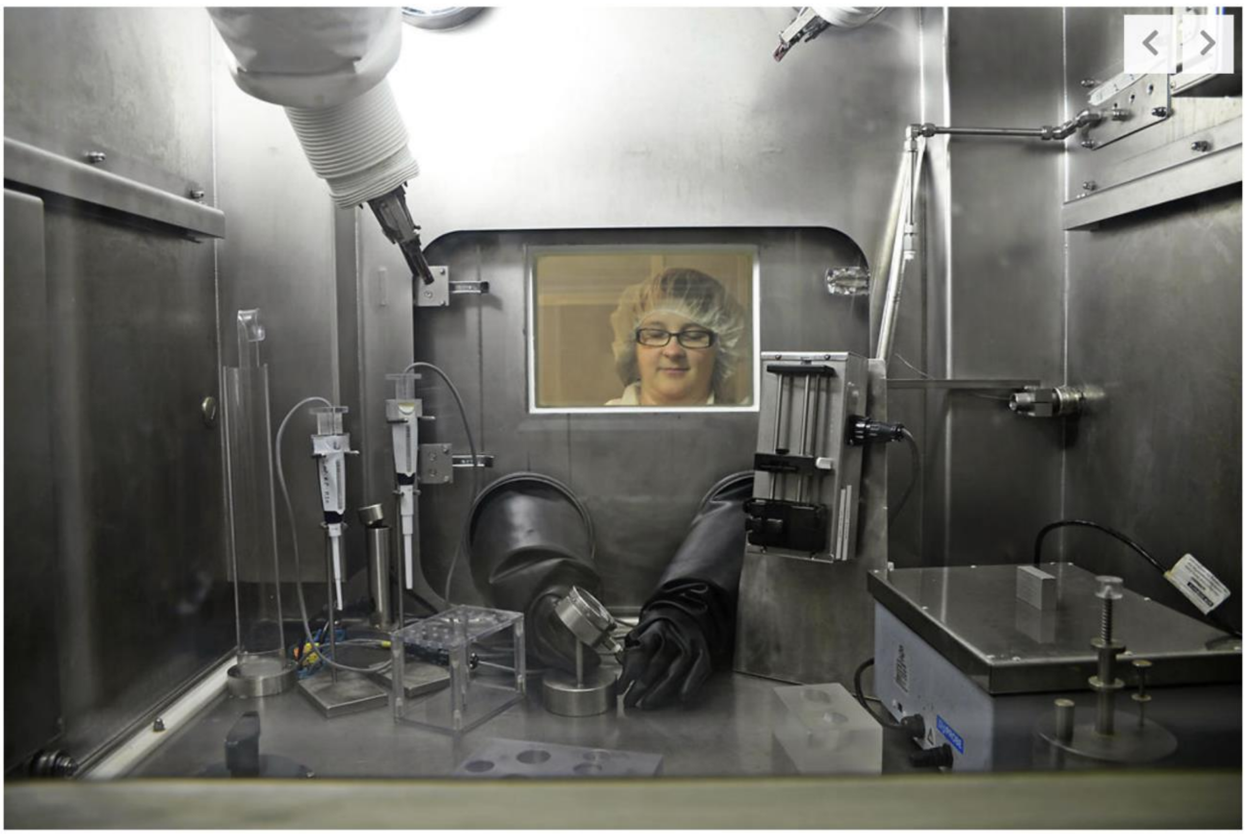
MISSOURIAN

MU reactor plays important role in nuclear medicine advancements

BY CLAIRE COLBY May 3, 2019 0



A scientist at the MU research reactor supervises the processing of Lutetium-177, the active ingredient in Lutathera.

