scopus rating (2010): SJR 3.449 SNIP 1.656
Web of Science (2010): Impact factor 4.279
Web of Science (2010): Indexed yes
BFI (2009): BFI-level 1
Imaging neuronal pathways with 52 Mn PET in rats

General information
State: Published
Organisations: Center for Nuclear Technologies, The Hevesy Laboratory, Eberhard-Karls-Universität Tübingen
Authors: Napieczynska, H. (Ekstern), Severin, G. W. (Intern), Fonslet, J. (Intern), Menegakis, A. (Ekstern), Wiehr, S. (Ekstern), Pichler, B. J. (Ekstern), Calaminus, C. (Ekstern)
Pages: 149
Publication date: 2017
Conference: Berlin BRAIN & BRAIN PET 2017, Berlin, Germany, 01/04/2017 - 01/04/2017
Main Research Area: Technical/natural sciences

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Journal: Journal of Cerebral Blood Flow and Metabolism
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BFI (2018): BFI-level 1
Web of Science (2018): Indexed yes
BFI (2017): BFI-level 1
Scopus rating (2017): CiteScore 5.07 SJR 2.558 SNIP 1.437
Web of Science (2017): Impact factor 6.045
Web of Science (2017): Indexed yes
BFI (2016): BFI-level 1
Scopus rating (2016): CiteScore 4.78 SJR 2.402 SNIP 1.396
Web of Science (2016): Impact factor 5.081
BFI (2015): BFI-level 1
Scopus rating (2015): SJR 3.112 SNIP 1.74 CiteScore 5.49
Web of Science (2015): Impact factor 4.929
BFI (2014): BFI-level 1
Scopus rating (2014): SJR 2.94 SNIP 1.652 CiteScore 5.15
Web of Science (2014): Impact factor 5.407
BFI (2013): BFI-level 1
Imaging neuronal pathways with $^{52}$Mn PET: Toxicity evaluation in rats

Manganese in its divalent state ($\text{Mn}^{2+}$) has features that make it a unique tool for tracing neuronal pathways. It is taken up and transported by neurons in an activity dependent manner and it can cross synapses. It also acts as a contrast agent for magnetic resonance imaging (MRI) enabling visualization of neuronal tracts. However, due to the limited sensitivity of MRI systems relatively high $\text{Mn}^{2+}$ doses are required. This is undesirable, especially in long-term studies, because of the known toxicity of the metal. In order to overcome this limitation, we propose $^{52}$Mn as a positron emission tomography (PET) neuronal tract tracer. We used $^{52}$Mn for imaging dopaminergic pathways after a unilateral injection into the ventral tegmental area (VTA), as well as the striatonigral pathway after an injection into the dorsal striatum (STR) in rats. Furthermore, we tested potentially noxious effects of the radioactivity dose with a behavioral test and histological staining. 24 h after $^{52}$Mn administration, the neuronal tracts were clearly visible in PET images and statistical analysis confirmed the observed distribution of the tracer. We noticed a behavioral impairment in some animals treated with 170 kBq of $^{52}$Mn, most likely caused by dysfunction of dopaminergic cells. Moreover, there was a substantial DNA damage in the brain tissue after applying 150 kBq of the tracer. However, all those effects were completely eliminated by reducing the $^{52}$Mn dose to 20-30 kBq. Crucially, the reduced dose was still sufficient for PET imaging.
Inter-laboratory exercise with an aim to compare methods for $^{90}$Sr and $^{239,240}$Pu determination in environmental soil samples

In order to deliver reliable results for a multitude of different scenarios, e.g. emergency preparedness, environmental monitoring, nuclear decommissioning and waste management, there is a constant process of method development in the field of radioanalytical chemistry. This work presents the results of a method comparison exercise aimed at quantifying $^{90}$Sr and $^{239,240}$Pu in environmental soil samples, with the intention of evaluating the performance and applicability of different methods. From the methods examined in this work, recommendations are given in order to find a radioanalytical measurement procedure, for $^{90}$Sr and $^{239,240}$Pu analysis, which is fit-for-purpose for a particular scenario.

General information

State: Published
Organisations: Center for Nuclear Technologies, The Hevesy Laboratory, Radioecology and Tracer Studies, University of Helsinki, Swedish Defence Research Agency, Institute for Energy Technology
Authors: Qiao, J. (Intern), Salminen-Paatero, S. (Ekstern), Rondahl, S. H. (Ekstern), Bourgeaux-Goget, M. (Ekstern), Roos, P. (Intern), Lagerkvist, P. (Ekstern), Strålberg, E. (Ekstern), Ramebäck, H. (Ekstern)
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Main Research Area: Technical/natural sciences

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BFI (2018): BFI-level 1
Web of Science (2018): Indexed yes
BFI (2017): BFI-level 1
Scopus rating (2017): CiteScore 1.14 SJR 0.47 SNIP 0.738
Web of Science (2017): Impact factor 1.181
Web of Science (2017): Indexed yes
BFI (2016): BFI-level 1
Scopus rating (2016): CiteScore 1.24 SJR 0.521 SNIP 0.831
Web of Science (2016): Impact factor 1.282
Web of Science (2016): Indexed yes
BFI (2015): BFI-level 1
Scopus rating (2015): SJR 0.454 SNIP 0.719 CiteScore 0.99
Web of Science (2015): Impact factor 0.983
BFI (2014): BFI-level 1
Scopus rating (2014): SJR 0.453 SNIP 0.826 CiteScore 1.09
Web of Science (2014): Impact factor 1.034
Web of Science (2014): Indexed yes
BFI (2013): BFI-level 1
Scopus rating (2013): SJR 0.502 SNIP 1.152 CiteScore 1.44
Web of Science (2013): Impact factor 1.415
ISI indexed (2013): ISI indexed yes
Web of Science (2013): Indexed yes
BFI (2012): BFI-level 1
Scopus rating (2012): SJR 0.542 SNIP 0.899 CiteScore 1.26
Web of Science (2012): Impact factor 1.467
ISI indexed (2012): ISI indexed yes
BFI (2011): BFI-level 1
Scopus rating (2011): SJR 0.526 SNIP 0.867 CiteScore 1.32
Web of Science (2011): Impact factor 1.52
ISI indexed (2011): ISI indexed yes
Web of Science (2011): Indexed yes
BFI (2010): BFI-level 1
Scopus rating (2010): SJR 0.493 SNIP 0.667
Web of Science (2010): Impact factor 0.777
Web of Science (2010): Indexed yes
BFI (2009): BFI-level 1
Scopus rating (2009): SJR 0.385 SNIP 0.723
Web of Science (2009): Indexed yes
BFI (2008): BFI-level 1
Scopus rating (2008): SJR 0.442 SNIP 0.804
Web of Science (2008): Indexed yes
Scopus rating (2007): SJR 0.441 SNIP 0.717
Web of Science (2007): Indexed yes
Scopus rating (2006): SJR 0.393 SNIP 0.645
Web of Science (2006): Indexed yes
Scopus rating (2005): SJR 0.397 SNIP 0.667
Scopus rating (2004): SJR 0.451 SNIP 0.656
Web of Science (2004): Indexed yes
Scopus rating (2003): SJR 0.397 SNIP 0.596
Scopus rating (2002): SJR 0.439 SNIP 0.664
Web of Science (2002): Indexed yes
Scopus rating (2001): SJR 0.396 SNIP 0.619
Web of Science (2001): Indexed yes
Scopus rating (2000): SJR 0.574 SNIP 0.674
Web of Science (2000): Indexed yes
Scopus rating (1999): SJR 0.556 SNIP 0.647
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Method comparison, Radiochemical analysis, Pu, Sr, Soil
Electronic versions:
JRNC_D_17_00408.pdf. Embargo ended: 04/08/2018
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10.1007/s10967-017-5385-9
Source: FindIt
Source-ID: 2372792712
Publication: Research - peer-review › Journal article – Annual report year: 2017
Local variance of atmospheric $^{14}$C concentrations around Fukushima Dai-ichi Nuclear Power Plant from 2010 to 2012

Radiocarbon ($^{14}$C) has been measured in single tree ring samples collected from the southwest of the Fukushima Dai-ichi Nuclear Power Plant. Our data indicate south-westwards dispersion of radiocarbon and the highest $^{14}$C activity observed so far in the local environment during the 2011 accident. The abnormally high $^{14}$C activity in the late wood of 2011 ring may imply an unknown source of radiocarbon nearby after the accident. The influence of $^{14}$C shrank from 30 km during normal reactor operation to 14 km for the accident in the northwest of FDNPP, but remains unclear in the southwest.

**General information**

**State:** Published
**Organisations:** Center for Nuclear Technologies, The Hevesy Laboratory, Radioecology and Tracer Studies, Scottish Universities Environmental Research Centre, Tianjin University, Fukushima University
**Authors:** Chen, B. (Ekstern), Xu, S. (Ekstern), Cook, G. T. (Ekstern), Freeman, S. P. H. T. (Ekstern), Hou, X. (Intern), Liu, C. (Ekstern), Naysmith, P. (Ekstern), Yamaguchi, K. (Ekstern)
**Number of pages:** 7
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- Web of Science (2018): Indexed yes
- BFI (2017): BFI-level 1
- Scopus rating (2017): CiteScore 1.14 SJR 0.47 SNIP 0.738
- Web of Science (2017): Impact factor 1.181
- Web of Science (2017): Indexed yes
- BFI (2016): BFI-level 1
- Scopus rating (2016): CiteScore 1.24 SJR 0.521 SNIP 0.831
- Web of Science (2016): Impact factor 1.282
- Web of Science (2016): Indexed yes
- BFI (2015): BFI-level 1
- Scopus rating (2015): SJR 0.454 SNIP 0.719 CiteScore 0.99
- Web of Science (2015): Impact factor 0.983
- BFI (2014): BFI-level 1
- Scopus rating (2014): SJR 0.453 SNIP 0.826 CiteScore 1.09
- Web of Science (2014): Impact factor 1.034
- Web of Science (2014): Indexed yes
- BFI (2013): BFI-level 1
- Scopus rating (2013): SJR 0.502 SNIP 1.152 CiteScore 1.44
- Web of Science (2013): Impact factor 1.415
- ISI indexed (2013): ISI indexed yes
- Web of Science (2013): Indexed yes
- BFI (2012): BFI-level 1
- Scopus rating (2012): SJR 0.542 SNIP 0.899 CiteScore 1.26
- Web of Science (2012): Impact factor 1.467
- ISI indexed (2012): ISI indexed yes
- BFI (2011): BFI-level 1
- Scopus rating (2011): SJR 0.526 SNIP 0.867 CiteScore 1.32
- Web of Science (2011): Impact factor 1.52
- ISI indexed (2011): ISI indexed yes
- Web of Science (2011): Indexed yes
- BFI (2010): BFI-level 1
- Scopus rating (2010): SJR 0.493 SNIP 0.667
- Web of Science (2010): Impact factor 0.777
Low-level gamma-ray spectrometry for the determination of $^{210}\text{Pb}$

A well High purity germanium (HPGe) gamma spectrometer with NaI(Tl) Compton anticoincidence shield recently installed at DTU Nutech and specially designed for low-level measurements was used for the $^{210}\text{Pb}$ determination in environmental samples. The system is compared to standard stand-alone HPGe spectrometers. The choice between high efficiency well and planar detectors as well as optimum sample size depending on available sample quantity are discussed. Results show that the only comparative advantage of the well anticoincidence system is when just small sample sizes are available.

General information
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Organisations: Center for Nuclear Technologies, The Hevesy Laboratory, Radioecology and Tracer Studies
Authors: Markovic, N. (Intern), Roos, P. (Intern), Nielsen, S. P. (Intern)
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BFI (2017): BFI-level 1
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Web of Science (2017): Impact factor 1.181
LSC methods for analysis of radionuclide impurity of $^{99m}$Tc eluate in quality control of $^{99Tc}$-$^{99m}$Tc generators

General information
State: Published
Organisations: Center for Nuclear Technologies, The Hevesy Laboratory, Radioecology and Tracer Studies
Authors: Hou, X. (Intern)
Number of pages: 3
Publication date: 2017
Event: Abstract from International Conference on Advances in Liquid scintillation Spectrometry 2017, Copenhagen, Denmark.
Main Research Area: Technical/natural sciences
Electronic versions:

Neodymium-140 DOTA-LM3: Evaluation of an In Vivo Generator for PET with a Non-Internalizing Vector

Neodymium ($^{140}$Nd) ($T_{1/2}=3.4$ days), owing to its short-lived positron emitting daughter $^{140}$Pr ($T_{1/2}=3.4$ min), has promise as an in vivo generator for positron emission tomography (PET). However, the electron capture decay of $^{140}$Nd is chemically disruptive to macrocycle-based radiolabelling, meaning that an in vivo redistribution of the daughter $^{140}$Pr is expected before positron emission. The purpose of this study was to determine how the delayed positron from the de-labeled $^{140}$Pr affects preclinical imaging with $^{140}$Nd. To explore the effect, $^{140}$Nd was produced at CERN-ISOLDE, reacted with the somatostatin analogue, DOTA-LM3 (1,4,7,10-tetraazacyclododecane, 1,4,7-triacetic acid, 10-acetamide N-p-Cl-Phe cyclo(D-Cys-Tyr-d-4-amino-Phe(carbamoyl)-Lys-Thr-Cys)D-Tyr-NH$_2$) and injected into H727 xenograft bearing mice. Comparative pre- and post-mortem PET imaging at 16 h postinjection was used to quantify the in vivo redistribution of $^{140}$Pr following $^{140}$Nd decay. The somatostatin receptor-positive pancreas exhibited the highest tissue accumulation of $^{140}$Nd-DOTA-LM3 (13% ID/g at 16 h) coupled with the largest observed redistribution rate, where 56 ± 7% (n=4, mean ± SD) of the in situ produced $^{140}$Pr washed out of the pancreas before decay. Contrastingly, the liver, spleen, and lungs acted as strong sink organs for free $^{140}$Pr$^{3+}$. Based upon these results, we conclude that $^{140}$Nd imaging with a non-internalizing vector convolutes the biodistribution of the tracer with the accumulation pattern of free $^{140}$Pr. This redistribution phenomenon may show promise as a probe of the cellular interaction with the vector, such as in determining tissue dependent internalization behavior.

General information
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Organisations: Center for Nuclear Technologies, The Hevesy Laboratory, Radioecology and Tracer Studies, University of Copenhagen, University Hospital Freiburg, CERN
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Publication date: 2017
Main Research Area: Technical/natural sciences

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$^{140}$Nd, $^{140}$Pr, DOTA-LM3, in vivo generator, Internalization, Positron emission tomography
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10.3389/fmed.2017.00098
Source: FindIt
Source-ID: 2372597751
Publication: Research - peer-review › Conference abstract for conference – Annual report year: 2017
Optimized procedures for manganese-52: Production, separation and radiolabeling

Pressed chromium-powder cyclotron targets were irradiated with 16MeV protons, producing $^{52}$Mn with average yields of 6.2±0.8MBq/µAh. Separation by solid-phase anion exchange from ethanol-HCl mixtures recovered 94.3±1.7% of $^{52}$Mn and reduced the chromium content by a factor of 2.2±0.4×10⁵. An additional AG 1-X8 column was used to remove copper, iron, cobalt, and zinc impurities from the prepared $^{52}$Mn in 8M HCl. The macrocyclic chelator DOTA was rapidly radiolabeled with $^{52}$Mn in aq. ammonium acetate (pH 7.5R.T.) with a radiochemical yield >99% within 1min and was stable for >2 days in bovine serum. The improved separation and purification methodology facilitates the use of 52Mn in basic science and preclinical investigations.

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Web of Science (2017): Indexed yes
BFI (2016): BFI-level 1
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Web of Science (2016): Indexed yes
BFI (2015): BFI-level 1
Scopus rating (2015): SJR 0.547 SNIP 0.999 CiteScore 1.15
Web of Science (2015): Impact factor 1.136
BFI (2014): BFI-level 1
Scopus rating (2014): SJR 0.574 SNIP 1.203 CiteScore 1.27
Web of Science (2014): Impact factor 1.231
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BFI (2013): BFI-level 1
Scopus rating (2013): SJR 0.526 SNIP 0.953 CiteScore 1.24
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ISI indexed (2013): ISI indexed yes
Web of Science (2013): Indexed yes
BFI (2012): BFI-level 1
Scopus rating (2012): SJR 0.671 SNIP 1.151 CiteScore 1.29
Web of Science (2012): Impact factor 1.179
ISI indexed (2012): ISI indexed yes
Web of Science (2012): Indexed yes
BFI (2011): BFI-level 1
Scopus rating (2011): SJR 0.644 SNIP 1.137 CiteScore 1.21
Web of Science (2011): Impact factor 1.172
ISI indexed (2011): ISI indexed yes
Web of Science (2011): Indexed yes
BFI (2010): BFI-level 1
PET imaging with copper-64 as a tool for real-time in vivo investigations of the necessity for crosslinking of polymeric micelles in nanomedicine: Imaging the influence of polymeric micelle crosslinking

Polymeric micelles in nanomedicine are often crosslinked to prevent disintegration in vivo. This typically requires clinically problematic chemicals or laborious procedures. In addition, crosslinking may interfere with advanced release strategies. Despite this, it is often not investigated whether crosslinking is necessary for efficient drug delivery. We used PET imaging with 64Cu to demonstrate general methodology for real-time in vivo investigations of micelle stability. Triblock copolymers with 4-methylcoumarin cores of ABC-type (PEG-PHEMA-PCMA) were functionalized in the handle region (PHEMA) with CB-TE2A chelators. Polymeric micelles were formed by dialysis and one half was core-crosslinked by UV light (CL) and the other half was not (nonCL). Both CL and nonCL were radiolabeled with 64Cu and compared in vivo in tumor-bearing mice, with free 64Cu as control. Accumulation in relevant organs was quantified by ROI analysis on PET images and ex vivo counting. It was observed that CL and nonCL showed limited differences in biodistribution from each other, whereas both differed markedly from control (free 64Cu). This demonstrated that 4-methylcoumarin core micelles may form micelles that are stable in circulation even without crosslinking. The methodology presented here where individual unimers are radiolabeled is applicable to a wide range of polymeric micelle types.

General information
State: Published
Organisations: Center for Nuclear Technologies, The Hevesy Laboratory, Department of Micro- and Nanotechnology, Colloids and Biological Interfaces, University of Copenhagen
Authors: Jensen, A. T. I. (Intern), Binderup, T. (Ekstern), Ek, P. K. (Intern), Grandjean, C. E. (Ekstern), Rasmussen, P. (Intern), Kjær, A. (Ekstern), Andresen, T. L. (Intern)
Number of pages: 9
Pages: 366-374
Publication date: 2017
Main Research Area: Technical/natural sciences

Publication information
Optically stimulated luminescence (OSL) dating was applied to the Neolithic Vinča culture's type-site, Vinča Belo-Brdo, to establish best protocols for routine luminescence dating of similar Holocene sites, critical in understanding Neolithic to Chalcolithic cultural development. Equivalent dose (De) values were investigated for sediment samples using 63–90 μm grains on large and small aliquots, and single-grain laser luminescence (SGLL), and for pottery samples using large aliquots of 4–11 μm grains. The effects of changing water content and the different techniques available to establish radionuclide concentration were explored for their impacts on dose rate (Dr) estimates.

Ages for two pottery samples of $6.74 \pm 0.37$ ka and $7.04 \pm 0.47$ ka are in line with the existing AMS radiocarbon chronology for the site and are regarded as the best dates available. Sediment samples at Vinča show poor signal strength, and the uncertainty over past water content, in addition to the possibility of mixing and/or partial bleaching of the quartz, means that we do not recommend the use of sediment-derived ages at complex archaeological sites such as Vinča. OSL dating of fired pottery however, presents a powerful tool for generating independent chronologies at archaeological sites as well as providing additional constraints for Bayesian age models.

**General information**
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Organisations: Center for Nuclear Technologies, Radiation Physics, The Hevesy Laboratory, Radioecology and Tracer Studies, Royal Holloway University of London, University of Novi Sad, University of Belgrade
Authors: Bate, S. (Ekstern), Stevens, T. (Ekstern), Buylaert, J. (Intern), Marković, S. B. (Ekstern), Roos, P. (Intern), Tasić, N. (Ekstern)
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Scopus rating (2016): CiteScore 2.19 SJR 1.121 SNIP 1.065
Web of Science (2016): Impact factor 2.199
BFI (2015): BFI-level 1
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Web of Science (2015): Impact factor 2.067
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Web of Science (2014): Impact factor 2.062
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BFI (2013): BFI-level 1
Scopus rating (2013): SJR 1.101 SNIP 1.222 CiteScore 2.12
Production and utilization of unconventional radiometals for advanced diagnostics and therapy

The continued development in biochemistry delivers vectors capable of specifically identifying foreign entities like malignancies and infections. Many of these vectors have long circulation time in vivo, resulting in optimal biodistribution for imaging several days post injection. The diagnostic potential of these can only be fully utilized if non-standard radionuclides with half-lives extending beyond those of the standard catalogue (\(^{11}C, {^{18}}F, {^{64}}Cu\)) are available. As for therapy, the increased specificity of new vectors strengthens the argument for using targeted radionuclide therapy, as they allow delivery of therapeutic doses to target tissues with minimal unspecific uptake and dose in healthy non-target tissues. This allows for the use of a wider range of radionuclides, like \(\alpha\)-emitters, for which high specificity is needed due to their high toxicity. The development of highly specific, internalizing vectors opens for use of Auger emitters. The therapeutic effect of these radionuclides most likely relies on internalization and translocation to the cell nucleus, because of their extremely localized, short-range dose deposition. Although the selection such vectors is still limited, the development of robust production methods for Auger emitters is crucial for investigating the basic principles of Auger therapy. The focus of this thesis has been expanding the number of isotopes and techniques available in the nuclear medicine toolbox.

The work performed using diagnostic isotopes includes:

\(^{52}\text{Mn}\): A production and separation method for high specific activity \(^{52}\text{Mn}\) was developed. Labeling conditions and serum stability for \(^{52}\text{Mn}\)-DOTA were investigated, and \(^{52}\text{Mn}\) was labeled to intact antibodies showing in vivo stability in mice.  
\(^{89}\text{Zr}\): Very high specific activity \(^{89}\text{Zr}\) was produced. A labeling method for sensitive metalloproteins was developed. Further, the potential pitfalls in quality control of \(^{89}\text{Zr}\) labeled proteins were documented.  
\(^{45}\text{Ti}\): A production and separation method for \(^{45}\text{Ti}\) was developed and optimized. This work includes one of the first ever in vivo studies of a \(^{45}\text{Ti}\)-compound.

The work performed using therapeutic isotopes includes:

\(^{177}\text{Lu}\): The sensitive metalloprotein FVIIai was conjugated with the chelator cDTPA and labeled with \(^{177}\text{Lu}\) for a therapeutic study. This included optimization of labeling conditions and development of quality control.  
\(^{135}\text{La}\): Pressed Ba-targets were produced and production and separation methods for high specific activity \(^{135}\text{La}\) were
developed. Labeling conditions were tested and cellular and human dosimetry of $^{135}$La was calculated. A production method for $^{165}$Er was developed, based on electron-capture-mediated release of $^{165}$Er from DOTA. Finally, a method was developed using $^{140}$Nd for assaying cellular internalization of a compound in vivo. General dosimetry calculations and considerations are further presented to aid selection of the radionuclide when designing a radiopharmaceutical. The combined work serves to aid further development in both pharmaceutical research, and diagnostic as well as therapeutic applications of radionuclides.

