

International Year of the Periodic Table 2019: Elements important for Life Sciences

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Technetium – Unstable in the Middle of the Periodic Table

Roger Alberto*^a and Ulrich Abram^b

*Correspondence: Prof. R. Alberto^a, E-mail: ariel@chem.uzh.ch; Prof. U. Abram^b, email: ulrich.abram@fu-berlin.de; ^aDepartment of Chemistry, University of Zurich, Winterthurerstr. 190, CH-8057 Zurich; ^bInstitute of Chemistry and Biochemistry, Freie Universität Berlin, Fabeckstrasse 34/36, D-14195 Berlin

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Element 43, technetium, may only have existed on earth at its very beginning since it does not have one single, stable isotope. Its longest-lived nuclide, ⁹⁸Tc, has a half-life time of 4.2·10⁶y, much too short for any primordial technetium to still exist in the earth crust. Albeit, it has been (falsely) reported in 1955 that ⁹⁸Tc was indeed present in some uranium or thorium ores.^[1] This ‘discovery’ was at least doubtful since more than one thousand half-life times have passed since the formation of earth. Nevertheless, ⁹⁹Tc is present in nature in minutest quantities since it is formed, in contrast to ⁹⁸Tc, in the spontaneous fission of ²³⁸U or from neutron-induced fission of natural ²³⁵U as already reported in 1961.^[2]

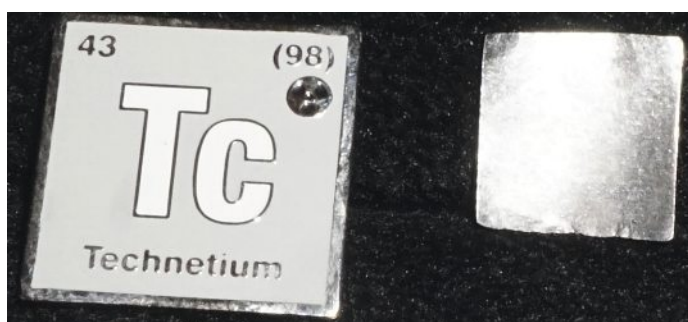


Fig. 1. A piece of elemental technetium from the author's collection.

The non-existence of technetium on earth is thus only known since the first half of the last century. Unaware that technetium does not exist, the search for element 43 was a persistent incentive for many chemists and mineralogists. Already before Mendeleev published his periodic table of the elements in 1869, the discovery of technetium had been claimed multiple times. Early discoveries named the new element Pluran after platinum and Ural.^[3] The ‘discoverer’ himself admitted later that his element was in fact a mixture of TiO₂, ZrO₂ and some silica.^[4] This was not the only false discovery as was the case for many other, then undiscovered elements. Technetium went through ilmenium reported in 1846^[5] together with an even newer element assigned as dwi-manganese and which Herrmann, the discoverer, named neptunium. Dwi-manganese would have been rhenium and dwi-technetium, in fact, became what is nowadays recognised as

element 93, neptunium. Technetium went through pelopium in 1847, davyum in 1877, lucium in 1897 and moseleyum in 1924, one year before rhenium was actually discovered.^[6] Most of these discoveries turned out to be impure group 4 or 5 oxides or some other mixtures. The name moseleyum was only a proposal for the case that element 43 would be discovered since the investigation by X-ray spectroscopy of different uranium and thorium ores did not reveal any trace of the missing element.^[7] The authors suggested to give the element this name to honour H.G. Moseley. Moseley was the first to relate the numbering in the periodic table of the elements to a physical meaning, the atomic number *Z* or the number of protons in the nucleus of the corresponding element. Distinct X-ray lines, emitted by the elements when bombarded with electrons, strictly correlate with this atomic number *Z*. It became thus evident that another element, undiscovered so far, must exist between the known elements 42 and 44. Only this relationship made a systematic search for the missing elements possible.^[8,9] Given the pivotal significance of his discovery, it would be indeed be timely to name an element after Moseley. Applying Moseley's system, Walter Noddack and Ida Tacke claimed in 1925 to have discovered both elements 43 and 75.^[10] They named them masurium and rhenium to honour Masuria, a province in then Eastern Prussia and the river Rhine. Whereas rhenium was soon substantiated by the isolation of weighable quantities, the discovery of masurium was heavily doubted and finally rejected. Still nowadays however, controversial discussions are ongoing if Noddack and Tacke had in fact discovered element 43 or not. In contrast to previous searches for new elements, they proceeded in a logical and scientific way by looking in ores in which these elements might indeed be found. They did not rely on ‘trial and error’ as had many before them. There is another rather tragic drama related to eka- and dwi-manganese; Masataka Ogawa, a student of Sir William Ramsay, the discoverer of the noble gases, continued his search for new elements after returning to Japan from the University College London. He claimed to have found element 43 in Japanese molybdenite, determined its atomic weight to be about 100 and showed that the chemistry would fit well into the manganese triad. He named element 43 nipponium (abbr. Np) to honour Nippon, an ancient name for Japan.^[11] He, and later his son, were however not able to confirm their claim by isolating weighable amounts of material and the name nipponium disappeared from the periodic table as did masurium.^[12] Re-evaluation evidenced that the Ogawas had in fact discovered ‘rhenium’ but this was evident only about five years after the claim of the Noddacks for rhenium, and then it was too late. At least, the element abbreviation ‘Np’ remains for neptunium which is in fact eka-rhenium. In 2016, IUPAC confirmed ‘nihonium’ (abbr. Nh) for element 113. The discoverer proposed the name not only for ‘Japan’ but they also paid respect to Ogawa's early work on nipponium.^[13]