Courtesy of MURR

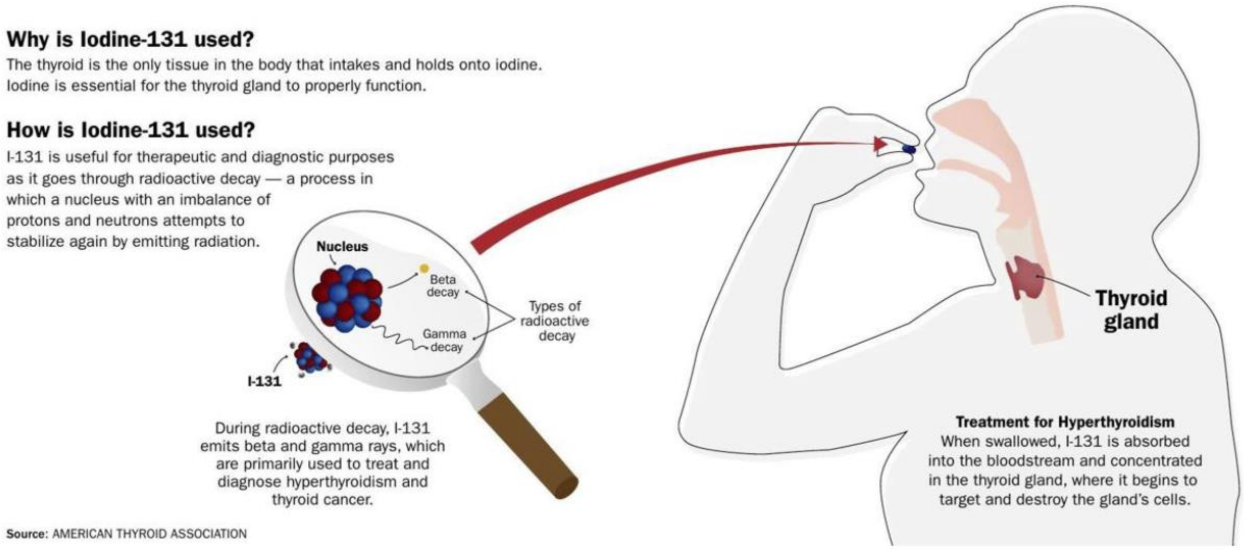
It looks like something out of a superhero movie. But the nuclear bright blue glow of the MU Research Reactor south of Memorial Stadium, isn't the stuff of science fiction.

It's being used to help create life-saving medicines today.

Since its creation in 1966, the MU Research Reactor has pumped out a steady supply of radioactive isotopes used in diagnostic and therapeutic medicine.

But its role in producing two innovative drugs used to treat hyperthyroidism and certain cancers has become even more crucial since 2018 when the reactor became the sole domestic supplier of two medical isotopes.

The reactor has supplied Iodine-131, which helps treat hyperthyroidism and thyroid cancer, since November. It has also supplied Lutetium-177, the active ingredient in Lutathera, a radiopharmaceutical used to treat neuroendocrine tumors of the midgut, including certain types of pancreatic cancer, since the U.S. patent for Lutathera was approved in January 2018.



Iodine-131 used to come from Canada, until the government decided to shut down its research reactor. “It was built in the ’50s, and they’re expensive to operate,” said Ken Brooks, associate director of the MU reactor. “As a result, their supply to the U.S. ended.”

Having a domestic supply prevents snags in the supply chain. Because these radioactive drugs have such a short shelf life, delays at any point in the process can be disastrous.

“It’s really good for patients in the U.S.,” Brooks said. “It’s a domestic supply, so you don’t have to worry about having international borders closed down for political or security reasons, whatever those look like.” For example, several years ago, volcanic ash in the air grounded planes and caused a shortage of nuclear drugs, he said.

The nuclear medicine market will be worth an estimated $15.2 billion by 2025, according to a report from Research and Markets. When other treatments have failed, radioactive drugs are being used to diagnose and treat ailments like hyperthyroidism and cancer. Nuclear reactors, like the reactor at MU, discover and produce the radioisotopes behind the powerful medicine.

A ticking clock

The process that takes radioisotopes from Missouri to clinically useful pharmaceuticals is complex and time sensitive. The active ingredient in Lutathera, for example, has a half life of just about six and a half days. The clock starts ticking once the isotopes are made radioactive at the reactor.

“Essentially, we take stable atoms and we add a neutron,” Brooks said. “When you insert a neutron, you have now created an unstable atom. We call that radioactive.”