### General information

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Organisations: Center for Nuclear Technologies, The Hevesy Laboratory
Authors: Fonslet, J. (Intern)
Number of pages: 77
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Production and utilization of unconventional radiometals for advanced diagnostics and therapy
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### Quantification of Radiation-induced DNA Damage following intracellular Auger-Cascades

Purpose: The aim my PhD study and the topic of this thesis is to investigate the radiotoxicity and the Relative Biological effectiveness (RBE) of intracellular Auger cascades. A special focus is kept on obtaining reliable absorbed dose calculations and using matched dose rate profiles for the Auger exposed cells and cells exposed to the reference radiation. In order to accomplish this, a new experimental model was developed. The Auger cascades were induced by intracellular decays of the electron-capture radionuclide $^{131}$Cs. The use of radiocaesium allowed me to develop new version of the cellular S-values ($S_C$-values). The work can be divided into three steps: Examination of the bio-kinetics of the Auger emitter $^{131}$Cs used in the study, calculations of the $S_C$-values and finally the measurement of the RBE of intracellular $^{131}$Cs decays, through $\gamma$H2AX and clonogenic cell survival assay. Methods: A series of experiments examining the cellular uptake, release rate and cellular accumulations of $^{131}$Cs in HeLa and V79 cell cultures were performed. The intracellular $^{131}$Cs activity was measured using liquid scintillation counting. The geometry used for the SC-values calculations were a confluent cellular monolayer, with the nuclei dispersed within. The height of this cellular monolayer and the shape and size of the nuclei were determined by confocal microscopy for both HeLa and V79 cell cultures. SC-values values were obtained for whole cell to nucleus, SC(N→CM), with $^{131}$Cs distributed homogeneously throughout the entire cellular monolayer. Monoenergetic electron emission dose kernels for a point source were calculated using the method applied by MIRD for cellular S-values and using Cole’s pseudo stopping power for electrons in water. K- and L-Auger electron energies and intensities (24.6 keV (9.3 %) and 3.43 keV (79.7 %) respectively) with an intensity normalisation factor of 1.17 were used as input for the SC value calculation. To measure the RBE of intracellular $^{131}$Cs decays, confluent cellular monolayers of HeLa and V79 cells were incubated with $^{131}$Cs containing medium. Using the obtained results of the $^{131}$Cs bio-kinetics, and the SC-values, dose rate profiles and absorbed doses for the $^{131}$Cs exposed cells could be calculated. HeLa and V79 cell cultures were then exposed to matched dose rate profiles using $^{137}$Cs $\gamma$-rays as the reference radiation. The biological effects of the two exposures were evaluated using $\gamma$H2AX and clonogenic cell survival assay. Results: $^{131}$Cs was taken up, accumulated and then released by both cell lines. The uptake and release could be described by exponential equations ($A = A_0 \cdot (1−e^{−t \cdot kc})$ and $A = A_0 \cdot e^{−t \cdot kout}$) with $kc$ and $kout$ having values of 1/293 min$^{-1}$ (HeLa), 1/294 min$^{-1}$ (V79) and 1/339 min$^{-1}$ (HeLa) , 1/256 min$^{-1}$ (V79) respectively. The cellular uptake of $^{131}$Cs was found to be mediated by the Na+K+-ATPase, supporting the hypothesis of a homogenous, intracellular distribution of $^{131}$Cs. The SC-values for 29 and 50 different sized nuclei were found to range from 7.83*10^{-4} to 7.83*10^{-4} Gy/(Bq*Sec)/pL for HeLa nuclei and from 7.45*10^{-4} to 7.63*10^{-4} Gy/(Bq*Sec)/pL for V79 nuclei. The SC-values were shown to be very robust and almost independent of cellular and nuclear size. A RBE value of 1 was obtained for HeLa cells using $\gamma$H2AX assays. RBE values of 4.5 ± 0.5 and 3.8 ± 0.8 were obtained for HeLa and V79 cells respectively, using clonogenic cell survival. The RBE values obtained in this study are higher than expected for Auger emitters located intracellularly but not directly intercalated to the DNA. Conclusions: The implication of this study is two-fold. The obtained RBE values give further hope for the development of future Auger therapy, as the Auger emitters might not be needed to bind to the DNA in order to achieve high radiotoxicity. At the same time these RBE values should raise concerns about in the ignorance of Auger electrons in dosimetry of diagnostic nuclear medicine procedures, as the risk associated with these might be underestimated. The RBE of Auger emitter decays clearly need to be further investigated. My new experimental method with the robust absorbed dose calculations, the new concept of SC-values, and the applicability to most cell types and all Auger emitters with homogeneous intracellular distribution, could be a valuable tool for such investigations.
Radioactivity in the Risø District July-December 2016
The environmental surveillance of the Risø environment was continued in July-December 2016. The mean concentrations in air were: 0.18±0.13 μBq m⁻³ of ¹³⁷Cs, 2.30±0.68 mBq m⁻³ of ⁷Be and 0.21±0.12 mBq m⁻³ of ²¹⁰Pb (±1 standard uncertainty). The depositions by precipitation at Risø in the second half of 2016 were: 0.046±0.006 Bq m⁻² of ¹³⁷Cs, 494±50 Bq m⁻² of ⁷Be, 24.9±2.2 Bq m⁻² of ²¹⁰Pb and <1.2 kBq m⁻² of ³H. The average background dose rate (TLD) at Risø (Zone I) was measured as 45 ± 2 nSv h⁻¹ compared with 45 ± 6 nSv h⁻¹ (±1 standard uncertainty) in the four zones around Risø.

Radionuclide therapy with tissue factor targeting Lu-177-FVIIai inhibits growth in an experimental mouse model of human pancreatic cancer
Objectives: Tissue factor (TF) is related to aggressiveness and invasiveness of cancer and there is a correlation between tumor TF expression, metastatic potential, and patient outcome. The aim of the study was to test the therapeutic potential and toxicity of a novel compound for localized TF targeted radionuclide therapy. The radionuclide therapy was based on Factor VII (FVII), the natural ligand to TF. In the current study, we investigated the biodistribution, therapeutic potential and toxicity of ¹⁷⁷Lu labeled active site inhibited FVIIa (¹⁷⁷Lu-FVIIai) in an experimental mouse model of pancreatic cancer.
Methods: p-SCN-Bn-CHX-A''-DTPA was conjugated to FVIIai followed by radiolabeling with ¹⁷⁷Lu (¹⁷⁷Lu-CHX-A''-DTPA-FVIIai). A pancreas xenograft mouse model (BxPC3) was used to assess the therapeutic potential of ¹⁷⁷Lu-FVIIai. NMRI nude mice with subcutaneous BxPC3 tumors were used. The mice were randomized into groups receiving ¹⁷⁷Lu-FVIIai, FVIIai, or vehicle when the tumor volumes were about 50 mm³. ¹⁷⁷Lu-FVIIai was administered in doses of 15 MBq, 7.5 MBq or 2 x 7.5 MBq (n=8 mice/group). Tumor growth was monitored three times weekly. Biodistribution of ¹⁷⁷Lu-FVIIai was studied ex vivo in several organs at 1, 4, 24, 72 and 168 hours after injection. The biodistribution of ¹⁷⁷Lu-FVIIai was evaluated by SPECT/CT imaging. Furthermore, competition and dose escalation experiments (1-30 MBq) were performed. A parallel set of NMRI mice, toxic effects of ¹⁷⁷Lu-FVIIai were evaluated by hematology, histology and ⁹⁹mTc-DMSA scintigraphy. Results: FVIIai was successfully radiolabeled with ¹⁷⁷Lu with a specific activity of 10-25 GBq/μmol after EDTA scavenging and PD-10 purification. Treatment with FVIIai did not change tumor growth compared to the vehicle groups. The mice that received 15 MBq ¹⁷⁷Lu-FVIIai had a significantly reduced tumor growth from day 0 to day 19 compared with mice from the control groups (425.5±44.8% versus 614.2±49.1%; p=0.02). The groups receiving
7.5 MBq or 2 x 7.5 MBq 177Lu-FVIIai had no significant different tumor growth compared with controls on day 19. Tumor uptake of 177Lu-FVIIai measured ex vivo was 1.16±0.04, 1.97±0.18, 1.95±0.07, 1.01±0.06, 0.31±0.02 percent injected dose per gram (%ID/g) at 1, 4, 24, 72 and 168 hours post-injection, respectively. Injection with unlabeled FVIIai 10 minutes before 177Lu-FVIIai injection significantly reduced tumor uptake of 177Lu-FVIIai (from 2.5±0.16 %ID/g to 1.7±0.05 %ID/g; p<0.05). Escalating the dose of 177Lu-ASIS from 1-30 MBq did not change tumor uptake (%ID/g). A transient decrease in leucocyte counts was observed for the mice receiving 15 and 7.5 MBq 177Lu-FVIIai. Ten weeks after injection of 177Lu-FVIIai kidney uptake of 99mTc-DMSA was significantly decreased in all the treatment groups compared to the vehicle group when measured by SPECT imaging. Conclusion: FVIIai was successfully radiolabeled with 177Lu. 177Lu-FVIIai showed anti-tumor activity in a mouse model of human pancreatic cancer. Treatment with 177Lu-ASIS induced a transient decrease in leucocyte counts and a decreased kidney function ten weeks after injection.

**General information**

**State:** Published

**Organisations:** Center for Nuclear Technologies, The Hevesy Laboratory, Department of Photonics Engineering, Administration, University of Copenhagen

**Authors:** Nielsen, C. (Ekstern), Jensen, M. (Ekstern), Fonslet, J. (Intern), Knudsen, C. (Ekstern), Jeppesen, T. (Ekstern), Jensen, A. (Intern), Severin, G. (Intern), Kjær, A. (Ekstern)

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- Web of Science (2017): Impact factor 7.439
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- Scopus rating (2016): CiteScore 5.06 SJR 2.313 SNIP 1.843
- Web of Science (2016): Impact factor 6.646
- Web of Science (2016): Indexed yes
- BFI (2015): BFI-level 2
- Scopus rating (2015): SJR 2.511 SNIP 1.887 CiteScore 4.83
- Web of Science (2015): Impact factor 5.849
- Web of Science (2015): Indexed yes
- BFI (2014): BFI-level 2
- Scopus rating (2014): SJR 2.461 SNIP 1.978 CiteScore 4.9
- Web of Science (2014): Impact factor 6.16
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- Scopus rating (2013): SJR 2.315 SNIP 1.982 CiteScore 4.66
- Web of Science (2013): Impact factor 5.563
- ISI indexed (2013): ISI indexed yes
- Web of Science (2013): Indexed yes
- BFI (2012): BFI-level 2
- Scopus rating (2012): SJR 2.787 SNIP 2.16 CiteScore 5
- Web of Science (2012): Impact factor 5.774
- ISI indexed (2012): ISI indexed yes
- Web of Science (2012): Indexed yes
- BFI (2011): BFI-level 2
- Scopus rating (2011): SJR 2.642 SNIP 2.092 CiteScore 5.08
- Web of Science (2011): Impact factor 6.381
Sixty Years of Environmental Radioactivity Research at Risø, Denmark and Future Guidelines

General information
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Organisations: Center for Nuclear Technologies, The Hevesy Laboratory, Radioecology and Tracer Studies
Authors: Hou, X. (Intern)
Number of pages: 2
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HOU_ICEG2017_Abstract.pdf
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233U/236U – A new tracer for environmental processes?

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Organisations: Center for Nuclear Technologies, The Hevesy Laboratory, Radioecology and Tracer Studies, University of Vienna, Hiroshima University, Australian National University, Karlsruhe Institute of Technology
Authors: Hain, K. (Ekstern), Steier, P. (Ekstern), Eigl, R. (Ekstern), Froehlich, M. (Ekstern), Golser, R. (Ekstern), Qiao, J. (Intern), Quinto, F. (Ekstern), Sakaguchi, A. (Ekstern)
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99Tc measurement with matrix-assisted low energy AMS

General information
The COOLER Code: A Novel Analytical Approach to Calculate Subcellular Energy Deposition by Internal Electron Emitters

COmputation of Local Electron Release (COOLER), a software program designed for dosimetry assessment at the cellular/subcellular scale, with a given distribution of administered low-energy electron-emitting radionuclides in cellular compartments, which remains a critical step in risk/benefit analysis for advancements in internal radiotherapy. The software is intended to overcome the main limitations of the medical internal radiation dose (MIRD) formalism for calculations of cellular S-values (i.e., dose to a target region in the cell per decay in a given source region), namely, the use of the continuous slowing down approximation (CSDA) and the assumption of a spherical cell geometry. To this aim, we developed an analytical approach, entrusted to a MATLAB-based program, using as input simulated data for electron spatial energy deposition directly derived from full Monte Carlo track structure calculations with PARTRAC. Results from PARTRAC calculations on electron range, stopping power and residual energy versus traveled distance curves are presented and, when useful for implementation in COOLER, analytical fit functions are given. Example configurations for cells in different culture conditions (V79 cells in suspension or adherent culture) with realistic geometrical parameters are implemented for use in the tool. Finally, cellular S-value predictions by the newly developed code are presented for different cellular geometries and activity distributions (uniform activity in the nucleus, in the entire cell or on the cell surface), validated against full Monte Carlo calculations with PARTRAC, and compared to MIRD standards, as well as results based on different track structure calculations (Geant4-DNA). The largest discrepancies between COOLER and MIRD predictions were generally found for electrons between 25 and 30 keV, where the magnitude of disagreement in S-values can vary from 50 to 100%, depending on the activity distribution. In calculations for activity distribution on the cell surface, MIRD predictions appeared to fail the most. The proposed method is suitable for Auger-cascade electrons, but can be extended to any energy of interest and to beta spectra; as an example, the 3H case is also discussed. COOLER is intended to be accessible to everyone (preclinical and clinical researchers included), and may provide important information for the selection of radionuclides, the interpretation of radiobiological or preclinical results, and the general establishment of doses in any scenario, e.g., with cultured cells in the laboratory or with therapeutic or diagnostic applications. The software will be made available for download from the DTU-Nutech website: http://www.nutech.dtu.dk/.

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Web of Science (2017): Impact factor 2.53
Web of Science (2017): Indexed yes
BFI (2016): BFI-level 1
The fate of fixed nitrogen in marine sediments with low organic loading: an in situ study
Given the increasing impacts of human activities on global nitrogen (N) cycle, investigations on N transformation processes in the marine environment have drastically increased in the last years. Benthic N cycling has mainly been studied in anthropogenically impacted estuaries and coasts, while its understanding in oligotrophic systems is still scarce. Here we report on rates of denitrification, anammox and dissimilatory nitrate reduction to ammonium (DNRA) studied by in situ incubations with benthic chamber landers during two cruises to the Gulf of Bothnia (GOB), a cold, oligotrophic basin located in the northern part of the Baltic Sea. Burial and benthic solute fluxes were also experimentally determined to investigate the fate of fixed N in these sediments. Average rates of N2 production by denitrification and anammox (range 53–360 µmol N m−2 d−1) were comparable to those from Arctic and subarctic sediments worldwide (range 34–344 µmol N m−2 d−1). Anammox accounted for 18–26 % of the total N2 production. Absence of free hydrogen sulfide and low concentrations of dissolved iron in sediment pore waters suggested that denitrification and DNRA were driven by organic.
matter oxidation rather than chemolithotrophy. DNRA was as important as denitrification at a shallow, coastal station situated in the northern Bothnian Bay. At this pristine and fully oxygenated site, ammonium regeneration through DNRA contributed more than one third to the total dissolved nitrogen (TDN) diffusing from the sediment to the water column, and accounted, on average, for 45% of total nitrate reduction. At the offshore stations, the proportion of DNRA in relation to denitrification was lower (0–16% of total nitrate reduction). Median value and range of benthic DNRA rates from the GOB were comparable to those from the southern and central eutrophic Baltic Sea and other temperate estuaries and coasts in Europe. Therefore, our results contrast with the view that DNRA is negligible in cold and well-oxygenated sediments with low organic carbon loads. However, the mechanisms behind the variability in DNRA rates between our sites were not resolved. The GOB sediments were a major source (237 kty⁻¹, which corresponds to 184% of the external N load) of fixed N to the water column through recycling mechanisms. To our knowledge, our study is the first to document the simultaneous contribution of denitrification, DNRA, anammox and TDN recycling combined with in situ measurements.

**General information**

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**Organisations:** Center for Nuclear Technologies, The Hevesy Laboratory, Radioecology and Tracer Studies, Stockholm University, University of Gothenburg, University of Southern Denmark

**Authors:** Bonaglia, S. (Ekstern), Hylén, A. (Ekstern), Rattray, J. E. (Ekstern), Kononets, M. (Ekstern), Ekeroth, N. (Ekstern), Roos, P. (Intern), Thamdrup, B. (Ekstern), Brüchert, V. (Ekstern), Hall, P. O. J. (Ekstern)

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- Web of Science (2017): Impact factor 3.441
- Web of Science (2017): Indexed yes
- BFI (2016): BFI-level 1
- Scopus rating (2016): CiteScore 4.25 SJR 2.397 SNIP 1.315
- Web of Science (2016): Impact factor 3.851
- Web of Science (2016): Indexed yes
- BFI (2015): BFI-level 1
- Scopus rating (2015): SJR 2.444 SNIP 1.326 CiteScore 4.04
- Web of Science (2015): Indexed yes
- BFI (2014): BFI-level 1
- Scopus rating (2014): SJR 2.237 SNIP 1.373 CiteScore 4.03
- Web of Science (2014): Indexed yes
- BFI (2013): BFI-level 1
- Scopus rating (2013): SJR 2.451 SNIP 1.422 CiteScore 4.21
- Web of Science (2013): Impact factor 3.753
- ISI indexed (2013): ISI indexed yes
- Web of Science (2013): Indexed yes
- BFI (2012): BFI-level 1
- Scopus rating (2012): SJR 2.4 SNIP 1.304 CiteScore 3.92
- Web of Science (2012): Impact factor 3.754
- ISI indexed (2012): ISI indexed yes
- Web of Science (2012): Indexed yes
- BFI (2011): BFI-level 1
- Scopus rating (2011): SJR 2.542 SNIP 1.164 CiteScore 3.86
- Web of Science (2011): Impact factor 3.859
Tissue factor targeted radionuclide therapy with $^{177}$Lu-FVIIai inhibits tumor growth of human pancreatic cancer xenografts

General information
State: Published
Organisations: Center for Nuclear Technologies, The Hevesy Laboratory, Minerva Imaging, University of Copenhagen
Publication date: 2017
Conference: AACR Annual Meeting 2017, Washington, United States, 01/04/2017 - 01/04/2017
Main Research Area: Technical/natural sciences

Publication information
Journal: Cancer Research
Volume: 77
Issue number: 13 Supplement
Article number: 5203
ISSN (Print): 0008-5472
Ratings:
BFI (2018): BFI-level 2
Web of Science (2018): Indexed yes
BFI (2017): BFI-level 2
Scopus rating (2017): CiteScore 7.35 SJR 4.26 SNIP 1.692
Web of Science (2017): Indexed yes
BFI (2016): BFI-level 2
Scopus rating (2016): CiteScore 8.55 SJR 4.908 SNIP 1.991
Web of Science (2016): Indexed yes
BFI (2015): BFI-level 2
Scopus rating (2015): SJR 5.358 SNIP 2.013 CiteScore 8.57
Web of Science (2015): Impact factor 8.556
BFI (2014): BFI-level 2
Scopus rating (2014): SJR 5.683 SNIP 2.087 CiteScore 8.69
Towards Translational ImmunoPET/MR Imaging of Invasive Pulmonary Aspergillosis: The Humanised Monoclonal Antibody JF5 Detects Aspergillus Lung Infections In Vivo

Invasive pulmonary aspergillosis (IPA) is a life-threatening lung disease of hematological malignancy or bone marrow transplant patients caused by the ubiquitous environmental fungus Aspergillus fumigatus. Current diagnostic tests for the disease lack sensitivity as well as specificity, and culture of the fungus from invasive lung biopsy, considered the gold standard for IPA detection, is slow and often not possible in critically ill patients. In a previous study, we reported the development of a novel non-invasive procedure for IPA diagnosis based on antibody-guided positron emission tomography and magnetic resonance imaging (immunoPET/MRI) using a $[^{64}\text{Cu}]$ DOTA-labeled mouse monoclonal
antibody (mAb), mJF5, specific to Aspergillus. To enable translation of the tracer to the clinical setting, we report here the development of a humanised version of the antibody (hJF5), and pre-clinical imaging of lung infection using a $[^{64}\text{Cu}]$ NODAGA-hJF5 tracer. The humanised antibody tracer shows a significant increase in in vivo biodistribution in A. fumigatus infected lungs compared to its radiolabeled murine counterpart $[^{64}\text{Cu}]$ NODAGA-mJF5. Using reverse genetics of the pathogen, we show that the antibody binds to the antigenic determinant beta 1,5-galactofuranose (Galf) present in a diagnostic mannoprotein antigen released by the pathogen during invasive growth in the lung. The absence of the epitope Galf in mammalian carbohydrates, coupled with the enhanced imaging capabilities of the hJF5 antibody, means that the $[^{64}\text{Cu}]$ NODAGA-hJF5 tracer developed here represents an ideal candidate for the diagnosis of IPA and translation to the clinical setting.
Tracing water exchange and circulation in the Antarctic using $^{129}$I

General information
State: Published
Organisations: Center for Nuclear Technologies, The Hevesy Laboratory, Radioecology and Tracer Studies, Uppsala University, Chinese Academy of Sciences, United Arab Emirates University
Authors: Hou, X. (Intern), Xing, S. (Ekstern), Aldahan, A. (Ekstern), Goran, P. (Ekstern), Weijian, Z. (Ekstern)
Publication date: 2017
Event: Abstract from 14th International Conference on Accelerator Mass Spectrometry, Ottawa, Canada.
Main Research Area: Technical/natural sciences
Electronic versions:

Bibliographical note
ID22
Source: PublicationPreSubmission
Source-ID: 142128782
Publication: Research - peer-review › Conference abstract for conference – Annual report year: 2017

Validation of radiochemical methods for the determination of difficult-to-measure nuclides using LSC

General information
State: Published
Organisations: Center for Nuclear Technologies, The Hevesy Laboratory, Radioecology and Tracer Studies, RadAnal Ltd., Hungarian Academy of Sciences, Isotoptech Zrt
Authors: Vajda, N. (Ekstern), Molnar, Z. (Ekstern), Bokori, E. (Ekstern), Osváth, S. (Intern), Párkányi, D. (Ekstern), Braun, M. (Ekstern)
Number of pages: 2
Publication date: 2017
Event: Abstract from International Conference on Advances in Liquid scintillation Spectrometry 2017, Copenhagen, Denmark.
Main Research Area: Technical/natural sciences
Electronic versions:

Bibliographical note
ID22
Source: PublicationPreSubmission
Source-ID: 141856953
Publication: Research - peer-review › Conference abstract for conference – Annual report year: 2017

Water Circulation and Marine Environment in the Antarctic Traced by Speciation of $^{129}$I and $^{127}$I

Emissions of anthropogenic $^{129}$I from human nuclear activities are now detected in the surface water of the Antarctic seas. Surface seawater samples from the Drake Passage, Bellingshausen, Amundsen, and Ross Seas were analyzed for total $^{129}$I and $^{127}$I, as well as for iodide and iodate of these two isotopes. The variability of $^{127}$I and $^{129}$I concentrations and their species ($^{127}$I$^{-/127}$IO$_3^-$, $^{129}$I$^{-/129}$IO$_3^-$) suggest limited environmental impact where ($1.15$-$3.15) $\times 10^6$ atoms/L for $^{129}$I concentration and $(0.61$-$1.98) \times 10^{-11}$ for $^{129}$I/$^{127}$I atomic ratios are the lowest ones compared to the other oceans. The iodine distribution patterns provide useful information on surface water transport and mixing that are vital for better understanding of the Southern Oceans effects on the global climate change. The results indicate multiple spatial interactions between the Antarctic Circumpolar Current (ACC) and Antarctic Peninsula Coastal Current (APCC). These interactions happen in restricted circulation pathways that may partly relate to glacial melting and icebergs transport. Biological activity during the warm season should be one of the key factors controlling the reduction of iodate in the coastal water in the Antarctic.

General information
State: Published
Organisations: Center for Nuclear Technologies, The Hevesy Laboratory, Radioecology and Tracer Studies, Chinese Academy of Sciences, United Arab Emirates University, Uppsala University
Authors: Xing, S. (Ekstern), Hou, X. (Intern), Aldahan, A. (Ekstern), Possnert, G. (Ekstern), Shi, K. (Intern), Yi, P. (Ekstern) Zhou, W. (Ekstern)
Number of pages: 9
Publication date: 2017
Main Research Area: Technical/natural sciences

Publication information
Journal: Scientific Reports
A Mouse Positron Emission Tomography Study of the Biodistribution of Gold Nanoparticles with Different Surface Coatings Using Embedded Copper-64

By taking advantage of the ability of (64)Cu to bind non-specifically to gold surfaces, we have developed a new methodology to embed this radionuclide inside gold nanoparticles (AuNPs). (64)Cu enables the in vivo imaging of AuNPs by positron emission tomography (PET). AuNPs have a multitude of uses within health technology and are useful tools for general nanoparticle research. (64)Cu-AuNPs were prepared by incubating AuNP seeds with (64)Cu(2+), followed by the entrapment of the radionuclide by grafting a second layer of gold on the surface. This resulted in radiolabeling efficiencies of 53 ± 6%. The radiolabel showed excellent stability when challenging with EDTA for two days (>95% radioactivity retention) and showed no loss of (64)Cu when incubated with 50% mouse serum for two days. The methodology was chelator-free, and circumvents traditional concerns over chelator instability and altered AuNP properties due to surface modification. Radiolabeled (64)Cu-AuNP cores were prepared in a biomedically relevant size of 30 nm and used to investigate the in vivo stability of three different AuNP coatings by PET imaging in a murine xenograft tumor model. We found the longest plasma half-life (T½ = 9 hours) and highest tumor accumulation (3.9 %ID/g) by using polyethylene glycol (PEG) coating, while faster elimination from the bloodstream was observed with both a Tween 20-stabilized coating and a zwitterionic coating based on a mixture of sulfonic acids and quaternary amines, which has previously been reported to be
superior to PEG. The new embedding method provides the utilization of PET imaging in combination with the multitude of uses that AuNPs have found in health technology, and the method can equally well be utilized for therapeutic copper radioisotopes for use in radiotherapy.
AMS and ICP-MS for measurement of low level radionuclides

General information
State: Published
Organisations: Center for Nuclear Technologies, The Hevesy Laboratory, Radioecology and Tracer Studies
Authors: Hou, X. (Intern)
Number of pages: 1
Pages: 53-54
Publication date: 2016

Host publication information
Title of host publication: Book of Abstracts. International Conference on Radioanalytical and Nuclear Chemistry, RANC 2016
Publisher: Akadémiai Kiadó
Main Research Area: Technical/natural sciences
Electronic versions: RANC_2016_Abstracts_57_58.pdf
Publication: Research - peer-review › Conference abstract in proceedings – Annual report year: 2016

Antibody-based PET of uPA/uPAR signaling with broad applicability for cancer imaging

Mounting evidence suggests that the urokinase plasminogen activator (uPA) and its receptor (uPAR) play a central role in tumor progression. The goal of this study was to develop an 89Zr-labeled, antibody-based positron emission tomography (PET) tracer for quantitative imaging of the uPA/uPAR system. An anti-uPA monoclonal antibody (ATN-291) was conjugated with a deferoxamine (Df) derivative and subsequently labeled with 89Zr. Flow cytometry, microscopy studies, and competitive binding assays were conducted to validate the binding specificity of Df-ATN-291 against uPA. PET imaging with 89Zr-Df-ATN-291 was carried out in different tumors with distinct expression levels of uPA. Biodistribution, histology examination, and Western blotting were performed to correlate tumor uptake with uPA or uPAR expression. ATN-291 retained uPA binding affinity and specificity after Df conjugation. 89Zr-labeling of ATN-291 was achieved in good radiochemical yield and high specific activity. Serial PET imaging demonstrated that, in most tumors studied (except uPA-LNCaP), the uptake of 89Zr-Df-ATN-291 was higher compared to major organs at 120 h post-injection, providing excellent tumor contrast. The tumor-to-muscle ratio of 89Zr-Df-ATN-291 in U87MG was as high as 45.2 ± 9.0 at 120 h p.i. In vivo uPA specificity of 89Zr-Df-ATN-291 was confirmed by successful pharmacological blocking of tumor uptake with ATN-291 in U87MG tumors. Although the detailed mechanisms behind in vivo 89Zr-Df-ATN-291 tumor uptake remained to be further elucidated, quantitative PET imaging with 89Zr-Df-ATN-291 in tumors can facilitate oncologists to adopt more relevant cancer treatment planning.

