

Impacts of 80 years of ORNL isotope production

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Carolyn Krause and I recently heard a fascinating talk on important radioisotopes and stable isotopes produced at Oak Ridge National Laboratory. Jeremy T. Busby, associate laboratory director for the Isotope Science and Enrichment Directorate (ISED) at ORNL, spoke to Friends of ORNL on "Isotopes: Vital to U.S. Success." His talk mentioned some history of the lab's isotope production and research, as well as current achievements.

At my request Carolyn conducted some additional research by delving into websites to learn more about the fascinating history and significance of certain ORNL-produced isotopes. ISED has fact-checked her series of three articles for this column to ensure its accuracy and clarity. ORNL has provided photos as well.

One answer to cancer is a selection of radiation-emitting forms of elements called radioisotopes. Over the past 80 years Oak Ridge National Laboratory has produced radioisotopes that have enabled many cancer patients to survive the disease and live longer lives.

Use of ORNL-produced radioisotopes for treatments of health issues, such as cancer, bone pain and even arthritis, is one of the examples of the beneficial impacts of the lab's reactor products. They were described recently by Jeremy T. Busby, associate laboratory director for ORNL's Isotope Science and Enrichment Directorate in his talk to Friends of ORNL titled "Isotopes: Vital to U.S. Success."

He said that other uses for ORNL isotopes include space exploration, energy production, national defense and research related to determining coordination chemistry and crystal structure in certain radioisotopes (radium and promethium) and making quantum devices and computers using an isotope called ytterbium-171 produced using electromagnetic separation at ORNL.

"ORNL has been and is one of the world's leading suppliers of isotopes," Busby said. "We have unique facilities for producing isotopes that have a variety of important and impactful applications. ORNL is producing 60 to 80 different isotopes every year for the nation. It's underappreciated how important isotopes are."

Birth of nuclear medicine. The first radioisotope shipped from a nuclear reactor for medical use—specifically for cancer research and treatment—was carbon-14. The historic shipment on Aug. 2, 1946, from the X-10 Graphite Reactor at Oak Ridge arrived at the Barnard Free Skin and Cancer Hospital in St. Louis, Missouri. It was celebrated that day under the leadership of Eugene Wigner, the ORNL research director and future Nobel Laureate.

The ORNL shipment is widely considered the birth of modern nuclear medicine. It highlighted the lab's shift from research to enable wartime weapon production to research leading to peacetime scientific and medical discoveries and technical developments.

Carbon-14, which was mentioned by Busby in his talk, is again being produced at ORNL in the High Flux Isotope Reactor, which began operation in 1965, but in greater amounts. The reason: Russia was historically the world's primary supplier of carbon-14 until it invaded Ukraine in 2022.

In the late 1940s it was discovered that carbon-14's radiation is too weak to kill cancer cells so production of it declined. However, HFIR can now make a more radioactive form of carbon-14 that is used to trace an experimental pharmaceutical's movement in the body and the body's responses to it. This valuable information will guide the U.S. Food and Drug Administration in deciding whether to approve the experimental drug for patients.

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Because of time limitations, Busby mentioned some but not every of the HFIR-produced radioisotopes cited on websites and on his slides that play a strong role in the treatment of cancers. HFIR makes desired radioisotopes by neutron irradiation of target materials including stable isotopes produced at the lab. Some radioisotopes are natural sources of neutrons that are stronger than X-rays.

Other ORNL radioactive products, including those from the lab's nuclear waste, are decaying radioisotopes that either are gamma-ray emitters, alpha emitters (releasers of helium nuclei, which consist of two protons and two neutrons) that kill small or resistant clusters of cancer cells, or beta emitters (releasers of low-energy electrons) that destroy large tumors.

Cancer treatments. HFIR has played a role in the production of the top three "gold standard" radioisotopes used in clinical practice and trials because of their high success rates in shrinking tumors and extending life. They are lutetium-177, actinium-225 and iodine-131.

"Lutetium-177 is in the drug Pluvicto advertised on TV commercials during National Football League games," Busby said. "It is used to treat advanced prostate cancer."