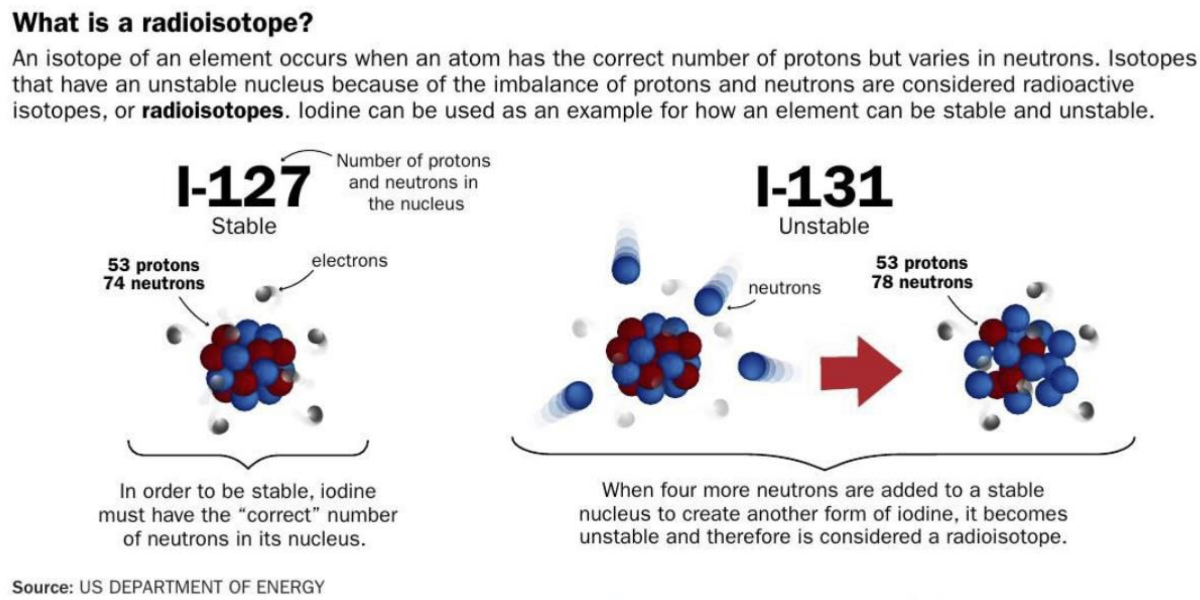
The radioactivity is short-lived.

“Everything that’s radioactive, or unstable, is then immediately on its path back to stable again,” Brooks said.

When the atom transitions back to a stable state, energy is released.

“What do we do with that energy release? That’s the focus of what’s happening in nuclear medicine,” Brooks said.

If the atom releases gamma ray energy, it’s useful for diagnostic purposes. Beta particles are useful in destroying diseased cells and treating certain illnesses.



The radioisotope is only half of the equation, however. In order to be effective, the isotope must be combined with a targeting molecule to hone in on the cells.

“We’ve got this ability to create a radioactive atom,” Brooks said. “Now, what we want to do is park it on a cancer cell.”

In the case of Lutathera, this process, called synthesis, happens through a “synthesis module” operated by Advanced Accelerator Applications in New Jersey. More than 2,000 U.S. patients have received the drug since its approval in early 2018. Before there was a domestic supply of Lutetium-177, also known as Lu-177, Advanced Accelerator Applications got the isotope from a reactor in the Netherlands and processed it in Italy.

After becoming radioactive, these isotopes are quickly back on the path to stability. It’s impossible to stockpile, so doses are literally made on demand. Doctors place orders for their individual patients two weeks in advance. The drug loses its effectiveness 48 hours after production, which must also include transit time.

Doses on demand

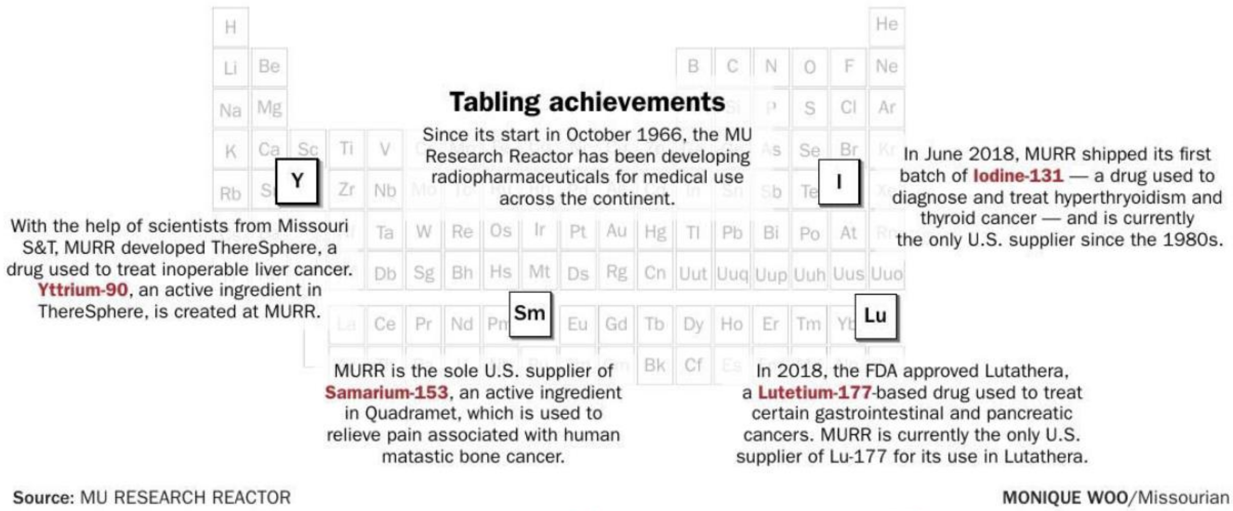
After processing, the drugs are delivered to more than 100 facilities across the country. Mayo Clinic in Rochester, Minnesota, receives air deliveries of Lutathera and administers the drug therapy five days a week.