General information
State: Published
Organisations: Center for Nuclear Technologies, The Hevesy Laboratory, University of Michigan, University of Wisconsin, Northwestern University
Pages: 73912-73924
Publication date: 2016
Main Research Area: Technical/natural sciences

Publication information
Journal: OncoTargets and Therapy
Volume: 7
Issue number: 45
ISSN (Print): 1178-6930
Ratings:
BFI (2018): BFI-level 1
Bioavailability Studies and in vitro Profiling of the Selective Excitatory Amino Acid Transporter Subtype 1 (EAAT1) Inhibitor UCPH-102

Although the selective excitatory amino acid transporter subtype 1 (EAAT1) inhibitor UCPH-101 has become a standard pharmacological tool compound for in vitro and ex vivo studies in the EAAT research field, its inability to penetrate the blood–brain barrier makes it unsuitable for in vivo studies. In the present study, per os (p.o.) administration (40 mg kg⁻¹) of the closely related analogue UCPH-102 in rats yielded respective plasma and brain concentrations of 10.5 and 6.67 μm after 1 h. Three analogue series were designed and synthesized to improve the bioavailability profile of UCPH-102, but none displayed substantially improved properties in this respect. In vitro profiling of UCPH-102 (10 μm) at 51 central nervous system targets in radioligand binding assays strongly suggests that the compound is completely selective for EAAT1. Finally, in a rodent locomotor model, p.o. administration of UCPH-102 (20 mg kg⁻¹) did not induce acute effects or any visible changes in behavior.

General information
State: Published
Organisations: Center for Nuclear Technologies, The Hevesy Laboratory, H. Lundbeck A/S, University of Copenhagen, University of Eastern Finland
Number of pages: 17
Pages: 403-419
Publication date: 2016
Main Research Area: Technical/natural sciences

Publication information
Journal: ChemMedChem
Volume: 11
Certified reference materials for radionuclides in Bikini Atoll sediment (IAEA-410) and Pacific Ocean sediment (IAEA-412)

The preparation and characterization of certified reference materials (CRMs) for radionuclide content in sediments collected offshore of Bikini Atoll (IAEA-410) and in the open northwest Pacific Ocean (IAEA-412) are described and the results of the certification process are presented. The certified radionuclides include: 40K, 210Pb (210Po), 226Ra, 228Ra, 228Th, 232Th, 234U, 238U, 239Pu, 239+240Pu and 241Am for IAEA-410 and 40K, 137Cs, 210Pb (210Po), 226Ra, 228Ra, 228Th, 232Th, 235U, 238U, 239Pu, 240Pu and 239+240Pu for IAEA-412. The CRMs can be used for quality assurance and quality control purposes in the analysis of radionuclides in sediments, for development and validation of analytical methods and for staff training.

General information

State: Published
Pages: 101–104
Publication date: 2016
Main Research Area: Technical/natural sciences

Publication information
Journal: Applied Radiation and Isotopes
Volume: 109
ISSN (Print): 0969-8043
Ratings:
BFI (2018): BFI-level 1
Web of Science (2018): Indexed yes
BFI (2017): BFI-level 1
Scopus rating (2017): CiteScore 1.15 SJR 0.528 SNIP 0.973
Web of Science (2017): Impact factor 1.123
Web of Science (2017): Indexed yes
BFI (2016): BFI-level 1
Scopus rating (2016): CiteScore 1.17 SJR 0.537 SNIP 1.027
Web of Science (2016): Impact factor 1.128
Web of Science (2016): Indexed yes
BFI (2015): BFI-level 1
Scopus rating (2015): SJR 0.547 SNIP 0.999 CiteScore 1.15
Web of Science (2015): Impact factor 1.136
BFI (2014): BFI-level 1
Scopus rating (2014): SJR 0.574 SNIP 1.203 CiteScore 1.27
Web of Science (2014): Impact factor 1.231
Web of Science (2014): Indexed yes
BFI (2013): BFI-level 1
Scopus rating (2013): SJR 0.526 SNIP 0.953 CiteScore 1.24
Determination of low level $^{129}$I in biological samples using accelerator mass spectrometry measurement

General information
State: Published
Organisations: Center for Nuclear Technologies, The Hevesy Laboratory, Radioecology and Tracer Studies, Chinese Academy of Sciences
Development of an experimental method using Cs-131 to evaluate radiobiological effects of internalized Auger-electron emitters.

General information
State: Published
Organisations: Center for Nuclear Technologies, The Hevesy Laboratory, Institut Laue-Langevin
Authors: Fredericia, P. (Intern), Severin, G. (Intern), Groesser, T. (Intern), Köster, U. (Ekstern), Jensen, M. (Intern)
Number of pages: 1
Pages: 114-114
Publication date: 2016

Host publication information
Title of host publication: 18th European Symposium on Radiopharmacy and Radiopharmaceuticals : Final programme
Article number: PP52
Main Research Area: Technical/natural sciences
Conference: 18th European Symposium on Radiopharmacy and Radiopharmaceuticals, Salzburg, Austria, 07/04/2016 - 07/04/2016
Electronic versions:
ESRR16_Final_Programme_1.pdf
Source: PublicationPreSubmission
Source-ID: 124105886
Publication: Research - peer-review › Conference abstract in proceedings – Annual report year: 2016

Distribution and sources of $^{226}$Ra groundwater of arid region
As a part of characterizing radioactivity in groundwater of the eastern Arabian Peninsula, a first systematic evaluation of $^{226}$Ra activity in groundwater indicates a wide range (0.65-203.66 mBq L$^{-1}$) with average of 17.56 mBq L$^{-1}$.

Adipsorption/desorption process, groundwater residence time and uranium concentration are the main controlling factors of $^{226}$Ra distribution in groundwater of the different aquifers. Estimation of $^{226}$Ra effective dose from water ingestion suggests potential risk of drinking water from the carbonate aquifer.

General information
State: Published
Organisations: Center for Nuclear Technologies, The Hevesy Laboratory, Radioecology and Tracer Studies, Hohai University, United Arab Emirates University
Number of pages: 9
Pages: 667-675
Publication date: 2016
Main Research Area: Technical/natural sciences

Publication information
Journal: Journal of Radioanalytical and Nuclear Chemistry
Volume: 309
Issue number: 2
ISSN (Print): 0236-5731
Ratings:
Electrosynthesis of acetate from CO₂ by a highly structured biofilm assembled with reduced graphene oxide–tetraethylene pentamine

Microbes can reduce CO₂ into multicarbon chemicals with electrons acquired from the cathode of a bioelectrochemical reactor. This bioprocess is termed microbial electrosynthesis (MES). One of the main challenges for the development of highly productive MES reactors is achieving efficient electron transfer from the cathode to microbes. Here, carbon cloth cathodes modified with reduced graphene oxide functionalized with tetraethylene pentamine (rGO-TEPA) were readily self-assembled in the cathodic chamber of a MES reactor. Electroactive biofilms with unique spatial arrangement were subsequently formed with Sporomusa ovata at the surface of rGO-TEPA-modified electrodes resulting in a more performant MES process. The acetate production rate from CO₂ was increased 3.6 fold with the formation of dense biofilms when wild type S. ovata was combined with rGO-TEPA. An improvement of 11.8 fold was observed with a highly structured biofilm including multiple spherical structures possibly consisting of bioinorganic networks of rGO-TEPA and bacterial cells from a novel strain of S. ovata adapted to reduce CO₂ faster. The three dimensional biofilms observed in this study enabled highly effective electric interactions between S. ovata and the cathode, demonstrating that the development of dense cathode biofilms is an effective approach to improve MES productivity.

General information
State: Published
Organisations: Novo Nordisk Foundation Center for Biosustainability, Research Groups, Bioelectrochemical Systems, BioLabChip, Department of Micro- and Nanotechnology, Center for Nuclear Technologies, The Hevesy Laboratory, Radioecology and Tracer Studies
Authors: Chen, L. (Intern), Tremblay, P. (Intern), Mohanty, S. (Intern), Xu, K. (Intern), Zhang, T. (Intern)
Number of pages: 7
Pages: 8395-8401
Publication date: 2016
Main Research Area: Technical/natural sciences

Publication information
Journal: Journal of Materials Chemistry A
Volume: 4
ISSN (Print): 2050-7488
Ratings:
BFI (2018): BFI-level 2
Web of Science (2018): Indexed yes
BFI (2017): BFI-level 1
Scopus rating (2017): CiteScore 9.61 SJR 3.488 SNIP 1.55
Web of Science (2017): Impact factor 9.931
Web of Science (2017): Indexed yes
BFI (2016): BFI-level 1
Scopus rating (2016): CiteScore 8.46 SJR 3.075 SNIP 1.479
Web of Science (2016): Impact factor 8.867
Web of Science (2016): Indexed yes
BFI (2015): BFI-level 1
Scopus rating (2015): SJR 2.62 SNIP 1.643 CiteScore 8.36
Web of Science (2015): Impact factor 8.262
Web of Science (2015): Indexed yes
BFI (2014): BFI-level 1
Scopus rating (2014): SJR 2.331 SNIP 1.514 CiteScore 7.27
Web of Science (2014): Impact factor 7.443
Web of Science (2014): Indexed yes
Environmental $^{129}$I: level, distribution and source in Northwestern China

General information
State: Published
Organisations: Center for Nuclear Technologies, The Hevesy Laboratory, Radioecology and Tracer Studies, Chinese Academy of Sciences
Authors: Zhang, D. (Ekstern), Hou, X. (Intern)
Number of pages: 2
Pages: 289-290
Publication date: 2016

Host publication information
Title of host publication: 9th International Conference on Nuclear and Radiochemistry - NRC9 : Abstracts
Main Research Area: Technical/natural sciences
Conference: 9th International Conference on Nuclear and Radiochemistry, Helsinki, Finland, 29/08/2016 - 29/08/2016
Electronic versions:
Environmental_129I_level_distribution_and_source_in_Northwestern_China.pdf
Publication: Research - peer-review › Conference abstract in proceedings – Annual report year: 2016

Environmental $^{129}$I: level, distribution and source in Qinghai region of China

General information
State: Published
Organisations: Center for Nuclear Technologies, The Hevesy Laboratory, Radioecology and Tracer Studies, Chinese Academy of Sciences
Authors: Zhang, D. (Ekstern), Hou, X. (Intern)
Number of pages: 1
Pages: 111
Publication date: 2016

Host publication information
Title of host publication: Book of Abstracts. International Conference on Radioanalytical and Nuclear Chemistry, RANC 2016
Publisher: Akadémiai Kiadó
Article number: 188
Main Research Area: Technical/natural sciences
Electronic versions:
RANC_2016_Abstracts_115.pdf
Source: PublicationPreSubmission
Source-ID: 123605693
Publication: Research - peer-review › Conference abstract in proceedings – Annual report year: 2016

Experimental implementation and proof of principle for a radionuclidic purity test solely based on half-life measurement
In this paper we present the results of an experimental implementation of the method (Jorgensen et al., 2012) for testing the radionuclidic purity (RNP) of F-18 compounds. The overall limitations of the experimental methods and their possible impacts on RNP detectability have been identified. We have developed an GUI application for use as an easy and automated test tool in the production procedure. The test results show that this method fully complies with the requirements in the European Pharmacopoeia (Eur. Ph.) for RNP of FDG and F-18 Sodium Fluoride. (C) 2015 Elsevier Ltd. All rights reserved.
Experimental study of Radiation induced DNA damage by internal Auger electron cascade compared to external γ-rays

General information
State: Published
Organisations: Center for Nuclear Technologies, The Hevesy Laboratory, Institut Laue-Langevin
Pages: s42-s43
Publication date: 2016
Conference: International Conference on Translational Research in Radio-Oncology / Physics for Health in Europe 2016, Geneva, Switzerland, 15/02/2016 - 15/02/2016
Main Research Area: Technical/natural sciences

Publication information
Journal: Radiotherapy & Oncology
Volume: 118
Issue number: s1
Article number: 87
ISSN (Print): 0167-8140
Ratings:
BFI (2018): BFI-level 1
Web of Science (2018): Indexed yes
BFI (2017): BFI-level 1
Scopus rating (2017): CiteScore 4.56 SJR 2.313 SNIP 1.612
Web of Science (2017): Impact factor 4.942
Web of Science (2017): Indexed yes
BFI (2016): BFI-level 1
Scopus rating (2016): CiteScore 4.36 SJR 2.099 SNIP 1.549
Web of Science (2016): Impact factor 4.328
Web of Science (2016): Indexed yes
BFI (2015): BFI-level 1
Scopus rating (2015): SJR 2.777 SNIP 1.707 CiteScore 4.87
Web of Science (2015): Impact factor 4.817
Exploiting the Metal-Chelating Properties of the Drug Cargo for In Vivo Positron Emission Tomography Imaging of Liposomal Nanomedicines

The clinical value of current and future nanomedicines can be improved by introducing patient selection strategies based on noninvasive sensitive whole-body imaging techniques such as positron emission tomography (PET). Thus, a broad method to radiolabel and track preformed nanomedicines such as liposomal drugs with PET radionuclides will have a wide impact in nanomedicine. Here, we introduce a simple and efficient PET radiolabeling method that exploits the metal-chelating properties of certain drugs (e.g., bisphosphonates such as alendronate and anthracyclines such as doxorubicin) and widely used ionophores to achieve excellent radiolabeling yields, purities, and stabilities with $^{89}$Zr, $^{52}$Mn, and $^{64}$Cu, and without the requirement of modification of the nanomedicine components. In a model of metastatic breast cancer, we demonstrate that this technique allows quantification of the biodistribution of a radiolabeled stealth liposomal nanomedicine containing alendronate that shows high uptake in primary tumors and metastatic organs. The versatility, efficiency, simplicity, and GMP compatibility of this method may enable submicrodosing imaging studies of liposomal...
nanomedicines containing chelating drugs in humans and may have clinical impact by facilitating the introduction of
image-guided therapeutic strategies in current and future nanomedicine clinical studies.

**General information**

**State:** Published

**Organisations:** Center for Nuclear Technologies, The Hevesy Laboratory, King's College London, Shaare Zedek Medical Center

**Authors:** Edmonds, S. (Ekstern), Volpe, A. (Ekstern), Shmeeda, H. (Ekstern), Parente-Pereira, A. C. (Ekstern), Radia, R. (Ekstern), Baguña-Torres, J. (Ekstern), Szanda, I. (Ekstern), Severin, G. (Intern), Livieratos, L. (Ekstern), Blower, P. J. (Ekstern), Maher, J. (Ekstern), Fruhwirth, G. O. (Ekstern), Gabizon, A. (Ekstern), T.M. de Rosales, R. (Ekstern)

**Pages:** 10294-10307

**Publication date:** 2016

**Main Research Area:** Technical/natural sciences

**Publication information**

**Journal:** A C S Nano

**Volume:** 10

**Issue number:** 11

**ISSN (Print):** 1936-0851

**Ratings:**

- BFI (2018): BFI-level 2
- Web of Science (2018): Indexed yes
- BFI (2017): BFI-level 2
- Web of Science (2017): Indexed yes
- Scopus rating (2017): CiteScore 14.29 SJR 7.203 SNIP 2.58
- Web of Science (2017): Impact factor 13.709
- Web of Science (2017): Indexed yes
- BFI (2016): BFI-level 2
- Scopus rating (2016): CiteScore 13.65 SJR 6.948 SNIP 2.604
- Web of Science (2016): Indexed yes
- BFI (2015): BFI-level 2
- Web of Science (2015): Indexed yes
- BFI (2014): BFI-level 2
- Scopus rating (2014): SJR 5.981 SNIP 2.721 CiteScore 12.49
- Web of Science (2014): Indexed yes
- BFI (2013): BFI-level 2
- Scopus rating (2013): SJR 6.672 SNIP 2.735 CiteScore 13.18
- Web of Science (2013): Impact factor 12.033
- ISI indexed (2013): ISI indexed yes
- Web of Science (2013): Indexed yes
- BFI (2012): BFI-level 2
- Scopus rating (2012): SJR 7.162 SNIP 2.685 CiteScore 11.92
- Web of Science (2012): Impact factor 12.062
- ISI indexed (2012): ISI indexed yes
- Web of Science (2012): Indexed yes
- Scopus rating (2011): SJR 6.282 SNIP 2.453 CiteScore 11.05
- Web of Science (2011): Impact factor 11.421
- ISI indexed (2011): ISI indexed yes
- Web of Science (2011): Indexed yes
- Scopus rating (2010): SJR 5.344 SNIP 2.069
- Web of Science (2010): Indexed yes
- Scopus rating (2009): SJR 4.114 SNIP 1.735
- Web of Science (2009): Indexed yes

Web of Science (2009): Indexed yes
Gold Nanoparticles with Stably Embedded Cu-64 and Their Use in Nanoparticle Research

Cu is a popular radionuclide for PET imaging and when Cu²⁺ is mixed with gold nanoparticles (AuNPs) it adheres to the gold surface. Taking advantage of this, we developed methods to trap the Cu within the AuNPs by embedding under additional layers of gold. This resulted in radiolabeling efficiencies around 53 ± 6%. EDTA challenge for two days revealed the embedded Cu to possess excellent stability with 94-98% of the radioactivity remaining associated with the AuNPs. Testing for two days against serum likewise showed no loss of Cu from the Cu-AuNPs. Accordingly, the technology was shown to yield a very stable radiolabel that can accurately trace AuNPs in vivo. Such chelator-free radiolabeling removes traditional concerns over the use of chelators for Cu, notably instabilities of chelators, such as DOTA, and their ability to alter the surface and thus the biodistribution of the compounds onto which they are attached. Radiolabeled Cu-AuNPs were prepared in biomedically relevant sizes of 20-30 nm and decorated with three different coatings, in order to investigate their in vivo performance by PET imaging in a murine xenograft model. We found the longest plasma half-life (T½ about 9 hours) to result from a polyethylene glycol (PEG) coating, while faster elimination from the bloodstream was observed for both a Tween-20 stabilized coating and a zwitterionic coating based on sulfonic acids and quaternary amines. Accordingly, our data concluded the PEG coating to be most beneficial for long circulation in vivo. In the in vivo model, the Cu was observed to closely follow the AuNPs for each coating, again attributing to the excellent stability of the radiolabel. Further, Cu-AuNPs were prepared in three different sizes ranging from 30 to 70 nm and injected intravenously (I.V.) or intratumorally (I.T.) in muring xenograft models, either coated with PEG or stabilized by citrate (only 30 nm). In the I.T. experiments, citrate-stabilized Cu-AuNPs were retained best in the tumors with about 100 %ID/g after 24 hours. For the PEG-coated Cu-AuNPs, a tendency for increased retention as larger particles were injected was observed (30 nm: ~ 30 %ID/g, 70 nm: ~ 60%ID/g). In the I.V. experiments, the opposite tendency was observed, with smaller particles showing higher tumor accumulation and citrate stabilized Cu-AuNPs being rapidly taken up in liver and spleen. Our group continues work with embedding of radionuclides in solid nanoparticles and further results will be presented as available.
Head-to-head comparison of $^{64}$Cu-DOTATATE and $^{68}$Ga-DOTATOC PET/CT: a prospective study of 59 patients with neuroendocrine tumors

Somatostatin receptor imaging is a valuable tool in the diagnosis, follow-up and treatment planning of neuroendocrine tumor (NET) patients. Positron emission tomography (PET) based tracers using $^{68}$Ga as the radioisotope have in most centers replaced single-photon emission tomography (SPECT) based tracers as the gold standard. $^{64}$Cu-DOTATATE is a new PET tracer that has been shown to be far superior compared to the SPECT tracer $^{111}$In-DTPA-octreotide. Due to advantages of $^{64}$Cu compared to $^{68}$Ga, we hypothesize that the tracer could have a higher sensitivity than $^{68}$Ga-based tracers. To test this hypothesis, we compared on a head-to-head basis the diagnostic performance of $^{64}$Cu-DOTATATE
with that of $^{68}$Ga -DOTATOC in NET patients.

**Objectives** $^{64}$Cu-DOTATATE is a new PET tracer for somatostatin receptor imaging. $^{64}$Cu-DOTATATE may potentially have a higher sensitivity than the current gold standards, due to advantages of $^{64}$Cu compared to $^{68}$Ga. The aim was to test this hypothesis on a head to head basis in neuroendocrine tumor patients (NET).

**Methods** Fifty-nine NET patients were scanned with $^{64}$Cu-DOTATATE and $^{68}$Ga-DOTATOC PET/CT and discordant lesions were verified through follow-up. Both scans were made within a week (1-5 days apart).

**Results** A total of 701 lesions were concordantly detected on both $^{64}$Cu-DOTATATE and $^{68}$Ga-DOTATOC PET/CT scans while additional 68 lesions were found by only one of the two scans. $^{64}$Cu-DOTATATE showed 42 discordant lesions of which 33 were found to be true positive on follow up. $^{68}$Ga-DOTATOC showed 26 discordant lesions, but only 7 were found to be true positive on follow up. False positives were mainly lymph node lesions. Eighty-three percent of the additional true positive lesions were found by $^{64}$Cu-DOTATATE. $^{64}$Cu-DOTATATE and $^{68}$Ga-DOTATOC discovered additional true lesions in 13 and 3 patients, respectively. All patients with additional lesions also had concordant lesions found by both scans.

**Conclusions** Although patient based sensitivity was the same for $^{64}$Cu-DOTATATE and $^{68}$Ga-DOTATOC in this cohort, more lesions were found by $^{64}$Cu-DOTATATE. Furthermore the shelf life of more than 24 hours and a scan window of at least 3 hours make $^{64}$Cu-DOTATATE logistically attractive to use in the clinic.

**General information**

State: Published
Organisations: Center for Nuclear Technologies, The Hevesy Laboratory, University of Copenhagen, Rigshospitalet
Authors: Johnbeck, C. (Ekstern), Knigge, U. (Ekstern), Loft, A. (Ekstern), Bertelsen, A. (Ekstern), Mortensen, J. (Ekstern), Oturai, P. (Ekstern), Langer, S. (Ekstern), Elema, D. R. (Intern), Kjaer, A. (Ekstern)
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  - BFI (2016): BFI-level 2
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  - Web of Science (2016): Indexed yes
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  - Scopus rating (2015): SJR 2.511 SNIP 1.887 CiteScore 4.83
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  - BFI (2014): BFI-level 2
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  - Web of Science (2014): Impact factor 6.16
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Immuno PET/MR imaging allows specific detection of Aspergillus fumigatus lung infection in vivo

Invasive pulmonary aspergillosis (IPA) is a life-threatening lung disease caused by the fungus Aspergillus fumigatus, and is a leading cause of invasive fungal infection-related mortality and morbidity in patients with hematological malignancies and bone marrow transplants. We developed and tested a novel probe for noninvasive detection of A. fumigatus lung infection based on antibody-guided positron emission tomography and magnetic resonance (immunoPET/MR) imaging. Administration of a [64Cu]DOTA-labeled A. fumigatus-specific monoclonal antibody (mAb), JF5, to neutrophil-depleted A. fumigatus-infected mice allowed specific localization of lung infection when combined with PET. Optical imaging with a fluorochrome-labeled version of the mAb showed colocalization with invasive hyphae. The mAb-based newly developed PET tracer [64Cu]DOTA-JF5 distinguished IPA from bacterial lung infections and, in contrast to [18F]FDG-PET, discriminated IPA from a general increase in metabolic activity associated with lung inflammation. To our knowledge, this is the first time that antibody-guided in vivo imaging has been used for non-invasive diagnosis of a fungal lung disease (IPA) of humans, an approach with enormous potential for diagnosis of infectious diseases and with potential for clinical translation.