Its prostate-specific membrane antigen combined with lutetium-177 seeks out cancer cells in the prostate and delivers radiation that destroys them. The lutetium-177 is produced at the University of Missouri Research Reactor by irradiating targets the company BWXT has made from a material it highly enriched in ytterbium-176. This isotope is obtained from HFIR.

Actinium-225. ORNL is the home of two sources of actinium-225: HFIR and the lab's nuclear waste containing mostly uranium-233 (from the Molten Salt Reactor Experiment) that decays to the first of a series of decay products including actinium-227, which has a half-life of 10 days.

When the decaying actinium-225 radioisotope is attached to a cancer-cell targeting molecule (like a nuclear warhead incorporated into a guided missile), the treatment called targeted alpha therapy (TAT) has demonstrated the ability of actinium-225 and its decay products to produce powerful alpha emissions that irreparably damage the double strands of DNA in pancreatic, prostate, lung and breast cancer cells. These cancer treatments will be on the market soon, according to Sarah Schaefer, president and project manager of Isotek Systems, LLC, which is based at ORNL.

Busby showed radiographs of a German patient's cancer treatment progress. "Every dark spot is a tumor formed from prostate cancer that spread throughout his body," Busby said. "Not a good prognosis.

"In December of 2014, the patient was given three rounds of TAT in which a special chelator directs actinium-225 to tumors. Seven months later, the tumors in the same patient were gone. After one more dose, less than a year later, the patient was declared cancer-free."

Busby said that actinium-225 is in short supply because of the expected demand for this "rarest drug on Earth," which is expected to have a market value exceeding \$1 billion in the 2030s. To increase supply, DOE is supporting development of accelerators to make the isotope.

Other anti-cancer isotopes. ORNL was the source of the first "miracle" reactor isotope for successfully treating cancer; it was iodine-131, which has long been used to cure thyroid cancer. It was shipped originally from ORNL's Graphite Reactor in late 1946 and 1947. Iodine-131 is still produced in HFIR today through the neutron irradiation of tellurium targets.

Other HFIR radioisotopes and neutron targets that contribute to the fight against cancer are actinium-227, which decays to radium-223 that is incorporated in the drug Xofigo for treatment of prostate cancer that has spread to the bone, helping to reduce pain and extend life; californium-252, a neutron source that is effective against advanced cervical cancers and certain types of brain and oral cancers resistant to

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traditional radiation; and tungsten-188, a producer of rhenium-188, a beta emitter that treats skin cancer and relieves cancer-caused bone pain.

Busby mentioned that xenon-129, a stable isotope, is a diagnostic tool for imaging lungs in a search for tumors and other disorders, and that the radioisotopes strontium-89 and tin-117m are used for palliative bone cancer treatments.

Through the University of Tennessee–Oak Ridge Innovation Institute, Busby said, ORNL is participating in efforts to target difficult-to-treat cancers and better understand the impacts of radiopharmaceutical therapy on cancer and normal cells.

Arthritis treatment. An injectable medicine containing tin-117m from HFIR is available commercially right now for treating arthritis in the joints of dogs, Busby said. “You can order this medicine approved for dogs. The FDA is working on using this beta emitter for treating arthritis in humans.” The treatment reduces inflammation in joints, providing long-lasting pain relief often up to a year.

Space exploration. Two radioisotopes produced only by ORNL have been essential for the scientific exploration of Earth’s moon and planets like Mars, Busby said. They are promethium-147 (Pm-147) and plutonium-238 (Pu-238).

Promethium-147, an element first discovered in 1945 at ORNL (which is the only source of promethium-147 today), was used on the Apollo Lunar Roving Vehicle in 1971 and 1972. This battery-powered buggy allowed the astronauts to explore the moon, take photos and collect samples during the final three Apollo lunar missions.

Because it is always dark on the moon, a luminescent paint was made that contained promethium-147 and a phosphor. Beta particles (electrons) emitted by promethium-147 strike the phosphor, making it glow continuously and serve as a light source for the lunar rover’s dashboard and control switches. (Busby said that promethium-147 is also used to measure the thickness of liquid crystal displays, or LCDs, to ensure the flat screens will produce sharp images in TVs, monitors, laptops and smartphones.)

