



Large-Scale Production of ^{119m}Te and ^{119}Sb for Radiopharmaceutical Applications

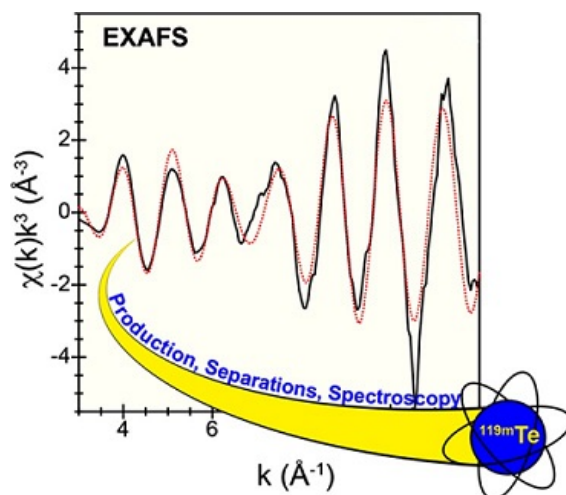
Radioisotope-based medical therapies rely upon the emission of radioactive particles to deliver a destructive radiation dose to diseased tissue while leaving adjacent healthy tissue unscathed. Auger-emitting isotopes could serve as excellent radiotherapeutic agents because their short path length in biological tissue ($\sim 10\ \mu\text{m}$) allows for precise targeting of cancer cells. This means that these therapies have many fewer side effects than traditional chemotherapies. One promising Auger-emitting isotope for medical therapies is ^{119}Sb , however, its use has been limited because its short half-life (~ 38 hours) makes access to it difficult at medical facilities. In this work, the researchers have developed a protocol for producing longer-lived ^{119}Te from an irradiated Sb metal target. ^{119}Te degrades to ^{119}Sb , so it can be shipped to medical facilities where it will produce the required ^{119}Sb for up to ~ 45 days.

To produce ^{119}Te , an Sb metal target was placed in the path of a high energy proton beam (42.5 MeV) at the Los Alamos Neutron Science Center (LANSCE). This generated a very small quantity ($\sim 10^{16}$ atoms) of highly radioactive ^{119}Te , which then had to be separated chemically from 25 grams of Sb. This work is done in Hot Cells so that the high levels of radioactivity (2.7 Ci) can be handled remotely.

One of the key challenges to obtaining ^{119}Te was to isolate it from the irradiated Sb target. A high level of purity is required in order to receive FDA approval, which is necessary for drug development. Radioisotope separations typically rely on the use of commercially available resins that preferentially bind the radioisotope of interest. Ideally, all other components of the mixture exhibit little or no reactivity towards the resin. In this case, the irradiated Sb metal target was dissolved in concentrated acid and then passed through a series of resins. However, the initial efforts were unsuccessful. The team therefore turned to x-ray absorption spectroscopy (Beam Line 11-2) to develop a protocol that took advantage of the different chemical properties of Te and Sb.

Extended x-ray absorption fine structure (EXAFS) and x-ray absorption near edge structure (XANES) spectroscopy were used to examine the speciation (oxidation state and coordination environment) of Sb and Te in the acid solutions used to load the resins. The spectroscopic analysis revealed that Te existed as a positively charged species at low acid concentrations and as a neutral species at high acid concentrations; whereas Sb transitioned from being neutral to carrying a negative charge as the acid concentration increased. This insight provided a method for separating Te and Sb based on the concentration of the acid used to load the resin.

EXAFS and XANES spectroscopies were also used to examine the speciation of Te sorbed by the separation resins. The first resin in the sequence ("CL" resin) separated out 99.994 % of the Sb from the ^{119}Te . Te K-edge EXAFS spectroscopy revealed that the reason for the remarkable efficiency of this



EXAFS was used to understand solution speciation to develop improved separation of the ^{119m}Te parent from the ^{119}Sb daughter.

step was the unexpected reduction of Te(IV) to Te(0), which entirely removed Te from solution. Sb, in contrast, remained in the +V oxidation state and was eluted in concentrated hydrofluoric acid. This result was entirely unexpected based on the reported reactivity of the resin; without EXAFS spectroscopy, the origin of this behavior would have been inscrutable.

Te(0) was removed from the first column using concentrated nitric acid, which oxidized it back into the +IV oxidation state. To purify this solution further, it was loaded onto a second resin- the "Rare Earth" resin, which was intended to covalently bind Te(IV). EXAFS spectroscopy, however, revealed that Te(IV) acquired a negative charge at the resin-solution interface. Under the acidic conditions present, the resin functional group became protonated, acquiring a positive charge that attracted the negatively charged Te species. Some Sb (also negatively charged) stuck to the Rare Earth resin, necessitating one final separation step.

Lastly, an anion exchange resin was used to remove Sb to acceptable levels. The anion exchange resin was loaded with relatively dilute hydrochloric acid. Under these conditions, Sb was neutrally charged and passed through the resin unhindered. Te, in contrast, was revealed to be a negatively charged species, and remained fixed to the resin.

In summary, x-ray absorption spectroscopy provided key insight into the speciation of Te and Sb during the separation process, which ultimately allowed for the development of a rapid (36 hour) procedure to purify ^{119}Te to a level that is consistent with the needs of drug manufacturers. This work therefore represents an important step in the development of Auger-emitting radiotherapies.

Primary Citation

K. T. Bennett, S. E. Bone, A. C. Akin, E. R. Birnbaum, A. V. Blake, M. Brugh, S. R. Daly, J. W. Engle, M. E. Fassbender, M. G. Ferrier, S. A. Kozimor, L. M. Lilley, C. A. Martinez, V. Mocko, F. M. Nortier, B. W. Stein, S. L. Thiemann and C. Vermeulen, "Large-scale Production of ^{119m}Te and ^{119}Sb for Radiopharmaceutical Applications", *ACS Cent. Sci.* **5**, 494 (2019) doi: 10.1021/acscentsci.8b00869

LA-UR-19-23603

Contacts

Sharon Bone, Stanford Synchrotron Radiation Lightsource

Stosh Kozimor, Los Alamos National Laboratory

SSRL is primarily supported by the DOE Offices of Basic Energy Sciences and Biological and Environmental Research, with additional support from the National Institutes of Health, National Institute of General Medical Sciences.