General information
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Organisations: Center for Nuclear Technologies, The Hevesy Laboratory, Eberhard-Karls-Universität Tübingen, University of Exeter, Chematech, Otto von Guericke University Magdeburg, Tübingen University Hospital, Friedrich-Alexander University Erlangen-Nürnberg, University of Duisburg-Essen, Paul Scherrer Institute
Authors: Rolle, A. (Ekstern), Hasenberg, M. (Ekstern), Thornton, C. R. (Ekstern), Solouk-Saran, D. (Ekstern), Mann, L. (Ekstern), Weski, J. (Ekstern), Maurer, A. (Ekstern), Fischer, E. (Ekstern), Spycher, P. R. (Ekstern), Schibli, R. (Ekstern), Boschetti, F. (Ekstern), Stegemann-Koniszewski, S. (Ekstern), Bruder, D. (Ekstern), Severin, G. W. (Intern), Autenrieth, S. E. (Ekstern), Krappmann, S. (Ekstern), Davies, G. (Ekstern), Pichler, B. J. (Ekstern), Gunzer, M. (Ekstern), Wiehr, S. (Ekstern)
ImmunoPET of urokinase plasminogen activator (uPA) system: broad applicability in cancer imaging

General information
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Organisations: Center for Nuclear Technologies, The Hevesy Laboratory, University of Michigan, Northwestern University
Authors: Yang, D. (Ekstern), Severin, G. (Intern), Dougherty, C. A. (Ekstern), Chen, D. (Ekstern), Mazar, A. P. (Ekstern), Hong, H. (Ekstern)
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Web of Science (2015): Impact factor 5.849
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BFI (2014): BFI-level 2
Scopus rating (2014): SJR 2.461 SNIP 1.978 CiteScore 4.9
Web of Science (2014): Impact factor 6.16
Web of Science (2014): Indexed yes
BFI (2013): BFI-level 2
Scopus rating (2013): SJR 2.315 SNIP 1.982 CiteScore 4.66
Web of Science (2013): Impact factor 5.563
ISI indexed (2013): ISI indexed yes
In vivo Evaluation of PEGylated $^{64}$Cu-liposomes with Theranostic and Radiotherapeutic Potential using Micro PET/CT

The objective of this study was to evaluate the potential of PEGylated $^{64}$Cu-liposomes in clinical diagnostic positron emission tomography (PET) imaging and PEGylated $^{177}$Lu-liposomes in internal tumor radiotherapy through in vivo characterization and dosimetric analysis in a human xenograft mouse model. Liposomes with 5 and 10 mol% PEG were characterized with respect to size, charge, and $^{64}$Cu- and $^{177}$Lu-loading efficiency. The tumor imaging potential of $^{64}$Cu-loaded liposomes was evaluated in terms of in vivo biodistribution, tumor accumulation and tumor-to-muscle (T/M) ratios, using PET imaging. The potential of PEGylated liposomes for diagnostic and therapeutic applications was further evaluated through dosimetry analysis using OLINDA/EXM software. The $^{64}$Cu-liposomes were used as biological surrogates to estimate the organ and tumor kinetics of $^{177}$Lu-liposomes. High remote loading efficiency (>95%) was obtained for both $^{64}$Cu and $^{177}$Lu radionuclides with PEGylated liposomes, and essentially no leakage of the encapsulated radionuclides was observed upon storage and after serum incubation for 24 h at 37 °C. The 10 mol% PEG liposomes showed higher tumor accumulation (6.2±0.2 %ID/g) than the 5 mol% PEG liposomes, as evaluated by PET imaging. The dosimetry analysis of the $^{64}$Cu-liposomes estimated an acceptable total effective dose of 3.3·10−2 mSv/MBq for diagnostic imaging in patients. A high absorbed tumor dose (114 mGy/MBq) was estimated for the potential radiotherapeutic $^{177}$Lu-liposomes. The overall preclinical profile of PEGylated $^{64}$Cu-liposomes showed high potential as a new PET/theranostic tracer for imaging in humans. Dosimetry results predicted that initial administered activity of 200 MBq of $^{64}$Cu-liposomes should be acceptable in patients. Work is in progress to validate the utility of PEGylated $^{64}$Cu-liposomes in a clinical research programme. The high absorbed tumor dose (114 mGy/MBq) estimated for $^{177}$Lu-liposomes and the preliminary dosimetric studies justify further therapeutic and dosimetry investigation of $^{177}$Lu-liposomes in animals before potential testing in man.

General information
State: Published
Organisations: Department of Micro- and Nanotechnology, Colloids and Biological Interfaces, Center for Nanomedicine and Theranostics, Department of Chemistry, Center for Nuclear Technologies, The Hevesy Laboratory, University of Copenhagen
In Vivo Radionuclide Generators for Diagnostics and Therapy

In vivo radionuclide generators make complex combinations of physical and chemical properties available for medical diagnostics and therapy. Perhaps the best-known in vivo generator is $^{212}\text{Pb}/^{212}\text{Bi}$, which takes advantage of the extended half-life of $^{212}\text{Pb}$ to execute a targeted delivery of the therapeutic short-lived $\alpha$-emitter $^{212}\text{Bi}$. Often, as in the case of $^{81}\text{Rb}/^{81}\text{Kr}$, chemical changes resulting from the transmutation of the parent are relied upon for diagnostic value. In other instances such as with extended alpha decay chains, chemical changes may lead to unwanted consequences. This article reviews some common and not-so-common in vivo generators with the purpose of understanding their value in medicine and medical research. This is currently relevant in light of a recent push for alpha emitters in targeted therapies, which often come with extended decay chains.

General Information

State: Published
Organisations: Center for Nuclear Technologies, The Hevesy Laboratory, University of Copenhagen
Authors: Edem, P. E. (Ekstern), Fonslet, J. (Intern), Kjær, A. (Ekstern), Herth, M. (Ekstern), Severin, G. (Intern)
Number of pages: 8
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Web of Science (2016): Impact factor 1.974
Web of Science (2016): Indexed yes
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Scopus rating (2014): SJR 0.339 SNIP 0.769 CiteScore 1.23
Web of Science (2014): Impact factor 2.081
Scopus rating (2013): SJR 0.246 SNIP 0.523 CiteScore 0.74
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Web of Science (2012): Impact factor 1.165
Scopus rating (2011): SJR 0.163 SNIP 0.13 CiteScore 0.28
Web of Science (2011): Impact factor 0.716
Scopus rating (2010): SJR 0.212 SNIP 0.318
Web of Science (2010): Impact factor 0.949
Large Gliadin Peptides Detected in the Pancreas of NOD and Healthy Mice following Oral Administration

Gluten promotes type 1 diabetes in nonobese diabetic (NOD) mice and likely also in humans. In NOD mice and in non-diabetes-prone mice, it induces inflammation in the pancreatic lymph nodes, suggesting that gluten can initiate inflammation locally. Further, gliadin fragments stimulate insulin secretion from beta cells directly. We hypothesized that gluten fragments may cross the intestinal barrier to be distributed to organs other than the gut. If present in pancreas, gliadin could interact directly with the immune system and the beta cells to initiate diabetes development. We orally and intravenously administered 33-mer and 19-mer gliadin peptide to NOD, BALB/c, and C57BL/6 mice and found that the peptides readily crossed the intestinal barrier in all strains. Several degradation products were found in the pancreas by mass spectroscopy. Notably, the exocrine pancreas incorporated large amounts of radioactive label shortly after administration of the peptides. The study demonstrates that, even in normal animals, large gliadin fragments can reach the pancreas. If applicable to humans, the increased gut permeability in prediabetes and type 1 diabetes patients could expose beta cells directly to gliadin fragments. Here they could initiate inflammation and induce beta cell stress and thus contribute to the development of type 1 diabetes.

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Organisations: The Hevesy Laboratory, Biomedical Tracers, Center for Nuclear Technologies, Rigshospitalet, Novozymes AS, Statens Serum Institut
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Marine dispersion of $^{236}$U in Danish Straits

General information
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Organisations: Center for Nuclear Technologies, The Hevesy Laboratory, Radioecology and Tracer Studies, University of Vienna
Authors: Qiao, J. (Intern), Steier, P. (Ekstern), Nielsen, S. P. (Intern), Hou, X. (Intern), Roos, P. (Intern), Golser, R. (Ekstern)
Number of pages: 1
Non-catalytic Roles for XPG with BRCA1 and BRCA2 in Homologous Recombination and Genome Stability

XPG is a structure-specific endonuclease required for nucleotide excision repair, and incision-defective XPG mutations cause the skin cancer-prone syndrome xeroderma pigmentosum. Truncating mutations instead cause the neurodevelopmental progeroid disorder Cockayne syndrome, but little is known about how XPG loss results in this devastating disease. We identify XPG as a partner of BRCA1 and BRCA2 in maintaining genomic stability through homologous recombination (HRR). XPG depletion causes DNA double-strand breaks, chromosomal abnormalities, cell-cycle delays, defective HRR, inability to overcome replication fork stalling, and replication stress. XPG directly interacts with BRCA2, RAD51, and PALB2, and XPG depletion reduces their chromatin binding and subsequent RAD51 foci formation. Upstream in HRR, XPG interacts directly with BRCA1. Its depletion causes BRCA1 hyper-phosphorylation and persistent chromatin binding. These unexpected findings establish XPG as an HRR protein with important roles in genome stability and suggest how XPG defects produce severe clinical consequences including cancer and accelerated aging.
Radiochemical analysis plays a critical role in the determination of pure beta and alpha emitting radionuclides for environmental monitoring, radioecology, decommissioning, nuclear forensics and geological dating. A remarkable development on radiochemical analysis has been achieved in the past decades to meet the increased requirement. In the recent years, mass spectrometric techniques have been considerably improved and are widely employed for measurement of radionuclides. Analytical methods for rapid, automated and simultaneous determination of radionuclides have been extensively developed for emergency analysis. In Nordic countries, many laboratories are involved in the determination of radionuclides for various purposes, and a series of radiochemical analytical methods have been developed and applied. This article presents the present status and progress on radiochemical analysis of radionuclides, especially in Nordic countries; some requirements from nuclear industries and research organizations, as well as perspectives on the development of radiochemical analysis are discussed.

General information
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Present status and perspective of radiochemical analysis of radionuclides in Nordic countries
Radiochemical analysis plays a critical role in the determination of pure beta and alpha emitting radionuclides for environmental monitoring, radioecology, decommissioning, nuclear forensics and geological dating. A remarkable development on radiochemical analysis has been achieved in the past decades to meet the increased requirement. In the recent years, mass spectrometric techniques have been considerably improved and are widely employed for measurement of radionuclides. Analytical methods for rapid, automated and simultaneous determination of radionuclides have been extensively developed for emergency analysis. In Nordic countries, many laboratories are involved in the determination of radionuclides for various purposes, and a series of radiochemical analytical methods have been developed and applied. This article presents the present status and progress on radiochemical analysis of radionuclides, especially in Nordic countries; some requirements from nuclear industries and research organizations, as well as perspectives on the development of radiochemical analysis are discussed.
Radioactivity in the Risø District January-June 2016
The environmental surveillance of the Risø environment was continued in January-June 2016. The mean concentrations in air were: 0.28±0.17 μBq m⁻³ of ¹³⁷Cs, 2.58±1.21 mBq m⁻³ of ⁷Be and 0.23±0.15 mBq m⁻³ of ²¹⁰Pb (±1 S.D.). The depositions by precipitation at Risø in the first half of 2016 were: 0.058±0.007 Bq m⁻² of ¹³⁷Cs, 474±47 Bq m⁻² of ⁷Be, 27.5±2.5 Bq m⁻² of ²¹⁰Pb and <0.7 kBq m⁻² of ³H. The average background dose rate (TLD) at Risø (Zone I) was measured as 59 nSv h⁻¹ compared with 52 ± 2 nSv h⁻¹ (±1 S.D.) in the four zones around Risø.

General information
State: Published
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Authors: Nielsen, S. P. (Intern), Andersson, K. G. (Intern), Miller, A. (Intern)
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Electronic versions: Halv_rsrapport_December_2016.pdf
Publication: Research › Report – Annual report year: 2016

Radioactivity in the Risø District July-December 2015
The environmental surveillance of the Risø environment was continued in July-December 2015. The mean concentrations in air were: 0.24±0.18 μBq m⁻³ of ¹³⁷Cs, 2.71±0.88 mBq m⁻³ of ⁷Be and 0.28±0.20 mBq m⁻³ of ²¹⁰Pb (±1 S.D.). The depositions by precipitation at Risø in the second half of 2015 were: 0.085±0.011 Bq m⁻² of ¹³⁷Cs, 607±30 Bq m⁻² of ⁷Be, 59.6±4.2 Bq m⁻² of ²¹⁰Pb and 1.4±0.2 kBq m⁻² of ³H. The average background dose rate (TLD) at Risø (Zone I) was measured as 42 nSv h⁻¹ compared with 40 ± 2 nSv h⁻¹ (±1 S.D.) in the four zones around Risø.

General information
State: Published
Organisations: Center for Nuclear Technologies, The Hevesy Laboratory, Radioecology and Tracer Studies, Radiation Physics
Authors: Nielsen, S. P. (Intern), Andersson, K. G. (Intern), Miller, A. (Intern)
Number of pages: 26
Publication date: 2016
Radiochemical analysis for decommissioning of nuclear facilities

General information
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Organisations: Center for Nuclear Technologies, The Hevesy Laboratory, Radioecology and Tracer Studies
Authors: Hou, X. (Intern)
Number of pages: 2
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Publication date: 2016

Stable and high-yielding intrinsic $^{59}$Fe-radiolabeling of the intravenous iron preparations Monofer and Cosmofer: Intrinsic $^{59}$Fe-radiolabeling of Monofer and Cosmofer

Commercial iron supplements Monofer(R) and Cosmofer(R) were intrinsically radiolabeled with Fe-59 for the purpose of tracing iron absorption in vivo. Optimized procedures aimed at introducing Fe-59 into the macromolecular construct in a form that was as chemically equivalent to the matrix iron as possible. This was determined by challenging the labeled constructs with diethylenetriaminepentaacetic acid (DTPA) followed by separation by size-exclusion and measurements of radioactivity and iron in the eluted fractions. The final procedures were simple and involved heating aqueous dispersions of the supplements in the presence of $[\text{Fe-59}]\text{FeCl}_3$ for 24h at 95 degrees C for Monofer, and 85 degrees C for Cosmofer, resulting in radiochemical yields greater than 94%. High performance size exclusion chromatography, UV-VIS spectroscopy, and dynamic light scattering were used to show that the supplements remained unchanged after radiolabeling, underscoring the applicability of the methodology for radiolabeling commercial iron preparations.

General information
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Organisations: Center for Nuclear Technologies, The Hevesy Laboratory, Pharmacosmos A/S
Authors: Jensen, A. T. I. (Intern), Severin, G. (Intern), Andreasen, H. B. (Ekstern), Rasmussen, P. (Intern)
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Main Research Area: Technical/natural sciences

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Scopus rating (2017): CiteScore 1.35 SJR 0.477 SNIP 0.474
Web of Science (2017): Impact factor 1.423
129I and its species in the East China Sea: level, distribution, sources and tracing water masses exchange and movement

Anthropogenic 129I as a long-lived radioisotope of iodine has been considered as an ideal oceanographic tracer due to its high residence time and conservative property in the ocean. Surface water samples collected from the East China Sea...
(ECS) in August 2013 were analyzed for $^{129}$I, $^{127}$I and their inorganic chemical species in the first time. The measured $^{129}$I/$^{127}$I ratio is 1–3 orders of magnitude higher than the pre-nuclear level, indicating its dominantly anthropogenic sources. Relatively high $^{129}$I levels were observed in the Yangtze River and its estuary, as well as in the southern Yellow Sea, and $^{127}$I level in seawater declines towards the ECS shelf. In the open sea, $^{129}$I and $^{127}$I in surface water exists mainly as iodate, while in Yangtze River estuary and some locations, iodide is dominated. The results indicate that the Fukushima nuclear accident has no detectable effects in the ECS until August 2013. The obtained results are used for investigation of interaction of various water masses and water circulation in the ECS, as well as the marine environment in this region. Meanwhile this work provides essential data for evaluation of the possible influence of the increasing NPPs along the coast of the ECS in the future.

**General information**

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Organisations: Center for Nuclear Technologies, The Hevesy Laboratory, Radioecology and Tracer Studies, East China Normal University, Chinese Academy of Sciences
Authors: Liu, D. (Ekstern), Hou, X. (Intern), Du, J. (Ekstern), Zhang, L. (Ekstern), Zhou, W. (Ekstern)
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Web of Science (2017): Impact factor 4.122
Web of Science (2017): Indexed yes
BFI (2016): BFI-level 1
Scopus rating (2016): CiteScore 4.63 SJR 1.692 SNIP 1.354
Web of Science (2016): Impact factor 4.259
Web of Science (2016): Indexed yes
BFI (2015): BFI-level 1
Scopus rating (2015): SJR 2.034 SNIP 1.597 CiteScore 5.3
Web of Science (2015): Impact factor 5.228
Web of Science (2015): Indexed yes
BFI (2014): BFI-level 1
Scopus rating (2014): SJR 2.163 SNIP 1.554 CiteScore 4.75
Web of Science (2014): Impact factor 5.578
Web of Science (2014): Indexed yes
BFI (2013): BFI-level 1
Scopus rating (2013): SJR 1.998 SNIP 1.57 CiteScore 4.06
Web of Science (2013): Impact factor 5.078
ISI indexed (2013): ISI indexed yes
Web of Science (2013): Indexed yes
BFI (2012): BFI-level 1
Scopus rating (2012): SJR 1.531 SNIP 0.962 CiteScore 2.44
Web of Science (2012): Impact factor 2.927
ISI indexed (2012): ISI indexed yes
Web of Science (2012): Indexed yes
Web of Science (2011): Impact factor
ISI indexed (2011): ISI indexed no
Original language: English
Electronic versions:
Scientific_reports_2016_129I_and_its_species_in_the_East_China_Sea.pdf
DOIs:
10.1038/srep36611
14C levels in the vicinity of the Fukushima Dai-ichi Nuclear Power Plant prior to the 2011 accident

A 50-year-old Japanese cedar (Cryptomeria japonica) from Okuma, ∼1 km southwest of the Fukushima Dai-ichi Nuclear Power Plant, was cored and each annual ring was analysed for 14C. The 14C specific activity values varied from 330.4 Bq kg⁻¹ C in the tree ring formed in 1971 to 231.2 Bq kg⁻¹ C in the 2014 ring. During the periods 1971–1976 and 2011–2014, the 14C specific activities are indistinguishable from the ambient background values. However, compared with the ambient atmospheric levels, the 14C specific activities between 1977 and 2010 are significantly elevated, clearly indicating 14C discharges from the reactors during their normal operations. In addition, the specific activities are positively correlated with the annual electricity generation values. The excess 14C specific activities were <36 Bq kg⁻¹ C, corresponding to an additional annual effective dose of <2 μSv via the food ingestion pathway in the study location. The primary wind direction is east-southeast/southeast with a frequency of ∼30%, in comparison to ∼20% frequency for the direction of the site under study (north-northeast/northeast). This would tend to indicate a similar magnitude of additional effective dose and consequently no significant radiological impact of atmospheric 14C discharges from the FDNPP during the entire period of normal operations. Additionally, no 14C pulse in activity can be observed in the year 2011 ring. This might be caused by a limited 14C release from the damaged reactors during the accident or that the prevailing wind during the short period of release (11th–25th March 2011) was not in the direction of Okuma.
Cellulose, Cryptomeria japonica tree ring, Fukushima nuclear reactors, Anthropogenic 14C

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52\textsuperscript{Mn} – a new PET tracer for imaging neural pathways

**General information**
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Authors: Napieczynska, H. (Ekstern), Severin, G. (Intern), Fonslet, J. (Intern), Menegakis, A. (Ekstern), Pichler, B. J. (Ekstern), Calaminus, C. (Ekstern)
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Synthesis and pharmacological characterization of the selective GluK1 radioligand (S)-2-amino-3-(6-[3H]-2,4-dioxo-3,4-dihydrothieno.3,2-d] pyrimidin1(2H)- yl) propanoic acid ([3H]-NF608)

The kainic acid receptors belong to the class of ionotropic glutamate receptors and comprise five subunits named GluK1-5. Radioligands are essential tools for use in binding assays aimed at ligand-receptor structure-activity-relationship studies. Previous work has led to the synthesis of GluK1 radioligands [H-3]SYM2081, [H-3]-UBP310 and [H-3]-ATPA, however all strategies were work-intensive and thus not attractive. Herein, we report the synthesis of [H-3]-NF608 and subsequent pharmacological evaluation at homomeric recombinant rat GluK1 receptors. Binding affinities of a series of standard GluK1 ligands were shown to be in line with previously reported affinities obtained by use of already reported radioligands.
The labeling of unsaturated γ-hydroxybutyric acid by heavy isotopes of hydrogen: iridium complex-mediated H/D exchange by C─H bond activation vs reduction by boro-deuterides/tritides

3-Hydroxycyclopent-1-ene-1-carboxylic acid (HOCPCA (1)) is a potent ligand for high-affinity γ-hydroxybutyric acid binding sites in the central nervous system. Various approaches to the introduction of a hydrogen label onto the HOCPCA skeleton are reported. The outcomes of the feasible C─H activation of olefin carbon (C-2) by iridium catalyst are compared with the reduction of the carbonyl group (C-3) by freshly prepared borodeuterides. The most efficient iridium catalysts proved to be Kerr bulky phosphine N-heterocyclic species providing outstanding deuterium enrichment (up to 91%) in a short period of time. The highest deuterium enrichment (>99%) was achieved through the reduction of ketone precursor 2 by lithium trimethoxyborodeuteride. Hence, analogical conditions were used for the tritiation experiment. [3H]-HOCPCA selectively labeled on the position C-3 was synthetized with radiochemical purity >99%, an isolated yield of 637 mCi and specific activity = 28.9 Ci/mmol.

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Organisations: The Hevesy Laboratory, Center for Nuclear Technologies, University of Copenhagen, Czech Academy of Sciences
Authors: Marek, A. (Intern), Pedersen, M. H. F. (Intern), Vogensen, S. B. (Ekstern), Clausen, R. P. (Ekstern), Frølund, B. (Ekstern), Elbert, T. (Ekstern)
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Web of Science (2015): Impact factor 1.532
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Transferrin receptor expression and role in transendothelial transport of transferrin in cultured brain endothelial monolayers

Receptor-mediated transcytosis of the transferrin receptor has been suggested as a potential transport system to deliver therapeutic molecules into the brain. Recent studies have however shown that therapeutic antibodies, which have been reported to cross the brain endothelium, reach greater brain exposure when the affinity of the antibodies to the transferrin receptor is lowered. The lower affinity of the antibodies to the transferrin receptor facilitates the dissociation from the receptor within the endosomal compartments, which may indicate that the receptor itself does not necessarily move across the endothelial cells by transcytosis. The aim of the present study was to investigate transferrin receptor expression and role in transendothelial transferrin transport in cultured bovine brain endothelial cell monolayers.

Transferrin receptor mRNA and protein levels were investigated in endothelial mono-cultures and co-cultures with astrocytes, as well as in freshly isolated brain capillaries using qPCR, immunocytochemistry and Western blotting. Transendothelial transport and luminal association of holo-transferrin was investigated using $^{[125]}$Iholo-transferrin or $^{[59]}$Fe]-transferrin. Transferrin receptor mRNA expression in all cell culture configurations was lower than in freshly isolated capillaries, but the expression slightly increased during six days of culture. The mRNA expression levels were similar in mono-cultures and co-cultures. Immunostaining demonstrated comparable transferrin receptor localization patterns in mono-cultures and co-cultures. The endothelial cells demonstrated an up-regulation of transferrin receptor mRNA after...
treatment with the iron chelator deferoxamine. The association of $^{125}$I-holo-transferrin and $^{59}$Fe-transferrin to the endothelial cells was inhibited by an excess of unlabeled holo-transferrin, indicating receptor mediated association. However, over time the cell associated $^{59}$Fe-label exceeded that of $^{125}$I-holo-transferrin, which could indicate release of iron in the endothelial cells and receptor recycling. Luminal-to-abluminal transport of $^{125}$I-holo-transferrin across endothelial cell monolayers was low and not inhibited by unlabeled holo-transferrin. This indicated that transendothelial transferrin transport was independent of transferrin receptor-mediated transcytosis.