The Voyager 1 and 2 spacecraft, which were both launched in 1977, are still being powered deep into space by plutonium-238. This decaying radioactive fuel had been placed inside radioisotope thermoelectric generators (RTGs) made elsewhere, where the significant heat it emits is constantly converted into electricity. However, ORNL is now developing a prototype of a next-generation RTG called a portable thermoelectric generator demonstration unit. It could lead to a commercial device that would meet the needs of people in remote areas.

ORNL did not produce plutonium-238 for the Voyagers. However, the lab did develop the specialized iridium alloy cladding and carbon-fiber insulation that safely contained the plutonium fuel in the RTGs. These robust power sources have enabled the probes’ almost-five decades of continuous deep-space travel beyond our solar system.

In 2015, because of a NASA-DOE agreement, ORNL started producing plutonium-238 for space exploration. That year HFIR made a 50-gram sample, marking the United States’ first domestic production of plutonium-238 in nearly 30 years. ORNL-produced plutonium-238 loaded into RTGs power NASA’s recent Mars rovers Curiosity (launched in 2011) and Perseverance (launched in 2020).

Plutonium-238 already produced at ORNL will be used to power NASA’s Dragonfly mission. It is a rotorcraft drone set to be launched around July 2028 by a SpaceX Falcon Heavy rocket. Starting in 2034, Dragonfly will use power from ORNL’s plutonium-238 to explore Saturn’s moon Titan. It will fly to various locations and investigate Titan’s prebiotic chemistry and potential for life.

Energy production. Tiny amounts of californium-252 (Cf-252), a strong neutron generator from HFIR, not only treats cancer patients but also contributes to energy production. Its neutron emissions have been

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used to start up new nuclear reactors. (Note: The berkelium-249 that is available only from HFIR during its production of californium-252 was essential for the 2010 discovery and synthesis in Russia of the new element 117, named tennessine.)

"Our administration is pushing hard to unleash American energy, such as oil and gas," Busby said. "To meet demands for oil and gas, the U.S. must be a dominant producer of the domestic isotopes needed."

Californium-252 is used to help engineers determine whether it's worth drilling further for oil and gas known to be in underground reservoirs. Fast neutrons that californium-252 emits in an underground "scanning" logging tool are slowed down when they strike hydrogen in the oil and gas below.

Detection of a high concentration of reflected, slowed-down neutrons tells engineers that the underground rocks are highly porous and contain fluids. That's an indication drilling would likely trigger the flow of oil and gas and make these fluids easy to access.

Barium-133, an emitter of gamma rays, is used to calibrate flow meters for measuring the individual flow rates of oil, water and gas as they emerge together from a well. Iridium-192 from HFIR is a source of gamma rays for nondestructive evaluation of oil and gas pipelines to determine if they have cracks and weld defects that later could cause leaks if not repaired.

Oak Ridge National Laboratory is the nation's largest science and energy research institution, and HFIR plays a major role in enabling its science and technology achievements for enhancing human health, exploring space and improving energy production.

Next: ORNL produces radioisotopes that contribute to homeland and national security.

Thanks, Carolyn. These examples of radioisotopes being used in so many ways makes it plain that ORNL is a huge contributor to cancer research and treatment. The fact that plutonium-238 is used by NASA to power deep space exploration is amazing. But the most significant thing may well be nuclear medicine.

Many of you readers may well recall the famous quote from Alvin Weinberg, who was mentioned at the very first of this series. Alvin was asked, "What is the most important thing Oak Ridge has done for the world?" Without hesitation he replied, "Nuclear Medicine! It helps millions of people every year!" I always add that some of the stable isotopes placed in the reactors at ORNL to produce radioisotopes for nuclear medicine came from the same equipment that separated uranium-235 for the atomic bomb, Little Boy. Same equipment, same science produced both the atomic bomb and nuclear medicine.

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Jeremy Busby, ORNL associate laboratory director for the Isotope Science and Enrichment Directorate
(Courtesy of Carolyn Krause)

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This purified promethium-147 has gone through several steps during processing in ORNL's Radiochemical Engineering Development Center. ORNL is working to re-establish domestic production of Pm-147, used for thin-film measurements, nuclear batteries and other applications. (Courtesy of Carlos Jones/ORNL, U.S. Dept. of Energy)