After Mattauch published his empirical rule about the existence of stable nuclides in 1934, it became clear that no stable isotope of technetium (and promethium) would exist.^[14] Emilio Segrè, researcher at Ernest Lawrence's Radiation Lab in

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Please contact: Dr. Cornelia Zumbrunn, Idorsia Pharmaceuticals Ltd., Hegenheimermattweg 91, CH-4123 Allschwil, E-mail: cornelia.zumbrunn@idorsia.com

Berkeley, California, took with him a piece of molybdenum foil which had been irradiated at the Livermore Cyclotron facility for months. After radiochemical workup together with Carlo Perrier, they found different unknown activities which they assigned to isotopes of element 43. They stated that the chemical behaviour of the isolated fraction resembled closely that of rhenium. They also pointed out in their 20-line publication that it can be separated from rhenium, experimental art at its highest perfection, given the minutest quantities they had in hand.^[15] According to the half-life times, they probably had ^{97m}Tc , ^{95m}Tc and ^{94}Tc without being aware of the metastable nature of some of their isotopes. They could confirm the existence of a new element on multiple occasions and the results were reproduced by others. At that time, they did not propose a name since the claim by Noddack and Tacke was still on the table. Only in 1947 and on an initiative by F.A. Paneth, Segrè and Perrier proposed the name ‘technetium’ for element 43 (abbr. Tc), a proposal officially accepted by the IUPAC in 1949.^[16,17]

If cyclotrons would have remained the only source for preparing isotopes of element 43 at that time, it would have remained irrelevant for medical application. Segrè and co-workers, however, already showed in 1938 that technetium or its mother nuclide molybdenum were also produced in nuclear fission.^[18] Then this was a nice scientific result but without any prospective significance. ^{99}Mo is produced with about 6% fission yield in nuclear reactors and its daughter ^{99}Tc remains one of the major concerns of nuclear waste due to its long half-life time. Technetium (^{99}Tc) only became available in visible quantities during the 1950s from spent nuclear fuel. It was at this time that the first chemical reactions and fundamental compounds such as $^{99}\text{Tc}_2\text{O}_7$, $^{99}\text{Tc}_2\text{S}_7$ or some binary halide complexes were published.^[19,20] Amongst them, some particularly ‘exotic’ studies appeared, likely worth reinvestigating. Geoffrey Wilkinson and co-workers reported that the polarographic reduction of technetium yields a compound they formulated as $[\text{Tc}(\text{OH})_4]^-$ or $[\text{HTc}(\text{OH})(\text{OH})_3]^-$ in parallel to the chemistry of ‘rhenides’ with rhenium.^[21] With the advent of organometallic chemistry, fundamental binary and ternary carbonyl complexes were prepared and characterized. Particularly nice is the synthesis of the first sandwich complex of ^{99}Tc by ‘element transmutation’, published by E.O. Fischer *et al.* Following the concept of sandwich complexes with cyclopentadienyl and benzene ligands, they irradiated $^{98}\text{Mo}(\eta^6\text{-C}_6\text{H}_6)_2$ with neutrons to yield radioactive $^{99}\text{Mo}(\eta^6\text{-C}_6\text{H}_6)_2$. The ^{99}Mo would β^- -decay to ^{99}Tc thereby producing the first ^{99}Tc sandwich complex $^{99}\text{Tc}(\eta^6\text{-C}_6\text{H}_6)_2^+$ which they analysed and substantiated by chromatographic methods; an alchemist’s dream became true.^[22] Only about one year later, they then synthesized the same compound on the gram scale but the X-ray structure was only solved 55 years later (Fig. 2).^[23,24]

The chemistry of technetium would probably have remained an exotic piece of science of exclusively fundamental interest with no means for application whatsoever. Along the advent of radiopharmaceutical chemistry with more and more radionuclides becoming available, researchers at Oak Ridge National Laboratory discovered the $^{99}\text{Mo}/^{99m}\text{Tc}$ generator. Since ^{99m}Tc has almost ideal properties for imaging purposes, this generator system made ^{99m}Tc widely available in hospitals at low cost. Whereas $^{99m}\text{TcO}_4^-$ has been used for thyroid imaging since the