General information
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Authors: Hersom, M. (Ekstern), Helms, H. C. (Ekstern), Pretzer, N. (Ekstern), Goldeman, C. (Ekstern), Jensen, A. T. I. (Intern), Severin, G. (Intern), Nielsen, M. S. (Ekstern), Holm, R. (Ekstern), Brodin, B. (Ekstern)
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BFI (2015): BFI-level 1
Scopus rating (2015): SJR 2.362 SNIP 0.926 CiteScore 3.86
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BFI (2013): BFI-level 1
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Scopus rating (2010): SJR 2.792 SNIP 0.911
BFI (2009): BFI-level 1
Scopus rating (2009): SJR 2.577 SNIP 0.896
BFI (2008): BFI-level 2
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135La for Auger-based therapy: preparation, imaging and emissions

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Organisations: Center for Nuclear Technologies, The Hevesy Laboratory, Department of Electrical Engineering, Lund University, Australian National University
Authors: Fonselet, J. (Intern), Tran, T. A. (Ekstern), Lee, B. Q. (Ekstern), Siikanen, J. (Ekstern), Larsson, E. (Ekstern), Kibédi, T. (Ekstern), Stuchbery, A. E. (Ekstern), Elema, D. R. (Intern), Severin, G. (Intern)
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64Cu-DOTATATE PET for Neuroendocrine Tumors: a Prospective Head-to-Head Comparison with 111In-DTPA-octreotide in 112 Patients

Neuroendocrine tumors (NETs) can be visualized using radiolabeled somatostatin analogs. We have previously shown the clinical potential of (64)Cu-DOTATATE in a small first-in-human feasibility study. The aim of the present study was, in a larger prospective design, to compare on a head-to-head basis the performance of (64)Cu-DOTATATE and (111)In-diethylenetriaminepentaacetic acid (DTPA)-octreotide ((111)In-DTPA-OC) as a basis for implementing (64)Cu-DOTATATE as a routine.

METHODS:

We prospectively enrolled 112 patients with pathologically confirmed NETs of gastroenteropancreatic or pulmonary origin. All patients underwent both PET/CT with (64)Cu-DOTATATE and SPECT/CT with (111)In-DTPA-OC within 60 d. PET scans were acquired 1 h after injection of 202 MBq (range, 183-232 MBq) of (64)Cu-DOTATATE after a diagnostic contrast-enhanced CT scan. Patients were followed for 42-60 mo for evaluation of discrepant imaging findings. The McNemar test was used to compare the diagnostic performance.

RESULTS:

Eighty-seven patients were congruently PET- and SPECT-positive. No SPECT-positive cases were PET-negative, whereas 10 false-negative SPECT cases were identified using PET. The diagnostic sensitivity and accuracy of (64)Cu-DOTATATE (97% for both) were significantly better than those of (111)In-DTPA-OC (87% and 88%, respectively, P = 0.017). In 64 patients (75%), (64)Cu-DOTATATE identified more lesions than (111)In-DTPA-OC and always at least as many. In total, twice as many lesions were detected with (64)Cu-DOTATATE than with (111)In-DTPA-OC. Moreover, in 40
of 112 cases (36%) lesions were detected by (64)Cu-DOTATATE in organs not identified as disease-involved by (111)In-DTPA-OC.

CONCLUSION:

With these results, we demonstrate that (64)Cu-DOTATATE is far superior to (111)In-DTPA-OC in diagnostic performance in NET patients. Therefore, we do not hesitate to recommend implementation of (64)Cu-DOTATATE as a replacement for (111)In-DTPA-OC.
Automated synthesis and PET evaluation of both enantiomers of [18F]FMISO

Introduction: [18F]FMISO, the widely used positron emission tomography (PET) hypoxia tracer, is a chiral compound clinically used as a racemic mixture. The purpose of this study was to synthesize the individual (R)- and the (S)-enantiomers of [18F]FMISO and compare their PET imaging characteristics.

Methods: The radiosynthesis of enantiopure (R)- and (S)-[18F]FMISO was based on Co(salen) (N,N'-bis(3,5-di-tert-butylsalicylidene)-1,2-cyclohexanediaminocobalt)-mediated opening of enantiopure epoxides with [18F]HF. The uptake and clearance of the individual [18F]FMISO antipodes were investigated using micro-PET/CT imaging performed on mice bearing FaDu tumors. Image-derived biodistribution was obtained from micro-PET/CT scans performed at 1 and 3 hours post injection (p.i.). In addition, the uptake patterns of each enantiomer were observed using two-hour dynamic micro-PET/CT scans and the time-activity curves from different organs were compared. Results: The individual (R)- and (S)-[18F]FMISO enantiomers were synthesized in one step with high enantiomeric excess (ee) > 99% and radiochemical purity > 97% using custom-made automation module. The dynamic micro-PET/CT scanning revealed a faster initial uptake of the (R)-[18F]FMISO enantiomer in tumor and muscle tissues, however the difference became progressively smaller with time. The tumor-to-muscle (T/M) and tumor-to-liver (T/L) ratios remained nearly identical for the (R)- and (S)-forms at all time points. The micro-PET/CT imaging at 1 and 3 hours p.i. did not show any significant enantioselective tissue uptake. Conclusions: Although the (R)-enantiomer of [18F]FMISO demonstrated a somewhat faster initial tumor and muscle uptake no significant enantioselective tissue uptake was observed at later time points. The T/M- and T/L- ratios for the (R)- and (S)-forms were the same within the experimental error at all times. Therefore, the use of enantiopure [18F]FMISO is unlikely to present any practical clinical benefit for PET imaging.

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Scopus rating (2013): SJR 0.874 SNIP 0.97 CiteScore 2.61
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ISI indexed (2013): ISI indexed yes
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Scopus rating (2012): SJR 0.943 SNIP 1.096 CiteScore 2.73
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Web of Science (2010): Impact factor 2.62
BFI (2009): BFI-level 1
Scopus rating (2009): SJR 0.738 SNIP 0.871
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Scopus rating (2008): SJR 0.975 SNIP 0.935
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Scopus rating (2006): SJR 1.036 SNIP 0.893
Scopus rating (2005): SJR 0.871 SNIP 0.937
Scopus rating (2004): SJR 0.985 SNIP 1.091
Scopus rating (2003): SJR 0.866 SNIP 0.991
Scopus rating (2002): SJR 0.811 SNIP 0.723
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Bringing Radiotracing to Titanium-Based Antineoplastics: Solid Phase Radiosynthesis, PET and ex Vivo Evaluation of Antitumor Agent \([{}^{45}\text{Ti}]\text{(salan)}\text{Ti(dipic)}\)

We present a novel solid-phase based \(^{45}\text{Ti}\) radiolabeling methodology and the implementation of \(^{45}\text{Ti}\)-PET in titanium-based antineoplastics using the showcase compound \([{}^{45}\text{Ti}]\text{(salan)}\text{Ti(dipic)}\). This development is intended to allow elucidation of the biodistribution and pharmacokinetics of promising new Ti-based therapeutics.
Decay induced de-chelation of positron-emitting electron-capture daughters and its use in preclinical PET

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Design and synthesis of new octadentate macrocyclic chelators for $^{89}$Zr

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Authors: Bonnaud, M. (Ekstern), Fleurat-Lessard, P. (Ekstern), Severin, G. W. (Intern), Jensen, A. T. I. (Intern), Boschetti, F. (Ekstern), Denat, F. (Ekstern)
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Engineered α4β2 nicotinic acetylcholine receptors as models for measuring agonist binding and effect at the orthosteric low-affinity α4-α4 interface

The nicotinic acetylcholine receptor alpha 4 beta 2 is important for normal mammalian brain function and is known to express in two different stoichiometries, (alpha 4)(2)(beta 2)(3) and (alpha 4)(3)(beta 2)(2). While these are similar in many aspects, the (alpha 4)(3)(beta 2)(2) stoichiometry differs by harboring a third orthosteric acetylcholine binding site located at the alpha 4-alpha 4 interface. Interestingly, the third binding site has, so far, only been documented using electrophysiological assays, actual binding affinities of nicotinic receptor ligands to this site are not known. The present study was therefore aimed at determining binding affinities of nicotinic ligands to the alpha 4-alpha 4 interface. Given that epibatidine shows large functional potency differences at alpha 4-beta 2 vs. alpha 4-alpha 4 interfaces, biphasic binding properties would be expected at (alpha 4)(3)(beta 2)(2) receptors. However, standard saturation binding experiments with [H-3]epibatidine did not reveal biphasic binding under the conditions utilized. Therefore, an engineered beta 2 construct (beta 2(HQT)), which converts the beta(-) face to resemble that of an alpha 4(-) face, was utilized to create (alpha 4)(3)(beta 2(HQT))(2) receptors harboring three alpha 4-alpha 4 interfaces. With this receptor, low affinity binding of epibatidine with a K_d of similar to 5 nM was observed in sharp contrast to a K_d value of similar to 10 pM observed for wild-type receptors. A strong correlation between binding affinities at the (alpha 4)(3)(beta 2(HQT))(2) receptor and functional potencies at the wild-type receptor of a range of nicotinic ligands highlighted the validity of using the mutational approach. Finally, large differences in activities at alpha 4-beta 2 vs. alpha 4-alpha 4 interfaces were observed for structurally related agonists underscoring the need for establishing all binding parameters of compounds at alpha 4 beta 2 receptors. Crown Copyright (C) 2015 Published by Elsevier Ltd. All rights reserved.
Frustrated Lewis pairs-assisted reduction of carbonyl compounds

An alternative and robust method for the reduction of carbonyl groups by frustrated Lewis pairs (FLPs) is reported in this paper. With its very mild reaction conditions, good to excellent yields, absolute regioselectivity and the non-metallic character of the reagent, it provides an excellent tool for H-1, H-2 as well as H-3 chemistry. It is a new strategy for the one-pot synthesis of aromatic alcohols selectively labeled with heavy isotopes of hydrogen. © 2015 Elsevier Ltd. All rights reserved.

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Authors: Marek, A. (Intern), Pedersen, M. H. F. (Intern)
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BFI (2016): BFI-level 1
Scopus rating (2016): CiteScore 2.54 SJR 0.91 SNIP 0.743
Web of Science (2016): Impact factor 2.651
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Scopus rating (2015): SJR 0.941 SNIP 0.83 CiteScore 2.72
Web of Science (2015): Impact factor 2.645
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BFI (2014): BFI-level 1
Scopus rating (2014): SJR 0.972 SNIP 0.888 CiteScore 2.79
Web of Science (2014): Impact factor 2.641
Web of Science (2014): Indexed yes
BFI (2013): BFI-level 1
Scopus rating (2013): SJR 1.106 SNIP 0.91 CiteScore 2.85
Web of Science (2013): Impact factor 2.817
ISI indexed (2013): ISI indexed yes
BFI (2012): BFI-level 1
Scopus rating (2012): SJR 1.329 SNIP 0.99 CiteScore 2.89
Web of Science (2012): Impact factor 2.803
ISI indexed (2012): ISI indexed yes
BFI (2011): BFI-level 1
Scopus rating (2011): SJR 1.473 SNIP 1.065 CiteScore 3.22
Web of Science (2011): Impact factor 3.025
ISI indexed (2011): ISI indexed yes
Web of Science (2011): Indexed yes
BFI (2010): BFI-level 1
Scopus rating (2010): SJR 1.526 SNIP 1.065
Web of Science (2010): Indexed yes
BFI (2009): BFI-level 1
Scopus rating (2009): SJR 1.545 SNIP 1.116
BFI (2008): BFI-level 1
Scopus rating (2008): SJR 1.605 SNIP 1.085
Scopus rating (2007): SJR 1.648 SNIP 1.099
Web of Science (2007): Indexed yes
Scopus rating (2006): SJR 1.524 SNIP 1.131
Scopus rating (2005): SJR 1.375 SNIP 1.124
Web of Science (2005): Indexed yes
Scopus rating (2004): SJR 1.466 SNIP 1.249
Web of Science (2004): Indexed yes
Scopus rating (2003): SJR 1.482 SNIP 1.246
Web of Science (2003): Indexed yes
Scopus rating (2002): SJR 1.598 SNIP 1.156
Scopus rating (2001): SJR 1.455 SNIP 1.147
Web of Science (2001): Indexed yes
Scopus rating (2000): SJR 1.363 SNIP 1.113
Improved sea level record over the satellite altimetry era (1993-2010) from the Climate Change Initiative project

Sea level is one of the 50 Essential Climate Variables (ECVs) listed by the Global Climate Observing System (GCOS) in climate change monitoring. In the past two decades, sea level has been routinely measured from space using satellite altimetry techniques. In order to address a number of important scientific questions such as "Is sea level rise accelerating?", "Can we close the sea level budget?", "What are the causes of the regional and interannual variability?", "Can we already detect the anthropogenic forcing signature and separate it from the internal/natural climate variability?", and "What are the coastal impacts of sea level rise?", the accuracy of altimetry-based sea level records at global and regional scales needs to be significantly improved. For example, the global mean and regional sea level trend uncertainty should become better than 0.3 and 0.5 mm year\(^{-1}\), respectively (currently 0.6 and 1-2 mm year\(^{-1}\)). Similarly, interannual global mean sea level variations (currently uncertain to 2-3 mm) need to be monitored with better accuracy. In this paper, we present various data improvements achieved within the European Space Agency (ESA) Climate Change Initiative (ESA CCI) project on "Sea Level" during its first phase (2010-2013), using multi-mission satellite altimetry data over the 1993-2010 time span. In a first step, using a new processing system with dedicated algorithms and adapted data processing strategies, an improved set of sea level products has been produced. The main improvements include: reduction of orbit errors and wet/dry atmospheric correction errors, reduction of instrumental drifts and bias, intercalibration biases, intercalibration between missions and combination of the different sea level data sets, and an improvement of the reference mean sea surface. We also present preliminary independent validations of the SL_cci products, based on tide gauges comparison and a sea level budget closure approach, as well as comparisons with ocean reanalyses and climate model outputs.

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Authors: Ablain, M. (Ekstern), Cazenave, A. (Ekstern), Larnicol, G. (Ekstern), Balmaseda, M. (Ekstern), Cipollini, P. (Ekstern), Faugere, Y. (Ekstern), Fernandes, M. J. (Ekstern), Henry, O. (Ekstern), Johannessen, J. A. (Ekstern), Knudsen, P. (Intern), Andersen, O. (Intern), Legeais, J. (Ekstern), Meyssignac, B. (Ekstern), Picot, N. (Ekstern), Roca, M. (Ekstern), Rudenko, S. (Ekstern), Scharffenberg, M. G. (Ekstern), Stammer, D. (Ekstern), Timms, G. (Ekstern), Benveniste, J. (Ekstern)
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Management of Tritium in European Spallation Source

The European Spallation Source (ESS) will produce tritium via spallation and activation processes during operational activities. Within the location of ESS facility in Lund, Sweden site it is mandatory to demonstrate that the management strategy of the produced tritium ensures the compliance with the country regulation criteria. The aim of this paper is to give an overview of the different aspects of the tritium management in ESS facility. Besides the design parameter study of the helium coolant purification system of the target the consequences of the tritium releasing into the environment were also analyzed. Calculations shown that the annual release of tritium during the normal operations represents a small fraction from the estimated total dose. However, more refined calculations of migration of activated-groundwater should be performed for higher hydraulic conductivities, with the availability of the results on soil examinations. With the assumption of 100% release of tritium to the atmosphere during the occurring of the extreme accidents, it was found as well that the total dose complies with the constraint.
Migration of radionuclides in a gas cooled solid state spallation target
The current design of the ESS (European Spallation Source) program proposes a rotating solid tungsten target cooled by helium gas and a pulsed beam of protons. For safety reasons any design has to address whether or not the induced radionuclidic isotopes in the target migrate. In this paper we have investigated the diffusion of (primarily) tritium in solid tungsten to see if a pulse driven short-term variation in temperature (temperature peaks separated by one turn of the wheel (2.36 s)) could possibly give rise to wave-like migration of the radionuclides, possibly accelerating the overall release. In order to calculate the diffusion in the solid tungsten target two approaches have been used. One neglecting the time structure of the beam and thermal cycling of the target, and one numerical, discrete time step simulation to capture the effects of the thermal cycling on the diffusion behavior. We found that the time structure of the temperature has a negligible impact on the diffusion, and that the radioactive release at the surface can be calculated safely by solving the differential equation (Fick's law) using an appropriate temperature to calculate the diffusion constant. © 2014 Elsevier B.V. All rights reserved.
Mn-52 as a PET Neural Tract Tracer

General information
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Organisations: Center for Nuclear Technologies, The Hevesy Laboratory, University of Tübingen, Eberhard-Karls-Universität Tübingen
Authors: Napieczynska, H. (Ekstern), Calaminus, C. (Ekstern), Severin, G. W. (Intern), Fonslet, J. (Intern), Pichler, B. J. (Ekstern)
Number of pages: 1
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Main Research Area: Technical/natural sciences
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New approaches to [18F]fluoride recovery and radiofluorination

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Organisations: Center for Nuclear Technologies, The Hevesy Laboratory
Authors: Mathiessen, B. I. (Intern), Zhuravlev, F. (Intern), Jensen, M. (Intern)
Number of pages: 194
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Main Research Area: Technical/natural sciences
Electronic versions:
New_approaches.pdf
Publication: Research › Ph.D. thesis – Annual report year: 2015

Novel Preparation Methods of 52Mn for ImmunoPET Imaging

52Mn (t1/2 = 5.59 d, β+ = 29.6%, Eβave = 0.24 MeV) shows promise in positron emission tomography (PET) and in dual-modality manganese-enhanced magnetic resonance imaging (MEMRI) applications including neural tractography, stem cell tracking, and biological toxicity studies. The extension to bioconjugate application requires high specific activity 52Mn in a state suitable for macromolecule labeling. To that end a 52Mn production, purification, and labeling system is presented, and its applicability in preclinical, macromolecule PET is shown using the conjugate 52Mn-DOTA-TRC105. 52 Mn is produced by 60 µA, 16 MeV proton irradiation of natural chromium metal pressed into a silver disc support. Radiochemical separation proceeds by strong anion exchange chromatography of the dissolved Cr target, employing a semi-organic mobile phase, 97:3 (v:v) ethanol: HCl (11M, aqueous). The method is 62 ± 14% efficient (n=7) in 52Mn recovery, leading to a separation factor from Cr of (1.6 ± 1.0) x10^6 (n = 4), and an average effective specific activity of 0.8 GBq/µmol (n = 4) in titration against DOTA. 52Mn-DOTA-TRC105 conjugation and labeling demonstrate the potential for chelation applications. In vivo images acquired using PET/CT in mice bearing 4T1 xenograft tumors are presented. Peak tumor uptake is 18.7 ± 2.7 %ID/g at 24 hours post injection and ex vivo 52Mn biodistribution validates the in vivo PET data. Free 52Mn^{2+} (as chloride or acetate) is used as a control in additional mice to evaluate the non-targeted biodistribution in the tumor model.

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Organisations: Center for Nuclear Technologies, The Hevesy Laboratory, Department of Electrical Engineering, University of Wisconsin-Madison, TRACON Pharmaceuticals, Inc.
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Web of Science (2017): Impact factor 4.485
Web of Science (2017): Indexed yes
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Optimized $^{52}$Mn Production for Longlived PET Applications

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Organisations: Center for Nuclear Technologies, The Hevesy Laboratory, Department of Electrical Engineering, University of Wisconsin-Madison
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Main Research Area: Technical/natural sciences
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Pathogen specific antibody-based molecular imaging of Invasive Aspergillosis with the newly developed PET tracer $[^{64}Cu]$DOTA-JF5 and its humanized variant $[^{64}Cu]$NODAGA-hJF5

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Organisations: Center for Nuclear Technologies, The Hevesy Laboratory, Eberhard-Karls-Universität Tübingen, University of Duisburg-Essen, Chematech
Authors: Rolle, A. (Ekstern), Hasenberg, M. (Ekstern), Thornton, C. R. (Ekstern), Maurer, A. (Ekstern), Fischer, E. (Ekstern), Spycher, P. R. (Ekstern), Schibli, R. (Ekstern), Boschetti, F. (Ekstern), Stegemann-Koniszewski, S. (Ekstern), Bruder, D. (Ekstern), Severin, G. (Intern), Elema, D. R. (Intern), Autenrieth, S. (Ekstern), Pichler, B. (Ekstern), Gunzer, M. (Ekstern), Wiehr, S. (Ekstern)
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Conference: World Molecular Imaging Congress 2015, Honolulu, HI, United States, 02/09/2015 - 02/09/2015

PET/CT Based In Vivo Evaluation of $^{64}$Cu Labelled Nanodiscs in Tumor Bearing Mice
$^{64}$Cu radiolabelled nanodiscs based on the 11 α-helix MSP1E3D1 protein and 1-palmitoyl-2-oleoyl-sn-glycero-3-phosphatidylcholine lipids were, for the first time, followed in vivo by positron emission tomography for evaluating the biodistribution of nanodiscs. A cancer tumor bearing mouse model was used for the investigations, and it was found that the approximately 13 nm nanodiscs, due to their size, permeate deeply into cancer tissue. This makes them promising candidates for both drug delivery purposes and as advanced imaging agents. For the radiolabelling, a simple approach for $^{64}$Cu radiolabelling of proteins via a chelating agent, DOTA, was developed. The reaction was performed at sufficiently mild conditions to be compatible with labelling of the protein part of a lipid-protein particle while fully conserving the particle structure including the amphipathic protein fold.

General information
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Organisations: Center for Nuclear Technologies, The Hevesy Laboratory, University of Copenhagen
Authors: Huda, P. (Forskerdatabase), Binderup, T. (Ekstern), Pedersen, M. C. (Forskerdatabase), Midtgaard, S. R. (Forskerdatabase), Elema, D. R. (Intern), Kjær, A. (Ekstern), Jensen, M. (Intern), Arleth, L. (Ekstern)
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Main Research Area: Technical/natural sciences
Positron Emission Tomography Based Elucidation of the Enhanced Permeability and Retention Effect in Dogs with Cancer Using Copper-64 Liposomes

Since the first report of the enhanced permeability and retention (EPR) effect, the research in nanocarrier based antitumor drugs has been intense. The field has been devoted to treatment of cancer by exploiting EPR-based accumulation of nanocarriers in solid tumors, which for many years was considered to be a ubiquitous phenomenon. However, the understanding of differences in the EPR-effect between tumor types, heterogeneities within each patient group, and dependency on tumor development stage in humans is sparse. It is therefore important to enhance our understanding of the EPR-effect in large animals and humans with spontaneously developed cancer. In the present paper, we describe a novel loading method of copper-64 into PEGylated liposomes and use these liposomes to evaluate the EPR-effect in 11 canine cancer patients with spontaneous solid tumors by PET/CT imaging. We thereby provide the first high-resolution analysis of EPR-based tumor accumulation in large animals. We find that the EPR-effect is strong in some tumor types but cannot be considered a general feature of solid malignant tumors since we observed a high degree of accumulation heterogeneity between tumors. Six of seven included carcinomas displayed high uptake levels of liposomes, whereas one of four sarcomas displayed signs of liposome retention. We conclude that nanocarrier-radiotracers could be important in identifying cancer patients that will benefit from nanocarrier-based therapeutics in clinical practice.

General information
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Organisations: Department of Micro- and Nanotechnology, Colloids and Biological Interfaces, Department of Chemistry, Center for Nuclear Technologies, The Hevesy Laboratory, University of Copenhagen, Copenhagen University Hospital
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Web of Science (2017): Indexed yes
BFI (2016): BFI-level 2
Scopus rating (2016): CiteScore 13.65 SJR 6.948 SNIP 2.604
Web of Science (2016): Impact factor 13.942
Web of Science (2016): Indexed yes
BFI (2015): BFI-level 2
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BFI (2014): BFI-level 2
Scopus rating (2014): SJR 5.981 SNIP 2.721 CiteScore 12.49
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BFI (2013): BFI-level 2
Scopus rating (2013): SJR 6.672 SNIP 2.735 CiteScore 13.18
Web of Science (2013): Impact factor 12.033
ISI indexed (2013): ISI indexed yes
Web of Science (2013): Indexed yes
BFI (2012): BFI-level 2
Predicted Radiation Exposure from Mining at Kvanefjeld: Introduction to Radiation, Review of Baseline Information, and Predicted Radiation Exposures from Kvanefjeld Mining, Mineral Processing and Refining

Baseline surveys of gamma radiation and environmental radioactivity have been carried out by Greenland Minerals and Energy Ltd (GMEL) to show existing levels in the town of Narsaq and in the Kvanefjeld project area. Radiation levels in Narsaq are low but elevated in the project area due to the presence of large uranium and thorium deposits in Kvanefjeld. These deposits are also the reason that radon in outdoor air show elevated concentrations in Narsaq and in the project area. It is recommended that future monitoring of external exposure and radon should be based on measurement techniques using integrating dosimeters.

The Technical University of Denmark (DTU) has reviewed the impact of Kvanefjeld operations on the future workforce to estimate radiation doses to individuals. Calculations were performed with conservative assumptions that reveal the annual radiation dose to workers to be between 1 and 5 millisieverts (mSv). This range of annual doses is below the internationally accepted limits for occupational exposure of 20 mSv averaged over five consecutive years and 50 mSv in any single year. The radiation dose estimates calculated by DTU are consistent with actual measured radiation doses from uranium mines in other developed countries such as Australia and Canada. From a radiation dose perspective Kvanefjeld operations are not expected to be any worse than current uranium mining operations elsewhere as the uranium content is significantly lower.

