Guest Edited Collection: Radioisotopes and radiochemistry in health science

Michael E. Fassbender

Radioisotopes can be produced artificially from stable nuclei through the interaction with particles or highly energetic photons. In combination with modern detection and counting techniques, radioisotopes and radiochemical methods uniquely contribute to the health sciences. This Collection showcases salient aspects of medical radioisotope science ranging from the production, recovery and purification of radioisotopes to the methods used to attach them to biomolecules. The Collection also presents studies that highlight the importance of radiochemistry in the assessment of environmental radioactivity.

The discovery of radioactivity dates back to the year 1896, when Antoine Henri Becquerel, now the eponym of the SI unit to quantify radioactive decay rate, first described the phenomenon of a mysterious penetrating radiation originating from uranium salt. This radiation was able to produce an image on a photographic plate. Radioactivity is a process where an unstable nucleus undergoes conversion to a different -energetically more favorable- nucleus, accompanied by the release of energy in the form of particles and photons.

The relationship between radioactivity and human health perception has been a bumpy ride. The radioactive element radium (half-life 1600 y) that was discovered in the year 1898 by Polish-French radiochemist Marie Sklodowska-Curie, the graduate student of Becquerel who would later earn herself the honour of becoming the first female Nobel prize laureate, was initially regarded as a harmless, even health-boosting natural agent. A few milligrams of radium chloride could be recovered from one metric ton of uranium ore through tedious radiochemical efforts. Grossly underestimating the hazards, radium was made a component of self-luminous paints; it was also the subject of flourishing radioactive quackery.

A later discovery, for which German radiochemist Otto Hahn received the Nobel Prize in the year 1944, ushered civilization into the “nuclear age”. Hahn –initially unknowingly- provided the radiochemical proof of barium as a product of neutron bombardment of uranium, which signalled the existence of a thitherto-unknown phenomenon: nuclear fission. Nuclear fission could be harnessed as a source of energy, but the wide range of unstable fission products associate it with quasi everlasting environmental impact -highly geochemically mobile isotopes- and dangerous levels of radioactivity.

Decades later there was the “Chernobyl disaster”. Still a high schooler in Cold-War era West Germany, I vividly recall the news streaming in that stoked the populace's fears of radioactivity like no other event before. And the event on April 26, 1986, made us Europeans think twice about what produce to eat and to better ask where it came from. Children were barred from entering playgrounds; the time span “eight days”, the half-life of volatile fission product 131I, kept circulating in people's heads. The “Chernobyl” and “Fukushima” disasters are certainly entries in the history annals of nuclear science and technology that bear witness to the blight of radioactivity.

The blessings of radioactivity, on the other hand, became apparent from the work of another radiochemist and Nobel Prize laureate, George de Hevesy. Hevesy pioneered the concept of radioactive tracers to study biological processes in vivo, and he is widely regarded as the “father of modern nuclear medicine”. Other sources name the Donner Laboratory at the University of California, Berkley, the “birthplace of nuclear medicine” and rather ascribe nuclear fatherhood to John Lawrence. The discovery of several well-known medical isotopes was claimed by the Donner Laboratory, including 14C, 18F, 15O and 201Tl. Also among them was “an isotope with a half-life of about one week”, as personally requested by Joseph G. Hamilton from Glenn T. Seaborg (1951 Chemistry Nobelist) for use in certain thyroid studies. Iodine-131 (half-life 8.0 d) was Seaborg’s legendary answer to his request, produced at Berkeley via deuteron irradiation of tellurium. The first use of 131I to treat hypothyroidism in humans was reported by Saul Hertz on January 1st, 1941, and a series of treatment studies was published in...
May 1946. Ironically, the later “Chernobyl scare” 111 had become the first U.S. Food and Drug Administration approved radiopharmaceutical in 1951. 11 Seaborg – along with Emilio Segré – also isolated metastable 99mTc (half-life 6.0 h) for the first time. 112 This isotope has become an invaluable tool for single photon computer tomography (SPECT). The last radioisotopes to mention in my almost chaotic introductory narrative are alpha emitters 222Ra and 212Ra 113 (half-lives 11.4 d and 3.7 d), thereby taking the reader’s attention back to the element that Madame Curie discovered. One of them, 222Ra, has recently become a U.S. FDA approved pharmaceutical for the treatment of bone metastases.