“It’s an exciting field to work in, with lutetium dotatate, because these patients — their cancer lives in them for a very long time, and some of them can become very ill,” said Dr. Geoffrey Johnson, chair of nuclear medicine at Mayo Clinic in Rochester.

For patients with certain types of metastatic cancer, Lutathera can be the difference between pain and productive lives. Before Lutathera, patients with these metastatic cancers had few — if any — treatment options.

"We receive it, we double check it, there are all kinds of regulations as to making sure it's the right amount of drug, and that it's stable and ready to be injected," Johnson said.

Strict scrutiny is standard for nuclear medicine at a hospital, Johnson said.



Patients interested in receiving Lutathera must schedule their appointments about a month in advance. It takes a few weeks to wash out any other drugs the patient may have been using to manage symptoms. And because of the drug's short half life — or the time it takes for half of the isotopes to transition back to stable — doses are made on demand.

"(The drug) is useful for about a day," Johnson said. "So if the patient isn't there and ready to go, we throw it out."

Each dose of Lutathera costs $47,500. Patients typically receive four doses, eight weeks apart which brings the total cost of treatment up to $190,000.

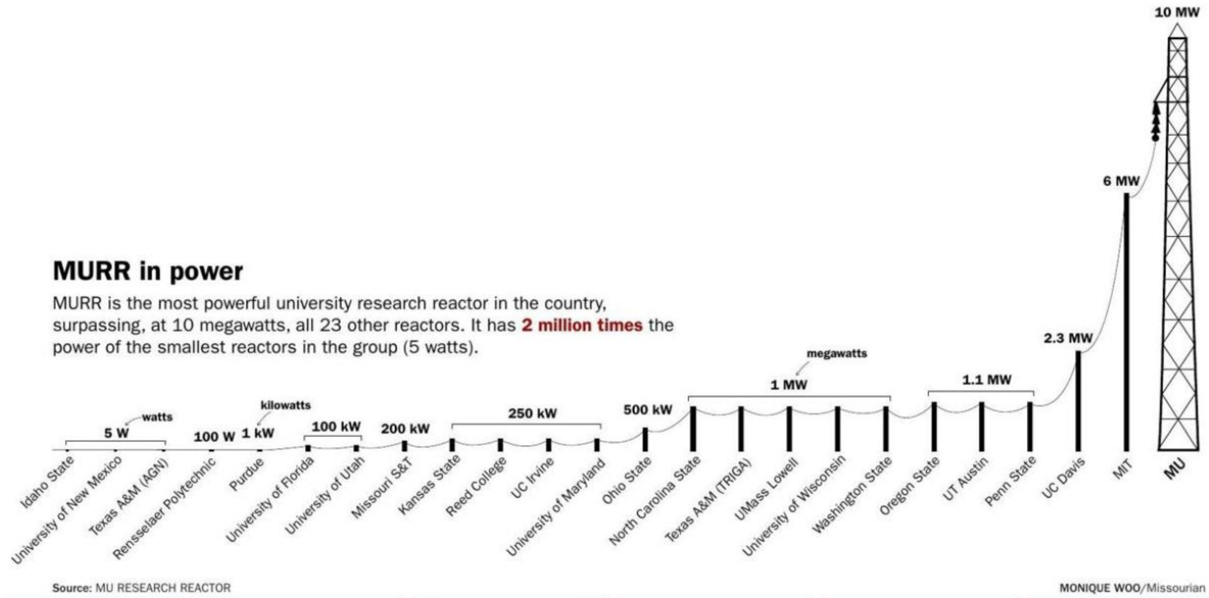
A well-tolerated treatment

On the day of treatment, doctors double check blood work and make sure patients are fit for treatment.

Patients get two IVs: One IV will run amino acids, which have been found to protect kidneys from potential damage from the drug, and the other will run Lutathera. Doctors typically keep patients for a few hours to administer more fluids and amino acids.

"It's very well-tolerate, and the patients can go back home after the therapy is done," Johnson said.

Radiopharmaceutical drugs are less toxic than many traditional cancer drugs, Johnson said.



One of the unique advantages of nuclear medicine is that doctors pretty much know right away if the drug isn't going to work. Imaging can show immediately if the drug is binding to a tumor, which removes a lot of the guesswork.