DTU was engaged by GMEL as an independent reviewer of baseline surveys carried out and data obtained. DTU (former Risø National Laboratory) has five-decades of experience in dealing with naturally-occurring and man-made radioactivity and radiation in the environment covering research and development as well as consultancy.
Radiosynthesis and in vitro validation of \(^3\)H-NS14492 as a novel high affinity alpha7 nicotinic receptor radioligand

The neuronal alpha 7 nicotinic acetylcholine receptor is a homo-pentameric ligand-gated ion channel that is a promising drug target for cognitive deficits in Alzheimer's disease and schizophrenia. We have previously described \(^{11}\)C-NS14492 as a suitable agonist radioligand for in vivo positron emission tomography (PET) occupancy studies of the alpha 7 nicotinic receptor in the pig brain. In order to investigate the utility of the same compound for in vitro studies, \(^3\)H-NS14492 was synthesized and its binding properties were characterized using in vitro autoradiography and homogenate binding assays in pig frontal cortex. \(^3\)H-NS14492 showed specific binding to alpha 7 nicotinic receptors in autoradiography, revealing a dissociation constant (K\(_d\)) of 2.1 ± 0.7 nM and a maximum number of binding sites (B\(_{\text{max}}\)) of 15.7±2.0 fmol/mg tissue equivalent. Binding distribution was similar to that of another selective ligand \(^{125}\)I-alpha-bungarotoxin (\(^{125}\)I-BTX) in autoradiography, and unlabeled NS14492 displaced \(^{125}\)I-BTX with an inhibition constant (K\(_i\)) of 23 nM. \(^3\)H-NS14492 bound to alpha 7 nicotinic receptors in homogenized pig frontal cortex with a K\(_d\) of 0.8±0.3 nM and a B\(_{\text{max}}\) of 30.2±11.6 fmol/mg protein. This binding assay further revealed the K\(_i\) rank order for a number of alpha 7 nicotinic receptor agonists, and positive allosteric modulators (PAMs). Further, we saw increased binding of \(^3\)H-NS14492 to pig frontal cortex membranes when co-incubated with PNU-120596, a type II PAM. Taken together, these findings show that \(^3\)H-NS14492 is a useful new in vitro radioligand for the pig alpha 7 nicotinic receptor. © 2015 Elsevier B.V. All rights reserved.

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  Web of Science (2017): Impact factor 3.04
  Web of Science (2017): Indexed yes
  BFI (2016): BFI-level 1
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  Web of Science (2016): Impact factor 2.896
  BFI (2015): BFI-level 1
  Scopus rating (2015): SJR 1.122 SNIP 1.014 CiteScore 2.93
  Web of Science (2015): Impact factor 2.73
  Web of Science (2015): Indexed yes
  BFI (2014): BFI-level 1
  Scopus rating (2014): SJR 1.027 SNIP 1.036 CiteScore 2.76
  Web of Science (2014): Impact factor 2.532
  BFI (2013): BFI-level 1
  Scopus rating (2013): SJR 1.068 SNIP 1.081 CiteScore 3
  Web of Science (2013): Impact factor 2.684
  BFI (2012): BFI-level 1
  Scopus rating (2012): SJR 0.989 SNIP 1.058 CiteScore 2.98
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  Scopus rating (2011): SJR 1.058 SNIP 1.069 CiteScore 3.03
Radiosynthesis and in vitro validation of [3H]-NS14492 as a novel high affinity α7 nicotinic receptor radioligand

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Organisations: Center for Nuclear Technologies, The Hevesy Laboratory, Copenhagen University Hospital, DanPET AB
Authors: Donat, C. K. (Ekstern), Magnussen, J. H. (Ekstern), Ettrup, A. (Ekstern), Peters, D. (Ekstern), Pedersen, M. H. F. (Intern), Knudsen, G. M. (Ekstern), Mikkelsen, J. D. (Ekstern)
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Web of Science (2017): Impact factor 4.235
Web of Science (2017): Indexed yes
BFI (2016): BFI-level 1
Scopus rating (2016): SJR 1.902 SNIP 1.335 CiteScore 4.75
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BFI (2015): BFI-level 1
Scopus rating (2015): SJR 2.286 SNIP 1.519 CiteScore 5.23
Web of Science (2015): Impact factor 5.091

Web of Science (2011): Impact factor 2.516
BFI (2010): BFI-level 1
Scopus rating (2010): SJR 1.043 SNIP 0.983
Web of Science (2010): Impact factor 2.737
BFI (2009): BFI-level 2
Scopus rating (2009): SJR 1.048 SNIP 0.968
BFI (2008): BFI-level 2
Scopus rating (2008): SJR 1.018 SNIP 0.905
Scopus rating (2007): SJR 1.002 SNIP 0.877
Scopus rating (2006): SJR 1.06 SNIP 0.941
Scopus rating (2005): SJR 1.022 SNIP 0.914
Scopus rating (2004): SJR 0.989 SNIP 0.897
Scopus rating (2003): SJR 0.971 SNIP 0.856
Scopus rating (2002): SJR 0.892 SNIP 0.816
Scopus rating (2001): SJR 0.94 SNIP 0.797
Scopus rating (2000): SJR 1.012 SNIP 0.84
Scopus rating (1999): SJR 0.953 SNIP 0.808
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Alpha7, Radioligand, Autoradiography, Binding assay, PET ligand

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Remote Loading of $^{64}$Cu$^{2+}$ into Liposomes without the Use of Ion Transport Enhancers

Due to low ion permeability of lipid bilayers, it has been and still is common practice to use transporter molecules such as ionophores or lipophilic chelators to increase transmembrane diffusion rates and loading efficiencies of radionuclides into liposomes. Here, we report a novel and very simple method for loading the positron emitter $^{64}$Cu$^{2+}$ into liposomes, which is important for in vivo positron emission tomography (PET) imaging. By this approach, copper is added to liposomes entrapping a chelator, which causes spontaneous diffusion of copper across the lipid bilayer where it is trapped. Using this method, we achieve highly efficient $^{64}$Cu$^{2+}$ loading (>95%), high radionuclide retention (>95%), and favorable loading kinetics, excluding the use of transporter molecule additives. Therefore, clinically relevant activities of 200-400 MBq/patient can be loaded fast (60-75 min) and efficiently into preformed stealth liposomes avoiding subsequent purification steps. We investigate the molecular coordination of entrapped copper using X-ray absorption spectroscopy and demonstrate high adaptability of the loading method to pegylated, nonpegylated, gel- or fluid-like, cholesterol rich or cholesterol depleted, cationic, anionic, and zwitterionic lipid compositions. We demonstrate high in vivo stability of $^{64}$Cu-liposomes in a large canine model observing a blood circulation half-life of 24 h and show a tumor accumulation of 6% ID/g in FaDu xenograft mice using PET imaging. With this work, it is demonstrated that copper ions are capable of crossing a lipid membrane unassisted. This method is highly valuable for characterizing the in vivo performance of liposome-based nanomedicine with great potential in diagnostic imaging applications.
Laboratory, University of Copenhagen
Authors: Henriksen, J. R. (Intern), Petersen, A. L. (Intern), Hansen, A. E. (Intern), Frankær, C. G. (Intern), Harris, P. (Intern), Elema, D. R. (Intern), Kristensen, A. T. (Ekstern), Kjær, A. (Ekstern), Andresen, T. L. (Intern)
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Web of Science (2017): Impact factor 8.097
Web of Science (2017): Indexed yes
BFI (2016): BFI-level 1
Scopus rating (2016): CiteScore 7.6 SJR 2.561 SNIP 1.536
Web of Science (2016): Impact factor 7.504
Web of Science (2016): Indexed yes
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Scopus rating (2015): SJR 2.262 SNIP 1.555 CiteScore 7.38
Web of Science (2015): Impact factor 7.145
Web of Science (2015): Indexed yes
BFI (2014): BFI-level 1
Scopus rating (2014): SJR 2.125 SNIP 1.636 CiteScore 6.88
Web of Science (2014): Impact factor 6.723
Web of Science (2014): Indexed yes
BFI (2013): BFI-level 1
Scopus rating (2013): SJR 1.992 SNIP 1.548 CiteScore 6.05
Web of Science (2013): Impact factor 5.9
ISI indexed (2013): ISI indexed yes
Web of Science (2013): Indexed yes
BFI (2012): BFI-level 1
Scopus rating (2012): SJR 2.199 SNIP 1.327 CiteScore 4.94
Web of Science (2012): Impact factor 5.008
ISI indexed (2012): ISI indexed yes
Web of Science (2012): Indexed yes
BFI (2011): BFI-level 1
Scopus rating (2011): SJR 2.046 SNIP 1.404 CiteScore 4.41
Web of Science (2011): Impact factor 4.525
ISI indexed (2011): ISI indexed no
Web of Science (2011): Indexed yes
Scopus rating (2010): SJR 1.597 SNIP 0.944
Web of Science (2010): Impact factor 2.925
Web of Science (2010): Indexed yes
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Diagnostic, Ion permeability, Molecular imaging, Nanoparticles, Positron emission tomography, Remote loading
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52gMn – a new PET tracer for preclinical in vivo neuroimaging

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Authors: Napieczynska, H. (Ekstern), Severin, G. (Intern), Fonslet, J. (Intern), Pichler, B. J. (Ekstern), Calaminus, C. (Ekstern)
Number of pages: 1
Publication date: 2015

The impact of weakly bound 89Zr on preclinical studies: Non-specific accumulation in solid tumors and aspergillus infection

Abstract
Preclinical studies involving 89Zr often report significant bone accumulation, which is associated with dissociation of the radiometal from the tracer. However, experiments determining the uptake of unbound 89Zr in disease models are not performed as routine controls. The purpose of the present study was to investigate the impact of free or weakly bound 89Zr on PET quantifications in disease models, in order to determine if such control experiments are warranted.

Methods
Chemical studies were carried out to find a 89Zr compound that would solubilize the 89Zr as a weak chelate, thus mimicking free or weakly bound 89Zr released in circulation. 89Zr oxalate had the desired characteristics, and was injected into mice bearing FaDu and HT29 solid tumor xenografts, and mice infected in the lungs with the mold Aspergillus fumigatus, as well as in healthy controls (naïve). PET/CT and PET/MR imaging followed to quantify the distribution of the radionuclide in the disease models.

Results
89Zr oxalate was found to have a plasma half-life of 5.1 ± 2.3 h, accumulating mainly in the bones of all animals. Both tumor types accumulated 89Zr on the order of 2-4% ID/cm3, which is comparable to EPR-mediated accumulation of certain species. In the aspergillosis model, the concentration of 89Zr in lung tissue of the naïve animals was 6.0 ± 1.1 %ID/g. This was significantly different from that of the animals with advanced disease, showing 11.6% ± 1.8 %ID/g.

Conclusions
Given the high levels of 89Zr accumulation in the disease sites in the present study, we recommend control experiments mapping the biodistribution of free 89Zr in any preclinical study employing 89Zr where bone uptake is observed. Aqueous 89Zr oxalate appears to be a suitable compound for such studies. This is especially relevant in studies where the tracer accumulation is based upon passive targeting, such as EPR.

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Towards automated solid phase radiofluorination for dose-on-demand PET: retention of activity by solid support

On-column $^{18}$F fluoride trapping and radiofluorination of 2-(naphthalen-1-yl)ethyl-4-methylbenzenesulfonate (C$_{10}$H$_{7}$CH$_2$OTs), performed on polystyrene supported phosphazene base PS-PbBu$_2$ yielded $^{18}$F1-(2-fluoroethyl)naphthalene (1$^{18}$F).
F\(\text{C}_{10}\text{H}_{7}\text{(CH}_{2}\text{)}_{2}\text{F}\) in 50% radiochemical yield but left up to 43% of activity unreacted on the resin. This activity could be eluted with Kryptofix/K\(\text{2CO}_{3}\) and then used for conventional radiofluorination of the same substrate, suggesting that the column-retained activity was present in the form of \([^{18}\text{F}]\)fluoride entrapped in polymer matrix. An approach to minimize the amount of entrapped \([^{18}\text{F}]\)fluoride by use of glass beads functionalized with alkylsilane-derivatized phosphazene residues was attempted but was stymied by fluorolysis/hydrolysis of the alkylsilane spacer. The results suggest that the key to high yield of on-column radiofluorination is to minimize the residual \([^{18}\text{F}]\)fluoride absorption in the matrix by the judicious choice of solid support.

**General information**
State: Published
Organisations: Center for Nuclear Technologies, The Hevesy Laboratory
Authors: Ingemann Mathiessen, B. (Intern), Severin, G. (Intern), Zhuravlev, F. (Intern)
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BFI (2017): BFI-level 1
Scopus rating (2017): SNIP 0.869 SJR 0.409 CiteScore 1.22
Web of Science (2017): Impact factor 1.202
Web of Science (2017): Indexed yes
BFI (2016): BFI-level 1
Scopus rating (2016): SJR 0.477 SNIP 0.749 CiteScore 1.2
Web of Science (2016): Impact factor 1.271
BFI (2015): BFI-level 1
Scopus rating (2015): SJR 0.464 SNIP 0.723 CiteScore 1.12
Web of Science (2015): Impact factor 1.1
Web of Science (2015): Indexed yes
BFI (2014): BFI-level 1
Scopus rating (2014): SJR 0.471 SNIP 0.773 CiteScore 1.26
Web of Science (2014): Impact factor 1.014
BFI (2013): BFI-level 1
Scopus rating (2013): SJR 0.633 SNIP 0.92 CiteScore 1.49
Web of Science (2013): Impact factor 1.411
ISI indexed (2013): ISI indexed yes
Web of Science (2013): Indexed yes
BFI (2012): BFI-level 1
Scopus rating (2012): SJR 0.675 SNIP 0.954 CiteScore 1.45
Web of Science (2012): Impact factor 1.373
ISI indexed (2012): ISI indexed yes
BFI (2011): BFI-level 1
Scopus rating (2011): SJR 0.678 SNIP 0.908 CiteScore 1.65
Web of Science (2011): Impact factor 1.575
ISI indexed (2011): ISI indexed yes
BFI (2010): BFI-level 1
Scopus rating (2010): SJR 0.823 SNIP 1.036
Web of Science (2010): Impact factor 1.128
BFI (2009): BFI-level 1
Scopus rating (2009): SJR 0.64 SNIP 1.044
BFI (2008): BFI-level 1
A radionuclide generator of Erbium-165, an isotope for Auger Therapy

General information
State: Published
Organisations: Center for Nuclear Technologies, The Hevesy Laboratory
Authors: Severin, G. (Intern), Jensen, M. (Intern)
Pages: S88-S89
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Conference: International Conference on Translational Research in Radio-Oncology / Physics for Health in Europe 2014, Geneva, Switzerland, 10/02/2014 - 10/02/2014
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BFI (2017): BFI-level 1
Scopus rating (2017): CiteScore 4.56 SJR 2.313 SNIP 1.612
Web of Science (2017): Impact factor 4.942
Web of Science (2017): Indexed yes
BFI (2016): BFI-level 1
Scopus rating (2016): CiteScore 4.36 SJR 2.099 SNIP 1.549
Web of Science (2016): Impact factor 4.328
Web of Science (2016): Indexed yes
BFI (2015): BFI-level 1
Scopus rating (2015): SJR 2.777 SNIP 1.707 CiteScore 4.87
Web of Science (2015): Impact factor 4.817
Web of Science (2015): Indexed yes
BFI (2014): BFI-level 1
Scopus rating (2014): SJR 2.605 SNIP 1.706 CiteScore 4.46
Web of Science (2014): Impact factor 4.363
Web of Science (2014): Indexed yes
BFI (2013): BFI-level 1
Auger Emitter Based Radiotherapy- A Possible New Treatment for Cancer

Cancer is a major cause of mortality worldwide (1). A large fraction of cancer patients undergo external radiotherapy, delivering a lethal dose of radiation to the patient’s tumour(s). The main problem with this approach is the collateral damage caused to healthy, surrounding tissue and the side effects, which result. Auger emitters decay by internal conversion (IC) or electron capture (EC) producing a number of Auger cascade electrons (5-8 electrons per decay). These electrons are so low in energy that their range in tissue is in the order of nm-μm. Due to this short range Auger emitters may be able to kill only the target cell while sparing the surrounding healthy tissue. In addition due to the multiple electrons released during the decay these emitters are more likely to produce at cluster of complex DNA damage which are considered to be much more harmful to the cell than dispersed DNA damage produced by Low-LET radiation used in current radiotherapy (2-3) Considerable efforts have been made in the past twenty years to develop Auger emitter-based radiotherapy However, previous studies lack precise measurement of RBE, which is the fundamental factor defining the relationship between local radiation dose and biological damage done for the given Auger emitter, thereby brought the development to a halt. We believe we have the techniques to quantify the biological damage done for a given Auger emitter and thereby pushing the development of Auger emitterbased radiotherapy into reality (4-10).

General information

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Organisations: Center for Nuclear Technologies, The Hevesy Laboratory, Department of Micro- and Nanotechnology, Institut Laue-Langevin
Number of pages: 1
Publication date: 2014
Biodistribution of 89Zr-oxalate in tumor bearing mice

General information
State: Published
Organisations: Center for Nuclear Technologies, The Hevesy Laboratory, Copenhagen University Hospital
Authors: Severin, G. (Intern), Jørgensen, J. (Ekstern), Hansen, A. (Ekstern), Kjær, A. (Ekstern), Jensen, A. (Intern)
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BFI (2018): BFI-level 2
Web of Science (2018): Indexed yes
BFI (2017): BFI-level 2
Scopus rating (2017): CiteScore 5.12 SJR 2.307 SNIP 1.705
Web of Science (2017): Impact factor 7.439
Web of Science (2017): Indexed yes
BFI (2016): BFI-level 2
Scopus rating (2016): CiteScore 5.06 SJR 2.313 SNIP 1.843
Web of Science (2016): Impact factor 6.646
Web of Science (2016): Indexed yes
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Scopus rating (2015): SJR 2.511 SNIP 1.887 CiteScore 4.83
Web of Science (2015): Impact factor 5.849
Web of Science (2015): Indexed yes
BFI (2014): BFI-level 2
Scopus rating (2014): SJR 2.461 SNIP 1.978 CiteScore 4.9
Web of Science (2014): Impact factor 6.16
Web of Science (2014): Indexed yes
BFI (2013): BFI-level 2
Scopus rating (2013): SJR 2.315 SNIP 1.982 CiteScore 4.66
Web of Science (2013): Impact factor 5.563
ISI indexed (2013): ISI indexed yes
Web of Science (2013): Indexed yes
BFI (2012): BFI-level 2
Scopus rating (2012): SJR 2.787 SNIP 2.16 CiteScore 5
Web of Science (2012): Impact factor 5.774
ISI indexed (2012): ISI indexed yes
Web of Science (2012): Indexed yes
BFI (2011): BFI-level 2
Scopus rating (2011): SJR 2.642 SNIP 2.092 CiteScore 5.08
Web of Science (2011): Impact factor 6.381
Dosimetry of $^{64}$Cu-DOTA-AE105, a PET tracer for uPAR imaging

$^{64}$Cu-DOTA-AE105 is a novel positron emission tomography (PET) tracer specific to the human urokinase-type plasminogen activator receptor (uPAR). In preparation of using this tracer in humans, as a new promising method to distinguish between indolent and aggressive cancers, we have performed PET studies in mice to evaluate the in vivo biodistribution and estimate human dosimetry of $^{64}$Cu-DOTA-AE105.

Methods
Five mice received iv tail injection of $^{64}$Cu-DOTA-AE105 and were PET/CT scanned 1, 4.5 and 22h post injection. Volume-of-interest (VOI) were manually drawn on the following organs: heart, lung, liver, kidney, spleen, intestine, muscle, bone and bladder. The activity concentrations in the mentioned organs [%ID/g] were used for the dosimetry calculation. The %ID/g of each organ at 1, 4.5 and 22h was scaled to human value based on a difference between organ and body weights. The scaled values were then exported to OLINDA software for computation of the human absorbed doses. The residence times as well as effective dose equivalent for male and female could be obtained for each organ.

To validate this approach, of human projection using mouse data, five mice received iv tail injection of another $^{64}$Cu-DOTA peptide-based tracer, $^{64}$Cu-DOTA-TATE, and underwent same procedure as just described. The human dosimetry estimates were then compared with observed human dosimetry estimate recently found in a first-in-man study using $^{64}$Cu-DOTA-TATE.

Results
Human estimates of $^{64}$Cu-DOTA-AE105 revealed the heart wall to receive the highest dose (0.0918mSv/MBq) followed by the liver (0.0815mSv/MBq). All other organs/tissue were estimated to receive doses in the range of 0.02–0.04mSv/MBq. The mean effective whole-body dose of $^{64}$Cu-DOTA-AE105 was estimated to be 0.0317mSv/MBq. Relatively good correlation between human predicted and observed dosimetry estimates for $^{64}$Cu-DOTA-TATE was found. Importantly, the effective whole body dose was predicted with very high precision (predicted value: 0.0252mSv/MBq, Observed value: 0.0315mSv/MBq) thus validating our approach for human dosimetry estimation.

Conclusion
Favorable dosimetry estimates together with previously reported uPAR PET data fully support human testing of $^{64}$Cu-DOTA-AE105.
Experimental yields of PET radioisotopes from a prototype 7.8 MeV cyclotron

General information
State: Published
Organisations: Center for Nuclear Technologies, The Hevesy Laboratory, GE Healthcare
Authors: Jensen, M. (Intern), Eriksson, T. (Ekstern), Severin, G. (Intern), Parnaste, M. (Ekstern), Norling, J. (Ekstern)
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Electronic versions:

Abstract
Source: PublicationPreSubmission
Source-ID: 115391337
Publication: Research - peer-review › Conference abstract in proceedings – Annual report year: 2015

Gamma camera imaging for studying intestinal absorption and whole-body distribution of selenomethionine
Se metabolism in humans is not well characterised. Currently, the estimates of Se absorption, whole-body retention and excretion are being obtained from balance and tracer studies. In the present study, we used gamma camera imaging to evaluate the whole-body retention and distribution of radiolabelled selenomethionine (SeMet), the predominant form of Se present in foods. A total of eight healthy young men participated in the study. After consumption of a meal containing 4MBq [75Se]L-SeMet ([75Se]SeMet), whole-body gamma camera scanning was performed for 45 min every hour over a 6 h period, every second hour for the next 18 h and once on each of the subsequent 6 d. Blood, urine and faecal samples were collected to determine the plasma content of [75Se]SeMet as well as its excretion in urine and faeces. Imaging showed that 87.9 (SD 3.3)% of the administered activity of [75Se]SeMet was retained within the body after 7 d. In contrast, the measured excretion in urine and faeces for the 7 d period was 8.2 (SD 1.1)% of the activity. Time–activity curves were generated for the whole body, stomach, liver, abdomen (other than the stomach and the liver), brain and femoral muscles. Gamma camera imaging allows for the assessment of the postprandial absorption of SeMet. This technique may also permit concurrent studies of organ turnover of SeMet.

General information
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Authors: Madsen, J. L. (Ekstern), Sjögreen-Gleisner, K. (Ekstern), Elema, D. R. (Intern), Søndergaard, L. R. (Ekstern), Rasmussen, P. (Intern), Fuglsang, S. (Ekstern), Ljungberg, M. (Ekstern), Damgaard, M. (Ekstern)
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BFI (2017): BFI-level 1
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Web of Science (2017): Indexed yes
BFI (2016): BFI-level 1
Scopus rating (2016): CiteScore 3.46 SJR 2.055 SNIP 1.535
Web of Science (2016): Impact factor 4.844
Web of Science (2016): Indexed yes
BFI (2015): BFI-level 1
Hydrolytically stable titanium-45

Introduction
Titanium-45, a candidate PET isotope, is under-employed largely because of the challenging aqueous chemistry of Ti(IV). The propensity for hydrolysis of Ti(IV) compounds makes radio-labeling difficult and excludes 45Ti from use in bio-conjugate chemistry. This is unfortunate because the physical characteristics are extremely desirable: 45Ti has a 3 hour half-life, a positron branching ratio of 85%, a low Eβmax of 1.04 MeV, and negligible secondary gamma emission. In terms of isotope production, 45Ti is transmuted from naturally mono-isotopic 45Sc by low energy proton irradiation. The high cross-section and production rates on an unenriched metal foil target contribute to make 45Ti an ideal PET radionuclide.

In order to bring 45Ti to even a preclinical platform, the hydrolytic instability of aqueous Ti(IV) needs to be addressed. Recently, the groups of Edit Tshuva (Hebrew University of Jerusalem) and Thomas Huhn (University of Konstanz) have synthesized several stable Ti(IV) compounds based upon the salan ligand [1,2]. Additionally, these compounds have shown heightened cytotoxicity against HT-29 (human colorectal cancer) cells, amongst others, as compared to traditional metal-based chemotherapeutics such as cisplatin.

The aim of our work has been to produce the radioactive analogue of one of these Ti(IV)-salan compounds, Ti-salan-dipic [2], which has hydro-lytic stability on the order of weeks. Not only will this allow us to shed some light on the still un-known mechanism of antiproliferative action of titanium-based chemotherapeutics, but it will also make progress toward bioconjugate 45Ti PET tracers.

In the current abstract, we present some of the methods we are using to separate 45Ti from irradiated Sc, and subsequent labeling conditions.

Material and Methods
45Ti was produced by proton irradiation of 250μm scandium foils at currents ranging from 10-20μA on a GE PETTrace. In order to increase production rate in the thin foil, an 800μm aluminum degrader was used to take the proton energy down from the nominal 16 MeV. The scandium was cooled by contact to a water-cooled silver plate.

