Providing isotopes that can pinpoint disease in the body

President Eisenhower's "atoms for Peace" initiative started the movement to explore peaceful uses of radioactive atoms, and today one use of radioactivity is to diagnose and treat diseases. Radioactive atoms are unstable atoms that decay by characteristic half-lives, and their decay involves the release of energy in the form of a gamma, X-ray, or a particle such as a positron (a positive electron), beta (electron) or alpha particle (Helium atom). Germanium-68 (^{68}Ge) has a half-life of 271 days, and decays to Gallium-68 (^{68}Ga) with a half-life of 68 minutes. The isotope pair is used to make a medical isotope generator that separates ^{68}Ga from ^{68}Ge, and the pure ^{68}Ga can be used in radiopharmaceuticals. These molecules can be used to identify disease in the body and evaluate the effectiveness of a treatment (Atlas of Science, December 2, 2015). A second use of ^{68}Ge /^{68}Ga is in the calibration of Positron Emission Tomography cameras which are used to image positron emitting isotopes on the radiopharmaceuticals. The production and use of ^{68}Ge is summarized in Figure 1.

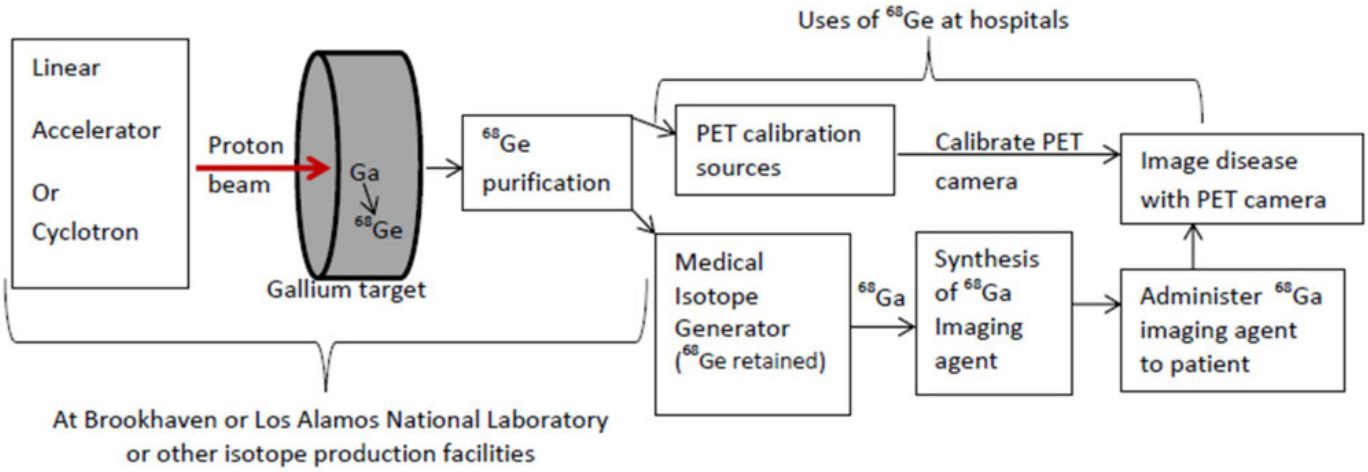

Fig. 1. Production and use of Germanium-68. PET = Positron Imaging Tomography.

Brookhaven and Los Alamos National Laboratories use a linear accelerator to accelerate protons to energies ≥100MeV. The proton beam passes through a target stack containing: rubidium chloride targets for production of Strontium-82 at proton energies from 42-90 MeV then a gallium target for production of ^{68}Ge at proton energies less than 40 MeV. The gallium target contains approximately 65 grams of natural gallium of which only a small amount of the gallium is converted to microgram quantities of ^{68}Ge. Natural gallium has two stable isotopes; gallium-69 and gallium-71, with natural abundances of 60.1% and 39.9%. Both gallium isotopes have a high "cross section" to capture the proton and be converted to ^{68}Ge. The cross section is a measure of the probability of such an encounter.. The nuclear reaction to produce ^{68}Ge is represented as ^{69}

Ga(p,2n)^{68}Ge. The nucleus of the ^{69}Ga atom is excited by absorbed kinetic energy from the incident proton and deexcites with the release of two neutrons to produce ^{68}Ge. The cross section of the reaction peaks around a proton energy of 22 MeV. During the irradiation of natural gallium, Zinc-65 (^{65}Zn) is coproduced in a ratio of ~4 to 1 of ^{68}Ge to ^{65}Zn.

The purification of ^{68}Ge involves a three step process: leaching to remove ^{68}Ge from the bulk of the natural gallium, an anion ion exchange resin to capture ^{65}Zn and a Sephadex©G25 resin to purify ^{68}Ge from residual natural gallium. During the leaching process hydrogen peroxide and 4 M hydrochloric acid are repeatedly used to recover ^{68}Ge and ^{65}Zn from the liquefied gallium. During this process we have found >95% of ^{68}Ge is removed from the gallium metal and from 0.5-3.5grams of natural gallium is present in the pooled leached solutions. To capture ^{65}Zn the solution is diluted to approximately 1.5 M hydrochloric acid, and the solution is passed through an anion exchange resin. The ^{65}Zn forms a negatively charged zinc complex which is retained by the anion exchange resin, and Gallium and ^{68}Ge species are not retained. The ^{65}Zn is eluted with water or nitric acid, the solution dried, re-dissolved in 0.1 M HCl and distributed to researchers. Citric acid is added to the ^{68}Ge solution to prevent the formation of insoluble gallium species [$Ga(OH)_3$], and the pH is raised to ~12.5 with sodium hydroxide. The solution is added to Sephadex©G25 resin; the ^{68}Ge is retained, and gallium is eluted. Pure ^{68}Ge is eluted from the resin with 0.1 M HCl and can be used in various nuclear medicine imaging applications.

Jonathan Fitzsimmons

Publication

Production scale separation of Ge-68 and Zn-65 from irradiated gallium metal.
Fitzsimmons JM, Mausner L.
Applied Radiation and Isotopes. 2015