"In other words, you can decide exactly how you're going to give therapy to a patient, and you'll know whether or not you think the drug is going to go to their cancer," Johnson said. "Sometimes, the cancers don't bind to the drug. And you don't want to waste the radiation exposure, the potential for negative side effects or the expense on a patient who isn't going to benefit from the therapy."

Back at MU, these new drugs aren't unique. The university has helped bring three radiopharmaceuticals to market: Ceretec was the first brain imaging agent, Quadramet is used for metastatic bone cancer and TheraSphere is used for inoperable liver cancer. The reactor operates 24 hours a day, 6½ days a week and 52 weeks a year to create the radioactive isotopes.

Going forward, researchers at MURR aim to produce targeting molecules, too. Brooks said that Discovery Ridge Research Park, an emerging research facility funded by MU, could be the perfect venue for this.

"This is our dream about what could happen out at Discovery Ridge," Brooks said.

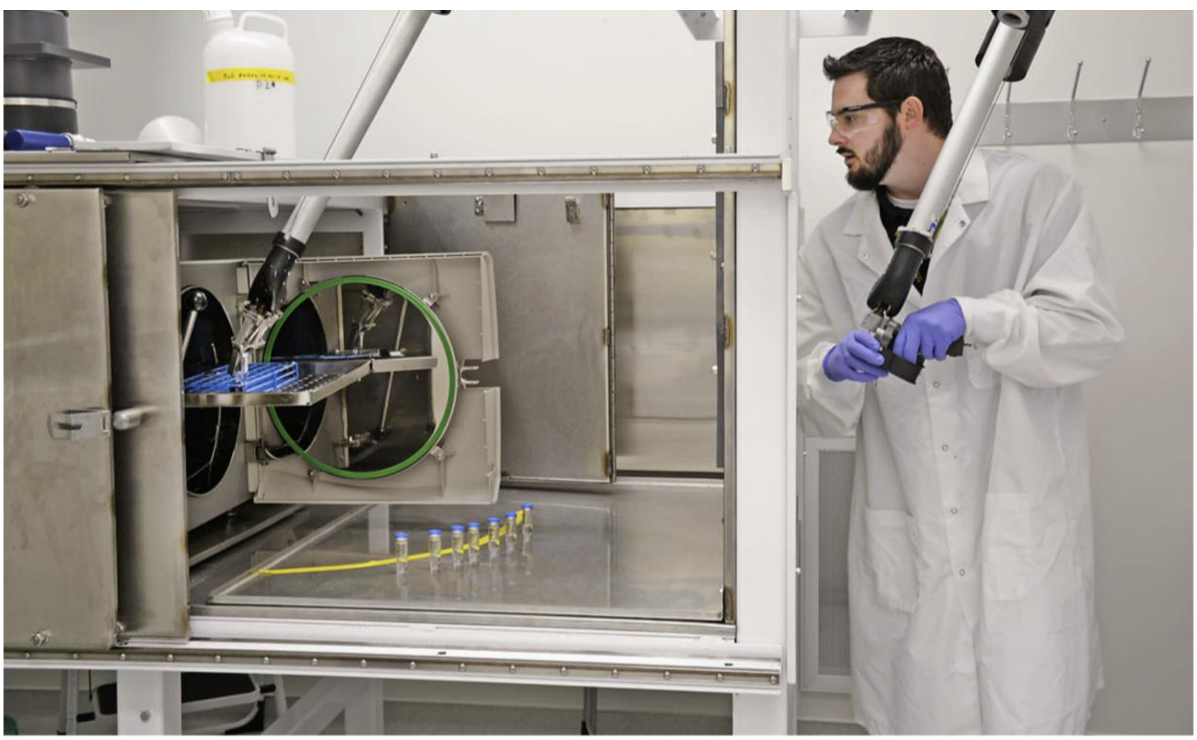
Northwest Medical Isotopes, a private company, received approval to build a facility at Discovery Ridge. The facility should be operational by 2021, according to previous Missourian reporting.

For Johnson, the Mayo nuclear medicine specialist, it's about alleviating suffering.

"(Cancer patients) were suffering, a lot of them were really suffering," Johnson said. "And it's really rewarding to see these patients have new hope and to see them get their lives back. It's a very rewarding field of medicine to be practicing."

A scientist at the MU research reactor supervises the processing of Lutetium-177.

Courtesy of MURR



A scientist supervises the processing of Iodine-131 at the MU research reactor. The drug is useful in treating hyperthyroidism and thyroid cancer.

Courtesy of MURR