The activated foil was dissolved in 4M HCl, dried under argon at 120 oC, and taken back up in 12M HCl. Here, four (i-iv below) different approaches to removing the Ti from the Sc and labeling were taken with varying success.

Briefly: i. 45Ti was separated on hydroxamate resin, as presented by K. Gagnon [3], only at 12M acid concentration followed by on-column radiolabeling. ii. 45Ti was extracted into 1-octanol [4], stripped with 12M HCl, and used directly for labeling from the organic phase. iii. 45Ti was trapped on a C-18 cartridge that had been pre-loaded with 1-octanol, similar to ion-pairing, and eluted with isopropanol. iv. 45Ti was extracted onto a polystyrene based 1,3 diol resin (RAPP polymers) and labeling commenced on the column.

Radiolabeling was slightly different in each condition, but in general the salan and dipic ligands were added to the 45Ti in pyridine and reacted at elevated temperature (60–100 oC) for several (10–30) minutes. Reaction progression and radiochemical purity were assessed with silica TLC in chloroform : ethyl acetate (1 : 1).

Results and Conclusion
The trap, release, and yields for the four methods listed above are shown in TABLE 1. The best result was with the 1,3 diol resin which had the added advantage of reacting on-column.

Further optimization is underway including a test of a solid supported 1,2 diol, and preclinical imaging with HT-29 xenografts.

We conclude that hydrolytically stable 45Ti com-pounds can be synthesized in high yield, and hope that this advances the radiochemistry and use of 45Ti toward more widespread applications.
Measurement of the shape factor for the β decay of $^{14}\text{O}$

We report results from an experiment designed to test the conserved vector current (CVC) hypothesis by measuring the shape of the β-decay spectrum for the allowed $0^+ \rightarrow 1^+$ ground state decay of $^{14}\text{O}$. Measurements of the spectrum intensity were obtained with a superconducting beta spectrometer and will be reported for positron kinetic energies ranging from 1.9 to 4.0 MeV. After dividing out phase space, Coulomb, and other correction factors, the resulting shape function has a negative slope of several percent per MeV. We define a parameter $a'$, which is essentially a measure of the average slope of the shape function over the energy range of the measurements, and determine its value to be $a' = -0.0290 \pm 0.0008$ (stat.) $\pm 0.0006$ (syst.). The measured slope parameter is in good agreement with predictions from shell model calculations that respect CVC.

General information
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Organisations: Center for Nuclear Technologies, The Hevesy Laboratory, Wittenberg University, University of Wisconsin-Madison
Authors: George, E. (Ekstern), Voytas, P. A. (Ekstern), Severin, G. (Intern), Knutson, L. D. (Ekstern)
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Scopus rating (2017): SNIP 1.29 SJR 1.443
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Scopus rating (2016): CiteScore 2.96 SJR 1.936 SNIP 1.747
Web of Science (2016): Impact factor 3.82
BFI (2015): BFI-level 1
Scopus rating (2015): SJR 1.993 SNIP 1.5 CiteScore 2.52
Web of Science (2015): Impact factor 3.146
Web of Science (2015): Indexed yes
BFI (2014): BFI-level 1
Scopus rating (2014): SJR 2.48 SNIP 1.77 CiteScore 3.25
Web of Science (2014): Impact factor 3.733
Web of Science (2014): Indexed yes
BFI (2013): BFI-level 1
Scopus rating (2013): SJR 2.584 SNIP 1.909 CiteScore 3.7
Web of Science (2013): Impact factor 3.881
ISI indexed (2013): ISI indexed yes
BFI (2012): BFI-level 1
Scopus rating (2012): SJR 2.769 SNIP 1.942 CiteScore 3.31
Web of Science (2012): Impact factor 3.715
ISI indexed (2012): ISI indexed yes
BFI (2011): BFI-level 1
Scopus rating (2011): SJR 2.962 SNIP 2.047 CiteScore 3.44
Positron Emission Tomography Based Analysis of Long-Circulating Cross-Linked Triblock Polymeric Micelles in a U87MG Mouse Xenograft Model and Comparison of DOTA and CB-TE2A as Chelators of Copper-64

Copolymers of ABC-type (PEG-PHEMA-PCMA) architecture were prepared by atom transfer radical polymerization and formulated as micelles with functionalizable primary alcohols in the shell-region (PHEMA-block) to which the metal-ion chelators DOTA or CB-TE2A were conjugated. Using this micelle system we compared the in vivo stabilities of DOTA and CB-TE2A as chelators of 64Cu in micelle nanoparticles. The coumarin polymer (PCMA-block) micelle core was cross-linked by UV irradiation at 2 W/cm² for 30 min. The cross-linked micelles were labeled with 64Cu at room temperature for 2 h (DOTA) or 80 °C for 3 h (CB-TE2A), giving labeling efficiencies of 60–76% (DOTA) and 40–47% (CB-TE2A). 64Cu-micelles were injected into tumor-bearing mice (8 mg/kg) and PET/CT scans were carried out at 1, 22, and 46 h postinjection. The micelles showed good blood stability (T1/2: 20–26 h) and tumor uptake that was comparable with other nanoparticle systems. The DOTA micelles showed a biodistribution similar to the CB-TE2A micelles and the tumor uptake was comparable for both micelle types at 1 h (1.9% ID/g) and 22 h (3.9% ID/g) but diverged at 46 h with 3.6% ID/g (DOTA) and 4.9% ID/g (CB-TE2A). On the basis of our data, we conclude that cross-linked PEG-PHEMA-PCMA micelles have long circulating properties resulting in tumor accumulation and that DOTA and CB-TE2A 64Cu-chelates show similar in vivo stability for the studied micelle system.
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</table>
Preparation of $^{45}$Ti Ti-salan-dipic

We report the carrier-free radiochemical synthesis of a neutral, bio-active, titanium-45 complex, $^{45}$Ti-salan-dipic. In 2012, the Huhn group at Universität Konstanz reported the non-radioactive compound, Ti-salan-dipic, and demonstrated therapeutic efficacy in a xenograft cervical cancer mouse model as well as enhanced in-vitro cytotoxicity over several other titanium-based chemotherapeutics [1]. The mechanism of action for this class of therapeutics is under investigation and the determination of which will be aided by radiotracing and PET with 45Ti.

45Ti was prepared by proton irradiation of natSc foil followed by extraction onto a polystyrene-based diol-resin (RAPP polymers) after dissolution of the foil in 37% HCl. Synthesis proceeded on the column after quenching the residual acidity with pyridine. The ligands, salan and dipic, were added sequentially in pyridine, with the release of the final compound upon ligand exchange to dipic. $^{45}$Ti-salan-dipic was characterized by radio-TLC on silica in 1:1 ethylacetate:chloroform in comparison to the cold compound.

This is a hydrolytically stable, cytotoxic, 45Ti compound. The solid-phase synthesis is robust, and provides opportunity for producing other 45Ti tracers. PET and radiotracer studies with $^{45}$Ti-salan-dipic and other Ti-based cytotoxic compounds will aid in mechanism determination, drug design, and eventually more effective treatment of cancer.

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Web of Science (2017): Indexed yes
BFI (2016): BFI-level 1
Scopus rating (2016): SJR 0.82 SNIP 0.798 CiteScore 2.39
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BFI (2015): BFI-level 1
Scopus rating (2015): SJR 0.76 SNIP 0.884 CiteScore 2.21
Web of Science (2015): Impact factor 2.429
Web of Science (2015): Indexed yes
BFI (2014): BFI-level 1
Scopus rating (2014): SJR 0.946 SNIP 0.959 CiteScore 2.53
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Web of Science (2014): Indexed yes
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Web of Science (2013): Impact factor 2.408
Radiofluorination method

A method of conducting radiofluorination of a substrate, comprising the steps of: (a) contacting an aqueous solution of [18F] fluoride with a polymer supported phosphazene base for sufficient time for trapping of [18F] fluoride on the polymer supported phosphazene base; and (b) contacting a solution of the substrate with the polymer supported phosphazene base having [18F] fluoride trapped thereon obtained in step (a) for sufficient time for a radiofluorination reaction to take place; an apparatus for conducting radiofluorination; use of the apparatus; and an apparatus for production of a dose of a radiotracer for administration to a patient.

General information

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Organisations: Center for Nuclear Technologies, The Hevesy Laboratory
Authors: Zhuravlev, F. (Intern), Ingemann Mathiessen, B. (Intern)
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Publication information

IPC: B01D15/36
Patent number: WO2014020035
Date: 06/02/2014
Priority date: 24/05/2013
Priority number: DK20130000319
Original language: English
Main Research Area: Technical/natural sciences
Publication: Research - peer-review › Conference abstract in journal – Annual report year: 2014
The ground state branch of the β decay of $^{66}$Ga is an allowed Fermi ($0^+ \rightarrow 0^+$) transition with a relatively high $f_t$ value. The large $f_t$ and the isospin-forbidden nature of the transition indicates that the shape of the β spectrum of this branch may be sensitive to higher order contributions to the decay. Two previous measurements of the shape have revealed deviations from an allowed spectrum but disagree about whether the shape factor has a positive or negative slope. As a test of a new iron-free superconducting β spectrometer, we have measured the shape of the ground state branch of the $^{66}$Ga β spectrum above a positron energy of 1.9 MeV. The spectrum is consistent with an allowed shape, with the slope of the shape factor being zero to within $\pm 3 \times 10^{-3}$ per MeV. We have also determined the endpoint energy for the ground state branch to be $4.1535 \pm 0.0003$ (stat.) $\pm 0.0007$ (syst.) MeV, in good agreement with and a factor of 3 more precise than the presently accepted value.
uPAR Targeted Radionuclide Therapy with $^{177}$Lu-DOTA-AE105 Inhibits Dissemination of Metastatic Prostate Cancer

The urokinase-type plasminogen activator receptor (uPAR) is implicated in cancer invasion and metastatic development in prostate cancer and provides therefore an attractive molecular target for both imaging and therapy. In this study, we provide the first in vivo data on an antimetastatic effect of uPAR radionuclide targeted therapy in such lesions and show the potential of uPAR positron emission tomography (PET) imaging for identifying small foci of metastatic cells in a mouse model of disseminating human prostate cancer. Two radiolabeled ligands were generated in high purity and specific activity: a uPAR-targeting probe ($^{177}$Lu-DOTA-AE105) and a nonbinding control ($^{177}$Lu-DOTA-AE105mut). Both uPAR flow cytometry and ELISA confirmed high expression levels of the target uPAR in PC-3M-LUC2.luc cells, and cell binding studies using $^{177}$Lu-DOTA-AE105 resulted in a specific binding with an IC50 value of 100 nM in a competitive binding experiment. In vivo, uPAR targeted radionuclide therapy significantly reduced the number of metastatic lesions in the disseminated metastatic prostate cancer model, when compared to vehicle and nontargeted $^{177}$Lu groups ($p < 0.05$) using bioluminescence imaging. Moreover, we found a significantly longer metastatic-free survival, with 65% of all mice without any disseminated metastatic lesions present at 65 days after first treatment dose ($p = 0.047$). In contrast, only 30% of all mice in the combined control groups treated with $^{177}$Lu-DOTA-AE105mut or vehicle were without metastatic lesions. No treatment-induced toxicity was observed during the study as evaluated by observing animal weight and H&E staining of kidney tissue (dose-limiting organ). Finally, uPAR PET imaging using $^{64}$Cu-DOTA-AE105 detected all small, disseminated metastatic foci when compared with bioluminescence imaging in a cohort of animals during the treatment study. In conclusion, uPAR targeted radiotherapy resulted in a significant reduction in the number of metastatic lesions in a human metastatic prostate cancer model. Furthermore, we have provided the first evidence of the potential for identification of small metastatic lesions using uPAR PET imaging in disseminated prostate cancer, illustrating the promising strategy of uPAR theranostics in prostate cancer.
An in-vivo PET study of DOTA vs. CB-TE2A and the effect of crosslinking using core-crosslinked ny triblock polymeric micelles labeled with Cu-64 in the shell-region

Original language: English

Cancer, Metastases, Urokinase-type plasminogen activator receptor, CD87, Radionuclide therapy, Radiation therapy, Positron emission tomography, Prostate cancer, Theranostics

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Automated Solid-Phase Radiofluorination Using Polymer-Supported Phosphazenes

The polymer supported phosphazene bases PS-P2tBu and the novel PS-P2PEG allowed for efficient extraction of [18F]F− from proton irradiated [18O]H2O and subsequent radiofluorination of a broad range of substrates directly on the resin. The highest radiochemical yields were obtained with aliphatic sulfonates (69%) and bromides (42%); the total radiosynthesis time was 35–45 min. The multivariate analysis showed that the radiochemical yields and purities were controlled by the resin load, reaction temperature, and column packing effects. The resins could be reused several times with the same or different substrates. The fully automated on-column radiofluorination methodology was applied to the radiosynthesis of the important PET radiotracers [18F]FLT and [18F]FDG. The latter was produced with 40% yield on a 120 GBq scale and passed GMP-regulated quality control required for commercial production of [18F]FDG. The combination of compact form factor, simplicity of [18F]F− recovery and processing, and column reusability can make solid phase radiofluorination an attractive radiochemistry platform for the emerging dose-on-demand instruments for bedside production of PET radiotracers.

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Organisations: Center for Nuclear Technologies, The Hevesy Laboratory
Authors: Mathiessen, B. (Intern), Zhuravlev, F. (Intern)
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BFI (2016): BFI-level 1
Scopus rating (2016): CiteScore 3.09 SJR 0.825 SNIP 1.257
Web of Science (2016): Impact factor 2.861
Web of Science (2016): Indexed yes
BFI (2015): BFI-level 1
Scopus rating (2015): SJR 0.57 SNIP 1.164 CiteScore 2.65
Web of Science (2015): Impact factor 2.465
Web of Science (2015): Indexed yes
BFI (2014): BFI-level 1
Scopus rating (2014): SJR 0.738 SNIP 1.3 CiteScore 2.62
Web of Science (2014): Impact factor 2.416
Web of Science (2014): Indexed yes
BFI (2013): BFI-level 1
Co(salen)-mediated enantioselective radiofluorination of epoxides. Radiosynthesis of enantiomerically enriched $[^{18}\text{F}]$-MISO via kinetic resolution

The first example of transition metal mediated enantioselective radiofluorination of epoxides is reported. The procedure utilizes gaseous $[^{18}\text{F}]$HF in a combination with $(-)$-tetramisole and (R,R)-Co(salen), giving the corresponding (S,S)-$^{18}\text{F}$-fluorohydrines in 78–93% radiochemical yield (RCY) and 20–46% enantioselectivities (ee). The use of this methodology allowed for a single step radiosynthesis of $[^{18}\text{F}]$-MISO, which took 1.5h and after solid phase-based purification delivered $[^{18}\text{F}]$-MISO in 81%/45% analytical/preparative RCY and 55% ee.
Dependence of (anomalous) fading of infra-red stimulated luminescence on trap occupancy in feldspars

Dose dependency of anomalous fading of infra-red stimulated luminescence (IRSL) from feldspars has been investigated using radiations of different ionisation qualities. The rate of fading of the IRSL signal after proton irradiation (9.4–30%/decade) is on an average almost twice compared to that after 90Sr/90Y beta particle irradiation (3.5–15%/decade) for all the measured feldspar mineral specimens. Similarly, the fading rates after x-rays of 50 kV and 10 kV fall in between those of beta particle and proton irradiations. Our results suggest that rate of anomalous fading in feldspars depends on the number density of the trapped charge carriers. These results support the hypothesis that anomalous fading occurs across randomly distributed donor-acceptor distances as opposed to pairs with a fixed distance.
Design, Synthesis, and Pharmacological Characterization of N- and O-Substituted 5,6,7,8-Tetrahydro-4H-isoxazolo[4,5-d]azepin-3-ol Analogues: Novel 5-HT2A/5-HT2C Receptor Agonists with Pro-Cognitive Properties

The isoxazol-3-one tautomer of the bicyclic isoxazole, 5,6,7,8-tetrahydro-4H-isoxazolo[4,5-d]azepin-3-ol (THAZ), has previously been shown to be a weak GABAA and glycine receptor antagonist. In the present study, the potential in this scaffold has been explored through the synthesis and pharmacological characterization of a series of N- and O-substituted THAZ analogues. The analogues N-Bn-THAZ (3d) and O-Bn-THAZ (4d) were found to be potent agonists of the human 5-HT2A and 5-HT2C receptors. Judging from an elaborate pharmacological profiling at numerous other CNS targets, the 3d analogue appears to be selective for the two receptors. Administration of 3d substantially improved the cognitive performance of mice in a place recognition Y-maze model, an effect fully reversible by coadministration of the selective 5-HT2C antagonist SB242084. In conclusion, as novel bioavailable cognitive enhancers that most likely mediate their effects through 5-HT2A and/or 5-HT2C receptors, the isoxazoles 3d and 4d constitute interesting leads for further medicinal chemistry development.
ESS Technical Design Report

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Organisations: Center for Nuclear Technologies, Radioecology and Tracer Studies, Department of Physics, Neutrons and X-rays for Materials Physics, The Hevesy Laboratory, Radiation Physics, Department of Energy Conversion and Storage, Atomic scale modelling and materials, European Spallation Source ESS AB, University of London, CEA, Helmholtz-Zentrum Berlin für Materialien und Energie, Paul Scherrer Institute, Linköping University, Technical University of Denmark
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Authors: Revunov, E. V. (Intern), Zhuravlev, F. (Intern)
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BFI (2017): BFI-level 1
Scopus rating (2017): CiteScore 1.35 SJR 0.477 SNIP 0.474
Web of Science (2017): Impact factor 1.423
Web of Science (2017): Indexed yes
BFI (2016): BFI-level 1
Scopus rating (2016): CiteScore 1.65 SJR 0.603 SNIP 0.627
Web of Science (2016): Impact factor 1.745
Web of Science (2016): Indexed yes
BFI (2015): BFI-level 1
Induction of Anti-Tumor Immune Responses by Peptide Receptor Radionuclide Therapy with (177)Lu-DOTATATE in a Murine Model of a Human Neuroendocrine Tumor

Peptide receptor radionuclide therapy (PRRT) is a relatively new mode of internally targeted radiotherapy currently in clinical trials. In PRRT, ionizing radioisotopes conjugated to somatostatin analogues are targeted to neuroendocrine tumors (NETs) via somatostatin receptors. Despite promising clinical results, very little is known about the mechanism of tumor control. By using NCI-H727 cells in an in vivo murine xenograft model of human NETs, we showed that 177Lu-DOTATATE PRRT led to increased infiltration of CD86+ antigen presenting cells into tumor tissue. We also found that following treatment with PRRT, there was significantly increased tumor infiltration by CD49b+/FasL+ NK cells potentially capable of tumor killing. Further investigation into the immunomodulatory effects of PRRT will be essential in improving treatment efficacy.

General information
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Organisations: The Hevesy Laboratory, Center for Nuclear Technologies, Guy's Hospital, University of Copenhagen, Næstved Hospital
Authors: Wu, Y. (Ekstern), Pfeifer, A. K. (Ekstern), Myschetzky, R. (Ekstern), Garbyal, R. S. (Ekstern), Rasmussen, P. (Intern), Knigge, U. (Ekstern), Bzorek, M. (Ekstern), Kristensen, M. H. (Ekstern), Kjær, A. (Intern)
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Scopus rating (2017): SNIP 0.788 SJR 0.669 CiteScore 2.43
Web of Science (2017): Indexed yes
Scopus rating (2016): SNIP 0.539 SJR 0.453
Scopus rating (2015): SNIP 0.147 SJR 0.206
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Web of Science (2013): Indexed yes
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Source: FindIt
Source-ID: 247936530
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Introduction to DTU Nutech – Center for Nuclear Technologies

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Authors: Lynov, J. (Intern)
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Original language: English
Main Research Area: Technical/natural sciences
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Labeling of gold nanoparticles with Cu-64 and Zr-89 for combined CT/PET-imaging

General information
State: Published
Organisations: Center for Nuclear Technologies, The Hevesy Laboratory, Department of Micro- and Nanotechnology, Colloids and Biological Interfaces
Authors: Frellsen, A. F. (Intern), Jolck, R. I. (Ekstern), Andresen, T. L. (Intern), Rasmussen, P. (Intern)
New Synthesis and Tritium Labeling of a Selective Ligand for Studying High-Affinity γ-Hydroxybutyrate (GHB) Binding Sites

3-Hydroxycyclopent-1-enecarboxylic acid (HOCPCA, 1) is a potent ligand for the high-affinity GHB binding sites in the CNS. An improved synthesis of 1 together with a very efficient synthesis of [3H]-1 is described. The radiosynthesis employs in situ generated lithium trimethoxyborotritide. Screening of 1 against different CNS targets establishes a high selectivity, and we demonstrate in vivo brain penetration. In vitro characterization of [3H]-1 binding shows high specificity to the high-affinity GHB binding sites.

General information
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Organisations: The Hevesy Laboratory, Center for Nuclear Technologies, H. Lundbeck A/S, University of Copenhagen
Authors: Vogensen, S. B. (Forskerdatabase), Marek, A. (Intern), Bay, T. (Forskerdatabase), Wellendorph, P. (Forskerdatabase), Kehler, J. (Forskerdatabase), Bundgaard, C. (Forskerdatabase), Frølund, B. (Forskerdatabase), Pedersen, M. H. F. (Intern), Clausen, R. P. (Forskerdatabase)
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BFI (2017): BFI-level 2
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Web of Science (2017): Indexed yes
BFI (2016): BFI-level 2
Scopus rating (2016): CiteScore 6.06
Web of Science (2016): Impact factor 6.259
BFI (2015): BFI-level 2
Scopus rating (2015): SJR 2.529 SNIP 1.631 CiteScore 5.66
Web of Science (2015): Impact factor 5.589
Web of Science (2015): Indexed yes
BFI (2014): BFI-level 2
Scopus rating (2014): SJR 2.259 SNIP 1.693 CiteScore 5.55
Web of Science (2014): Impact factor 5.447
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Scopus rating (2013): SJR 2.293 SNIP 1.78 CiteScore 5.65
Web of Science (2013): Impact factor 5.48
ISI indexed (2013): ISI indexed yes
Web of Science (2013): Indexed yes
BFI (2012): BFI-level 2
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Web of Science (2012): Impact factor 5.614
Non-targeted effects of ionising radiation—Implications for low dose risk

Non-DNA targeted effects of ionising radiation, which include genomic instability, and a variety of bystander effects including abscopal effects and bystander mediated adaptive response, have raised concerns about the magnitude of low-dose radiation risk. Genomic instability, bystander effects and adaptive responses are powered by fundamental, but not clearly understood systems that maintain tissue homeostasis. Despite excellent research in this field by various groups, there are still gaps in our understanding of the likely mechanisms associated with non-DNA targeted effects, particularly with respect to systemic (human health) consequences at low and intermediate doses of ionising radiation. Other outstanding questions include links between the different non-targeted responses and the variations in response observed between individuals and cell lines, possibly a function of genetic background. Furthermore, it is still not known what the initial target and early interactions in cells are that give rise to non-targeted responses in neighbouring or descendant cells. This paper provides a commentary on the current state of the field as a result of the non-targeted effects of ionising radiation (NOTE) Integrated Project funded by the European Union. Here we critically examine the evidence for non-targeted effects, discuss apparently contradictory results and consider implications for low-dose radiation health effects. © 2012 Elsevier B.V. All rights reserved.

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Authors: Kadhim, M. (Ekstern), Salomaa, S. (Ekstern), Wright, E. (Ekstern), Hildebrandt, G. (Ekstern), Belyakov, O. V. (Intern), Prise, K. M. (Ekstern), Little, M. P. (Ekstern)
Pages: 84–98
Publication date: 2013
Main Research Area: Technical/natural sciences
Radionuclides for nuclear medicine: a nuclear physicists’ view

NuPECC (the Nuclear Physics European Collaboration Committee, an expert committee of the European Science Foundation) has the mission to strengthen European Collaboration in nuclear science through the promotion of nuclear physics and its trans-disciplinary use and application. NuPECC is currently working on a report on “Nuclear Physics for Medicine” and has set up a working group to review the present status and prospects of radionuclides for nuclear medicine. An interim report will be presented to seek comments and constructive input from EANM members. In particular it is investigated how nuclear physics Methods and nuclear physics facilities are supporting the development and supply of medical radionuclides and how this support could be further strengthened in future.