1960s, the preparation of more specific compounds for functional imaging was the incentive which boosted technetium chemistry over the following decades.^[25,26] This research comprised all fields; organometallic chemistry and coordination chemistry, thermodynamics and kinetics and even catalysis was an issue. The motivation, however, was mainly the discovery of new imaging agents. One of the most prominent and elegant discoveries was that of Sestamibi by Davison and co-workers.^[27] Sestamibi, trade name Cardiolite[®], is a binary isocyanide cation which accumulates in the myocardium and allows visualization of the heart function. Cardiolite, developed at MIT, still is one of the most beneficial ^{99m}Tc radiopharmaceutical ever produced (Fig. 3). Its beauty is not only the structure, but also the synthetic approach. Any useful radiopharmaceutical based on ^{99m}Tc must be synthesized in one step, in water and in quantitative yield on a reproducibility level which allows for its preparation at any hospital. Low valent and of organometallic nature, one would not expect that this is chemically feasible but Davison and co-workers achieved exactly this.^[28]

The preparation of Cardiolite inspired then generations of researchers, *e.g.* also the authors of this report,^[30,31] search for new and unexpected structures by direct preparation from water. Despite enormous research efforts and the fact that still nowadays more than 80% of all imaging procedures in hospitals are done with ^{99m}Tc , hardly any new ^{99m}Tc radiopharmaceuticals were introduced to the market over the last 10–20 years.^[32] Reasons for this are many, one certainly being the growing competition from other imaging modalities such as Positron Emission Tomography PET. The decline in fundamental ^{99}Tc chemistry as a model for ^{99m}Tc went along with the diminished interest in ^{99m}Tc radiopharmaceuticals. Nowadays, only a handful of groups are left worldwide doing technetium chemistry at the macroscopic level. Still, only recently a ^{99m}Tc -labelled PSMA agent finished phase III clinical trials and its eventual market introduction may give hope for the future of technetium chemistry.^[33,34]

Apart from its relevance for nuclear medicine, technetium’s place is in the middle of the periodic table. It is thus neither an early and nor a late transition element. Its chemistry is clearly distinct from its neighbouring elements and may offer some features of fundamental interest. Its radioactivity is prohibitive for general application, except for imaging purposes, but it might well serve for a core understanding of trends in d-element chemistry in gen-

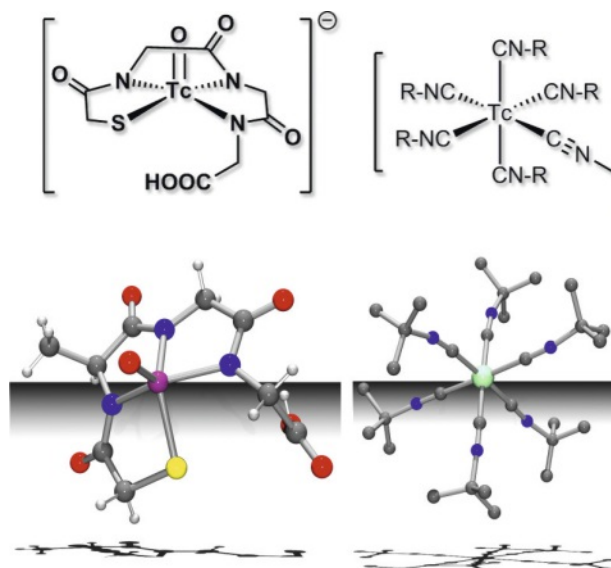


Fig. 3. Fully characterized ^{99m}Tc radiopharmaceuticals that are still in routine clinical application; top left, $^{99}\text{TcO}(\text{MAG3})^-$,^[29] top right Sestamibi (Cardiolite). Second row, X-ray structures of $^{99}\text{TcO}(\text{MAG3})^-$ and a binary $^{99}\text{Tc}(\text{I})$ isocyanide complex.

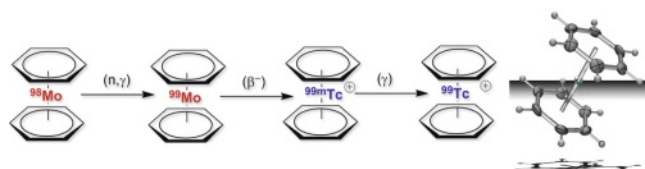


Fig. 2. Preparation of one of the first organometallic ^{99}Tc complexes by element transmutation^[22] and its X-ray structure from 55 years later.^[23]

eral.^[35–40] Technetium is a fascinating element, not only due to its artificial origin and its significance for human health care, but even more for its role in educating young students in how to work with small amounts of radioactive materials. Skilled researchers in this field will be more and more sought after in the future with *e.g.* the decommissioning of nuclear reactors in mind, and technetium offers the opportunity of learning to handle long-lived radionuclides for fundamental but also for applied purposes.

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