Collection Overview

As the ‘Radioisotopes and radiochemistry in health science’ Collection launches, applications of short-lived positron emitter fluorine-18 (half-life 109.8 min) naturally find the strongest representation. Certainly due to fluorine’s ability to rapidly form extremely stable F-C bonds via nucleophilic or electrophilic fluorination of organic molecules, 18F is undisputedly the most widely used positron emission tomography (PET) labelling agent. Advances in 18F labelling chemistry also shed light on the more fundamental chemistry of this most reactive halogen. For instance, a new route to [18F]fluoroform has been demonstrated, 19 where the trifluoromethyl synthon is formed in the gas phase by passing [18F]fluoromethane over heated COF3, one of the few binary phases that release elemental fluorine (F2) upon heating. The introduction of new 18F-labelled triazolyl-linked arginine peptides to target neuropeptides for the imaging of mammary carcinoma 20 serves as an apt example of click chemistry-based 18F-labelling, and a Design of Experiments (DoE) approach has been reported to optimize copper-mediated radiolabelling. 21 The evaluation of new 18F-labelled melanoma xenograft targeting peptides is the subject of an imaging study 22 that is also published as part of this Collection.

While the lightest halogen has become the workhorse of PET imaging, the heaviest (natural) halogen, astatine, has been advancing as a therapy agent. This Collection includes reports on optimized 210Bi(α,2n) cyclotron production and recovery of targeted alpha therapy (TAT) isotope 211At (7.2 h) 23 and an investigation into astatine’s solvent extraction behaviour. 24 Radioiodine still plays an important role; beyond historic 131I, other iodine isotopes 25 are now utilized for SPECT imaging (123I, 13.3 h) and treatment (Auger emitter 129I, 59.4 d).

Radioisotopes have their deserved place in the toolbox of nuclear medicine: cobalt (57Co, 271.8 d; as a surrogate for 59Co, 17.5 h) and indium (111In, 2.8 d) were used as labels for affibody monomers targeting tumours in BxPC-3 xenografted mice. 27 A further contribution broaches the application of nanospheres labelled with 89Zr (78.4 h) 28, a positron emitter with a half-life roughly matching the in vivo circulation of antibodies.

Lanthanides are represented, as many of their easily accessible chemically similar - and thus interchangeableregioisotopes constitute versatile agents for diagnostics and therapy. The purification of SPECT isotope 155Tb (5.3 d) is featured, 29 and a method for the production and recovery of the theranostic pair 120,121La (4.8 h and 19.5 h) with initial imaging and biodistribution evaluation is reported. 30 Alpha emitter 212Ac (10.6 d) has emerged as a TAT isotope: one contribution looks into the in-vivo redistribution of 212Ac daughter isotopes in a mouse model; 31 another study reports the purification of accelerator produced 212Ac using a silicotitanate sorbent. 32 Surveys into the distribution and detection of naturally occurring radioactivity are an important part of the Collection as well, as they demonstrate how radioisotope science helps assess radiation doses from natural radioactivity; the “isodose” concept to Swedish residential buildings was applied to optimize topsoil removal concepts. 33

As the Collection is still open for submissions on a rolling basis, this is only the beginning! May the interested colleague find in this “living” Collection a one-stop overview of the current research that puts radioactivity and radiochemistry to work for the sake of human health.

Published online: 10 January 2020

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Acknowledgements
I would like to extend my thanks to all colleagues for submitting their cutting edge contributions. My gratitude is also due to all peer reviewers who donated a share of their valuable time to assess and help improve these contributions, and to Nature Research as well as the staff editors of Scientific Reports for their kind invitation to propose and lead this Collection.

Author contributions
M.E.F. wrote the invited editorial.

Competing interests
The author declares no competing interests.

Correspondence and requests for materials should be addressed to M.E.F.

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