Aspects that will be addressed: • In recent years, the reactor-based supply chain of 99Mo/99mTc generators was repeatedly challenged by unforeseen outages. This triggered the proposition and development of complementary accelerator-based production Methods of 99mTc. Long-term prospects for 99mTc supply in Europe will be discussed. • The emergence of new applications as well as rising costs and regulations for radioactive transport of individual doses lead to a renewed interest in radionuclide generators such as 68Ge/68Ga, 82Sr/82Rb or even 44Ti/44Sc. For long time such generator nuclides were mainly produced at non-European accelerators (BNL, LANL, TRIUMF, iThemba Labs) that are mainly devoted to support nuclear physics facilities. The recent addition of ARRONAX, a dedicated production facility in Nantes, France, and the upcoming inauguration of a 70 MeV cyclotron at the nuclear physics facility SPES at Legnaro, Italy will greatly improve Europe’s production capabilities of these nuclides. • Ongoing accelerator R&D for new nuclear physics facilities led to improved technologies for linear accelerators which could in future be used for providing intense beams of alpha particles costefficiently, thus facilitating access to nuclides such as 211At, 43Sc, 67Cu, etc. • The evaluation of trends in radionuclide demand requires reliable statistical data. The working group is promoting the collection of data on the production and use of medical radionuclides in European countries. Trends and prospects, in particular for non-conventional radionuclides will be discussed. • Nuclear medicine departments interested in using or performing research with non-conventional radionuclides are sometimes faced with the problem of identifying an adequate supplier since many of these nuclides are not yet commercially available. The working group is preparing a database of regular and potential producers of emerging radionuclides such as 64Cu, 67Cu, 44Sc, 89Zr, 211At, etc. in Europe.
Szilard-Chalmers effect in DOTA-bound Sc-44m

General information
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Organisations: Center for Nuclear Technologies, The Hevesy Laboratory
Authors: Severin, G. (Intern), Munch, M. (Intern), Jensen, M. (Intern)
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Main Research Area: Technical/natural sciences

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Volume: 56
Article number: P133
An after-market, five-port vertical beam line extension for the PETtrace

Most commercial cyclotrons intended for medical isotope production provide a limited number of beam ports crowded into a minimal vault space. Taking advantage of our new lab construction, we planned and installed a beam-line on port #2 of our GEMS PETtrace to bring beam to an additional 5 target positions. These are oriented in the vertical plane, with the downward directed beam well suited for molten target substrates.

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Organisations: Center for Nuclear Technologies, The Hevesy Laboratory, University of Wisconsin-Madison, Los Alamos National Laboratory
Authors: Barnhart, T. E. (Ekstern), Engle, J. W. (Ekstern), Severin, G. (Intern), Valdovinos, H. F. (Ekstern), Gagnon, K. (Ekstern), Nickles, R. J. (Ekstern)
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Web of Science (2017): Indexed yes
BFI (2016): BFI-level 1
Scopus rating (2016): CiteScore 0.21 SJR 0.165 SNIP 0.246
BFI (2015): BFI-level 1
Scopus rating (2015): SJR 0.18 SNIP 0.218 CiteScore 0.18
BFI (2014): BFI-level 1
Scopus rating (2014): SJR 0.171 SNIP 0.202 CiteScore 0.17
BFI (2013): BFI-level 1
Scopus rating (2013): SJR 0.164 SNIP 0.187 CiteScore 0.16
ISI indexed (2013): ISI indexed no
BFI (2012): BFI-level 1
Scopus rating (2012): SJR 0.176 SNIP 0.193 CiteScore 0.14
ISI indexed (2012): ISI indexed no
BFI (2011): BFI-level 1
Scopus rating (2011): SJR 0.161 SNIP 0.16 CiteScore 0.12
ISI indexed (2011): ISI indexed no
Web of Science (2011): Indexed yes
BFI (2010): BFI-level 1
Scopus rating (2010): SJR 0.166 SNIP 0.158
BFI (2009): BFI-level 1
Scopus rating (2009): SJR 0.163 SNIP 0.156
BFI (2008): BFI-level 1
Scopus rating (2008): SJR 0.17 SNIP 0.132
Web of Science (2008): Indexed yes
Scopus rating (2007): SJR 0.171 SNIP 0.176
Scopus rating (2006): SJR 0.184 SNIP 0.187
Scopus rating (2005): SJR 0.217 SNIP 0.416
Scopus rating (2004): SJR 0.198 SNIP 0.249
Clinical PET of Neuroendocrine Tumors Using $^{64}$Cu-DOTATATE: First-in-Humans Study

The use of positron emitter–labeled compounds for somatostatin receptor imaging (SRI) has become attractive because of the prospect of improved spatial resolution, accelerated imaging procedures, and the ability to quantify tissue radioactivity concentrations. This paper provides results from first-in-humans use of $^{64}$Cu-DOTATATE, an avidly binding somatostatin receptor ligand linked to a radioisotope with intermediate half-life and favorable positron energy (half-life, 12.7 h; maximum positron energy, 0.653 MeV).

Methods: In a prospective setup, 14 patients with a history of neuroendocrine tumors underwent both PET/CT with $^{64}$Cu-DOTATATE and SPECT/CT with our current routine imaging agent $^{111}$In-diethylenetriaminepentaacetic acid–octreotide. After intravenous injection of 193–232 MBq of $^{64}$Cu-DOTATATE, whole-body PET scans were acquired at 1 h ($n = 14$), 3 h ($n = 12$), and 24 h ($n = 5$) after administration. Tissue radioactivity concentrations for normal organs and lesions were quantified, and standardized uptake values were calculated for the early (1 h) and delayed (3 h) scans. Using the data for 5 patients, we assessed the radiation dose with OLINDA/EXM software. Furthermore, the clinical performance of $^{64}$Cu-DOTATATE with respect to lesion detection was compared with conventional SRI. Results: SRI with $^{64}$Cu-DOTATATE produced images of excellent quality and high spatial resolution. Images were characterized by high and stable tumor-to-background ratios over an imaging time window of at least 3 h. Compared with conventional scintigraphy, $^{64}$Cu-DOTATATE PET identified additional lesions in 6 of 14 patients (43%). In 5 patients, lesions were localized in organs and organ systems not previously known as metastatic sites, including the early-stage detection of a secondary neuroendocrine tumor in a patient with a known mutation in the multiple endocrine neoplasia type I gene. All major additional findings seen only on PET could be confirmed on the basis of a clinical follow-up interval of 18 mo. Calculated radiation dose estimates yielded an effective dose of 6.3 mSv for an injected activity of 200 MBq of $^{64}$Cu-DOTATATE, with the liver being the organ with the highest absorbed radiation dose (0.16 mGy/MBq).

Conclusion: This first-in-humans study supports the clinical use of $^{64}$Cu-DOTATATE for SRI with excellent imaging quality, reduced radiation burden, and increased lesion detection rate when compared with $^{111}$In-diethylenetriaminepentaacetic acid–octreotide.
Dural mast cell degranulation is a putative mechanism for headache induced by PACAP-38

BACKGROUND: Pituitary adenylate cyclase activating peptide-38 (PACAP-38) has been shown to induce migraine in migraineurs, whereas the related peptide vasoactive intestinal peptide (VIP) does not. In the present study we examine the hypothesis that PACAP-38 and its truncated version PACAP-27 but not VIP cause degranulation of mast cells in...
peritoneum and in dura mater. METHODS: The degranulatory effects of PACAP-38, PACAP-27 and VIP were investigated by measuring the amount of N-acetyl-β-hexosaminidase released from isolated peritoneal mast cells and from dura mater attached to the skull of the rat in vitro. In peritoneal mast cells N-truncated fragments of PACAP-38 (PACAP(6–38), PACAP(16–38) and PACAP(28–38)) were also studied. To investigate transduction pathways involved in mast cell degranulation induced by PACAP-38, PACAP-27 and VIP, the phospholipase C inhibitor U-73122 and the adenylate cyclase inhibitor SQ 22536 were used. RESULTS: The peptides induced degranulation of isolated peritoneal mast cells of the rat with the following order of potency: PACAP-38 = PACAP(6–38) = PACAP(16–38) » PACAP-27 = VIP = PACAP(28–38). In the dura mater we found that 10–5 M PACAP-38 was significantly more potent in inducing mast cell degranulation than the same concentration of PACAP-27 or VIP. Inhibition of intracellular mechanisms demonstrated that PACAP-38-induced degranulation is mediated by the phospholipase C pathway. Selective blockade of the PAC1 receptor did not attenuate degranulation. CONCLUSION: These findings correlate with clinical studies and support the hypothesis that mast cell degranulation is involved in PACAP-induced migraine. PACAP-38 has a much stronger degranulatory effect on rat peritoneal and dural mast cells than VIP and PACAP-27. The difference in potency between PACAP-38- and PACAP-27/VIP-induced peritoneal mast cell degranulation is probably not related to the PAC1 receptor but is caused by a difference in efficacy on phospholipase C.
Entrapment of Radionuclides in Nanoparticle Compositions

The present invention is directed to the technical field of imaging compositions useful for diagnosing cancer and other diseases in a subject. In particular, the invention relates to a class of diagnostic compounds comprising a novel liposome composition with encapsulated metal entities such as radionuclides, for example 61Cu and 64Cu copper isotopes. The invention further relates to a novel method for loading delivery systems, such as liposome compositions, with metal entities such as radionuclides, and the use of liposomes for targeted diagnosis and treatment of a target site, such as cancerous tissue and, in general, pathological conditions associated with leaky blood vessels. The present invention provides a new diagnostic tool for the utilization of positron emission tomography (PET) imaging technique.

Flexible, durable proton energy degraders for the GE PETtrace

In order to limit the formation of radionuclotopic impurities during proton bombardments of solid targets, two methods of introducing degrader foils into the beam upstream of the target were tested. The first design uses a 445 μm thick fixed degrader machined from a single piece of aluminum. The second design permits introduction of foils made of any material and was tested with foils as thick as 635 μm (also aluminium). In both cases, the foils are cooled with by water flowing through an annular channel outside the radius of the beam. Both designs proved durable and tolerated proton beam currents in excess of 80 μA.
Improved methods to determine radionuclidic purity of F-18 compounds

Current revisions of monographs for F-18 pharmaceuticals in the European Pharmacopoeia (Ph. Eur.) (Ph. Eur., 2011) call for a radionuclidic purity (RNP) of or better than 99.9%. However, the current method is not sufficient nor effective for testing this required RNP level. We present a theoretical model leading to a practical procedure for a simple test of RNP for F-18 compounds that tells whether or not the sample is pure with a statistical confidence of 97.5% (P=0.975). (C) 2011 Elsevier Ltd. All rights reserved.

General information
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New peptide receptor radionuclide therapy of invasive cancer cells: in vivo studies using $^{177}$Lu-DOTA-AE105 targeting uPAR in human colorectal cancer xenografts

The proposition of uPAR as a potential target in cancer therapy is advanced by its predominant expression at the invasive front of colorectal cancer (CRC) and its value as prognostic biomarker for poor survival in this disease. In this study, we provide the first in vivo proof-of-concept for a theranostic approach as treatment modality in a human xenograft colorectal cancer model. Methods A DOTA-conjugated 9-mer high affinity uPAR binding peptide (DOTA-AE105) was radiolabeled with $^{64}$Cu and $^{177}$Lu, for PET imaging and targeted radionuclide therapy study, respectively. Human uPAR-positive CRC HT-29 cells were inoculated in Nude mice and treated with $^{177}$Lu-DOTA-AE105 once a visible tumor had formed. To evaluate the true effect of the targeted radiotherapy, two controls groups were included in this study, one receiving a $^{177}$Lu-labeled non-binding control peptide and one receiving vehicle. All animals were treated day 0 and 7. A parallel $^{18}$F-FLT PET/CT study was performed on day 0, 1, 3 and 6. Dosimetry calculations were based on a biodistribution study, where organs and tissue of interest were collected 0.5, 1.0, 2.0, 4.0 and 24h post injection of $^{177}$Lu-DOTA-AE105. Toxicity was assessed by recording mouse weight and by H&E staining of kidneys in each treatment group. Results uPAR-positive HT-29 xenograft was clearly visualized by PET/CT imaging using $^{64}$Cu-DOTA-AE105. Subsequently, these xenograft transplants were locally irradiated using $^{177}$Lu-DOTA-AE105, where a significant effect on tumor size and the number of uPAR-positive cells in the tumor was found ($p < 0.05$). A histological examination of the kidneys from one animal in each treatment group did not reveal any gross abnormalities and the general performance of all treated animals also showed no indications of radioactivity-induced toxicity. Conclusion: These findings document for the first time the in vivo efficacy of an uPAR-targeted radionuclide therapeutic intervention on both tumor size and its content of uPAR expressing cells thus setting the stage for future translation into clinical use. © 2012 Elsevier Inc. All rights reserved.
Particle Accelerators for PET radionuclides

The requirements set for particle accelerators for production of radioactive isotopes for PET can easily be derived from first principles. The simple general need is for proton beams with energy in the region 10–20 MeV and current 20–100 microAmps. This is most reliably and cost-effectively achieved by the well proven technology of the compact medical cyclotron, presently available from several companies. The main features of these cyclotrons are essential similar: resistive, sector focused iron magnets, internal negative ion sources and stripping extraction. The remaining differences between different manufacturers will be discussed the light of what is actually needed for a given PET site operation. Alternatives to the conventional cyclotron have been proposed and tested but have at present very limited use. These alternatives will be discussed, as well as the future possibilities of supplying point of demand tracer production with very small cyclotrons of energy well below 10 MeV. The authors best advice at present for new PET sites is to negotiate for conventional cyclotron solutions from experienced manufacturers. It is the combined performance of cyclotron and target in terms of available activity output and the specific activity that is the real figures of merit and it is recommended that cyclotron solutions are weighted according to this and that acceptance tests are set up to realistically evaluate the routine availability of this output.

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PET imaging of liposomes labeled with an $^{18}$F-fluorocholesteryl ether probe prepared by automated radiosynthesis

A novel $^{18}$F-labeled cholesteryl ether lipid probe was prepared by synthesis of the corresponding mesylate, which was $^{18}$F-fluorinated by a $^{18}$KF, Kryptofix-222, K$_2$CO$_3$ procedure. Fluorination was done for 10 minutes at 165 degrees C and took place with conversion between 3 and 17%, depending on conditions. Radiolabelling of the probe and subsequent in situ purification on SEP-Paks were done on a custom-built, fully automatic synthesis robot. Long-circulating liposomes were prepared by hydration (magnetic stirring) of a lipid film containing the radiolabeled probe, followed by fully automated extrusion through 100-nm filters. The $^{18}$F-labeled liposomes were injected into nude, tumor-bearing mice, and positron emission tomography (PET) scans were performed several times over 8 hours to investigate the in vivo biodistribution. Clear tumor accumulation, as well as hepatic and splenic uptake, was observed, corresponding to expected liposomal pharmacokinetics. The tumor accumulation 8 hours postinjection accounted for 2.25 +/- 0.23 (mean +/- standard error of the mean) percent of injected dose per gram (%ID/g), and the tumor-to-muscle ratio reached 2.20 +/- 0.24 after 8 hours, which is satisfactorily high for visualization of pathological lesions. Moreover, the blood concentration was still at a high level (13.9 +/- 1.5 %ID/g) at the end of the 8-hour time frame. The present work demonstrates the methodology for automated preparation of radiolabeled liposomes, and shows that $^{18}$F-labeled liposomes could be suitable as a methodology for visualization of tumors and obtaining short-term pharmacokinetics in vivo.
tumor Neoplasms (MeSH) neoplastic disease, Rodentia Mammalia Vertebrata Chordata Animalia (Animals, Chordates, Mammals, Nonhuman Vertebrates, Nonhuman Mammals, Rodents, Vertebrates) - Muridae [86375] mouse common, 10-cholesteryloxy-1-[fluorine-18]fluoro-decanol diagnostic-drug pharmacokinetics, [fluorine-18]-fluorocholesteryl ether probe, fluorine-18-labeled cholesteryl ether diagnostic-drug pharmacokinetics, Kryptofix-222 23978-09-8, liposome, potassium carbonate 584-08-7, 10511, Biophysics - Bioengineering, 12504, Pathology - Diagnostic, 12512, Pathology - Therapy, 14004, Digestive system - Physiology and biochemistry, 15002, Blood - Blood and lymph studies, 15004, Blood - Blood cell studies, 22002, Pharmacology - General, 24003, Neoplasms - Immunology, 24004, Neoplasms - Pathology, clinical aspects and systemic effects, 34502, Immunology - General and methods, 34508, Immunology - Immunopathology, tissue immunology, Pharmacology, liver digestive system, spleen immune system, blood and lymphatics, automated radiosynthesis method laboratory techniques, custom-built fully automatic synthesis robot laboratory equipment, magnetic stirring method laboratory techniques, positron emission tomography imaging PET imaging imaging and microscopy techniques, diagnostic techniques, Biomaterials, Methods and Techniques, Pharmaceuticals, Tumor Biology DOIs:

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Positron emission tomography evaluation of somatostatin receptor targeted (64)Cu-TATE-liposomes in a human neuroendocrine carcinoma mouse model.

Targeted therapeutic and diagnostic nanocarriers functionalized with antibodies, peptides or other targeting ligands that recognize over-expressed receptors or antigens on tumor cells have potential in the diagnosis and therapy of cancer. Somatostatin receptors (SSTRs) are over-expressed in a variety of cancers, particularly neuroendocrine tumors (NETs) and can be targeted with somatostatin peptide analogs such as octreotate (TATE). In the present study we investigate liposomes that target SSTR in a NET xenograft mouse model (NCI-H727) by use of TATE. TATE was covalently attached to the distal end of DSPE-PEG(2000) on PEGylated liposomes with an encapsulated positron emitter (64)Cu that can be utilized for positron emission tomography (PET) imaging. The biodistribution and pharmacokinetics of the (64)Cu-loaded PEGylated liposomes with and without TATE was investigated and their ability to image NETs was evaluated using PET. Additionally, the liposome accumulation and imaging capability was compared with free radiolabelled TATE peptide
administered as (64)Cu-DOTA-TATE. The presence of TATE on the liposomes resulted in a significantly faster initial blood clearance in comparison to control-liposomes without TATE. PEGylated liposomes with or without TATE accumulated at significantly higher quantities in NETs (5.1±0.3 and 5.8±0.2 %ID/g, respectively) than the free peptide (64)Cu-DOTA-TATE (1.4±0.3 %ID/g) 24h post-injection. Importantly, (64)Cu-loaded PEGylated liposomes with TATE showed significantly higher tumor-to-muscle (T/M) ratio (12.7±1.0) than the control-liposomes without TATE (8.9±0.9) and the (64)Cu-DOTA-TATE free peptide (7.2±0.3). The higher T/M ratio of the PEGylated liposomes with TATE suggests some advantage of active targeting of NETs, although no absolute benefit in tumor accumulation over the non-targeted liposomes was observed. Collectively, these data showed that (64)Cu-loaded PEGylated liposomes with TATE conjugated to the surface could be promising new imaging agents for visualizing tumor tissue and especially NETs using PET.
Prompt radiation detectors to monitor target conditions

Lessons learned by basic scientists in the study of experimental nuclear physics can often go unnoticed by cyclotron operator's intent on meeting a demanding schedule of tracer production. Prompt neutrons and gammas are the signature that the desired reaction is occurring, providing a robust measure of the expected yield.

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Radiolabeling of liposomes and polymeric micelles with PET-isotopes

This thesis is divided into three separate chapters that can be read independently. Chapter 1 is a general introduction, touching upon liposomes and polymeric micelles and radiolabeling with 18F and 64Cu. Chapter 2 and 3 address two separate research projects, each described below. A complete reference list is compiled in the end, immediately after the three chapters. This is followed by the supplementary information, divided into appropriate sections. Finally, the two first-authored manuscripts are attached as appendices.

Chapter 1. The field of nanoparticulate drug delivery has been hailed as a revolution in modern therapeutics, especially in chemotherapy. A major reason is the ability of nanoparticles to accumulate in tumor tissue. Liposomes are the classic nanoparticle, consisting of a lipid membrane with an aqueous core. Polymeric micelles are made from amphiphilic detergent-like copolymers, that self-assemble in water. Therapy with nanoparticles is hampered by often poor tumor accumulation, combined with massive uptake by macrophages in the liver and spleen. For this reason, visualizing nanoparticle pharmacokinetics in-vivo is a valuable tool in the on-going research. Such visualization can be done by labeling with radio isotopes. Isotopes that emit positrons (PET-isotopes) can be detected by PET (positron emission tomography) technology, an accurate technique that has gained popularity in recent years. PET-isotopes of interest include 18F and 64Cu. In addition to being a research tool, radiolabeled nanoparticles hold promise as a radiopharmaceutical in themselves, as a means of imaging tumor tissue, aiding in diagnosis and surgery.

Chapter 2. A method for labeling liposomes with 18F (97% positron decay, $T_1/2 = 110$ min) was investigated. 18F is widely available, but is hampered by a short half-life only allowing up to 8 hours scans. 18F must be covalently attached to components of the liposome. By binding to a lipid, it can be stably lodged in the membrane. A glycerolipid and a cholesteryl ether were synthesized with free primary alcohols and a series of their sulphonates (Ms, Ts, Tf) were prepared.
Radiofluorination of these substrates was performed on fully automated equipment using a classic Kryptofix222-mediated procedure in DMSO. Yields were poor, 3-17% depending on conditions. The [18F]fluorinated probes were purified in-situ on SEP-Paks. The cholesteryl ether mesylate performed best. This substrate was radiolabeled and formulated in long-circulating liposomes by drying the probe and the lipids together, followed by hydration by magnetic stirring. The liposomes were extruded through 100 nm filter on fully automated equipment. Animal studies were done in tumor-bearing mice, and PET-scans were performed over 8 hours. Clear tumor uptake, as well as hepatic and splenic uptake, was observed, corresponding to expected liposomal pharmacokinetics. Tumor uptake was quantifiable (tumor-to-muscle ratio at 8 h: 2.20), showing that the maximum scan duration with 18F is sufficient for visualizing tumor tissue. Because of the low [18F]radiofluorination yields obtained, we investigated ways of labeling lipophilic substrates in nonpolar solvents. This involved the transfer of [18]HF gas from a solution of concentrated sulphuric acid into a receiving vial containing the substrate in toluene. A phosphazene base was present to bind [18]HF and mediate fluorination. This procedure made it possible to fluorinate highly lipophilic substrates in 71% yields.

Chapter 3. Radiolabeling of polymeric micelles with 64Cu (18% positron decay, T½ = 12.7 h) was investigated. 64Cu allows longer scans (up to 48 hours), which mirrors the duration of nanoparticle pharmacokinetics. It is a metal and must be attached to polymeric micelles by covalently conjugated chelators. DOTA and CB-TE2A are two such chelators, but DOTA is widely believed to be unstable in-vivo. DOTA and CB-TE2A were conjugated to triblock polymeric micelles in the shellregion. Here, they were thought to be shielded by the outer PEG-layer. The micelles were crosslinked in their coumarin-containing cores by exposure to UV light. Subsequently, the micelles were labeled with 64Cu, followed by removal of unspecifically bound 64Cu by EDTA. Good labeling efficiency was achieved with both chelators (40-70%). Some of the prepared micelles were found to exhibit gross instabilities, especially with raised temperature, which prevented their in-vivo use. Other micelles were stable and were investigated in xenografted mice. These micelles were 20-45 nm. They showed good tumor uptake (4-5 %ID/g, 48h) and limited uptake in liver (5-7 %ID/g, 48h) and spleen (3-6 %ID/g, 48h). It was concluded that there did not seem to be a significant difference between DOTA and CB-TE2A in-vivo. In addition, crosslinked micelles (with 64Cu bound to CB-TE2A) were compared with non-crosslinked micelles. To our surprise, we found that the non-crosslinked micelles exhibited good stability in circulation and obtained a biodistribution very similar to the crosslinked micelles.

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Organisations: Department of Micro- and Nanotechnology, Center for Nuclear Technologies, The Hevesy Laboratory, Colloids and Biological Interfaces
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44gSc from metal calcium targets for PET
A low-cost and efficient method for producing pre-clinical scale quantities of 44gSc is presented. Production involves proton irradiation of natural unenriched calcium metal followed by rapid separation of radioscandium from the target using hydroxamate functionalized resin.© 2012 American Institute of Physics

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As an attractive radionuclide for positron emission tomography, this study explores the extraction and reactivity of $^{45}$Ti produced via the $^{44}$Sc(p,n)$^{45}$Ti reaction on a GE PETtrace. Using a small hydroxamate column, we have demonstrated an overall recovery of >50% of $^{45}$Ti in ~1 mL of 1M oxalic acid. Conditions for reacting with desferal were also explored, with effective specific activities up to 38 GBq/μmol obtained.
Tritium labelling of peptides using synthetic incorporated diiodinated tyrosine amino acid residues as precursor

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Electronic versions:
Tritium_labelling_of_peptides.pdf
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Loading technique for preparing radionuclide containing nanoparticles
Source: US2012213698A The present invention relates to a novel composition and method for loading delivery systems such as liposome compositions with radionuclides useful in targeted diagnostic and/or therapy of target site, such as cancerous tissue and, in general, pathological conditions associated with leaky blood vessels. The composition and methods of the invention find particular use in diagnosing and imaging cancerous tissue and, in general, pathological conditions associated with leaky blood vessels in a subject. The present invention provides a new diagnostic tool for the utilization of positron emission tomography (PET) imaging technique. One specific aspect of the invention is directed to a method of producing nanoparticles with desired targeting properties for diagnostic and/or radio-therapeutic applications.

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Teaching the physics of medical imaging: an active learning approach involving imaging of biological tissue
Introduction to medical imaging is an experimentally oriented course in the physics of medical imaging, where the students record, process and analyse 3D data of an unknown piece of formalin fixed animal tissue embedded in agar in order to estimate the tissue types present. Planar X-ray, CT, MRI, ultrasound and SPECT/PET images are recorded, showing the tissue in very different ways. In order for the students to estimate the tissue type, they need to study the physical principles of the imaging modalities. The “true” answer is subsequently revealed by slicing the tissue.

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Center for Nuclear Technologies

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Activity: Talks and presentations › Conference presentations

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