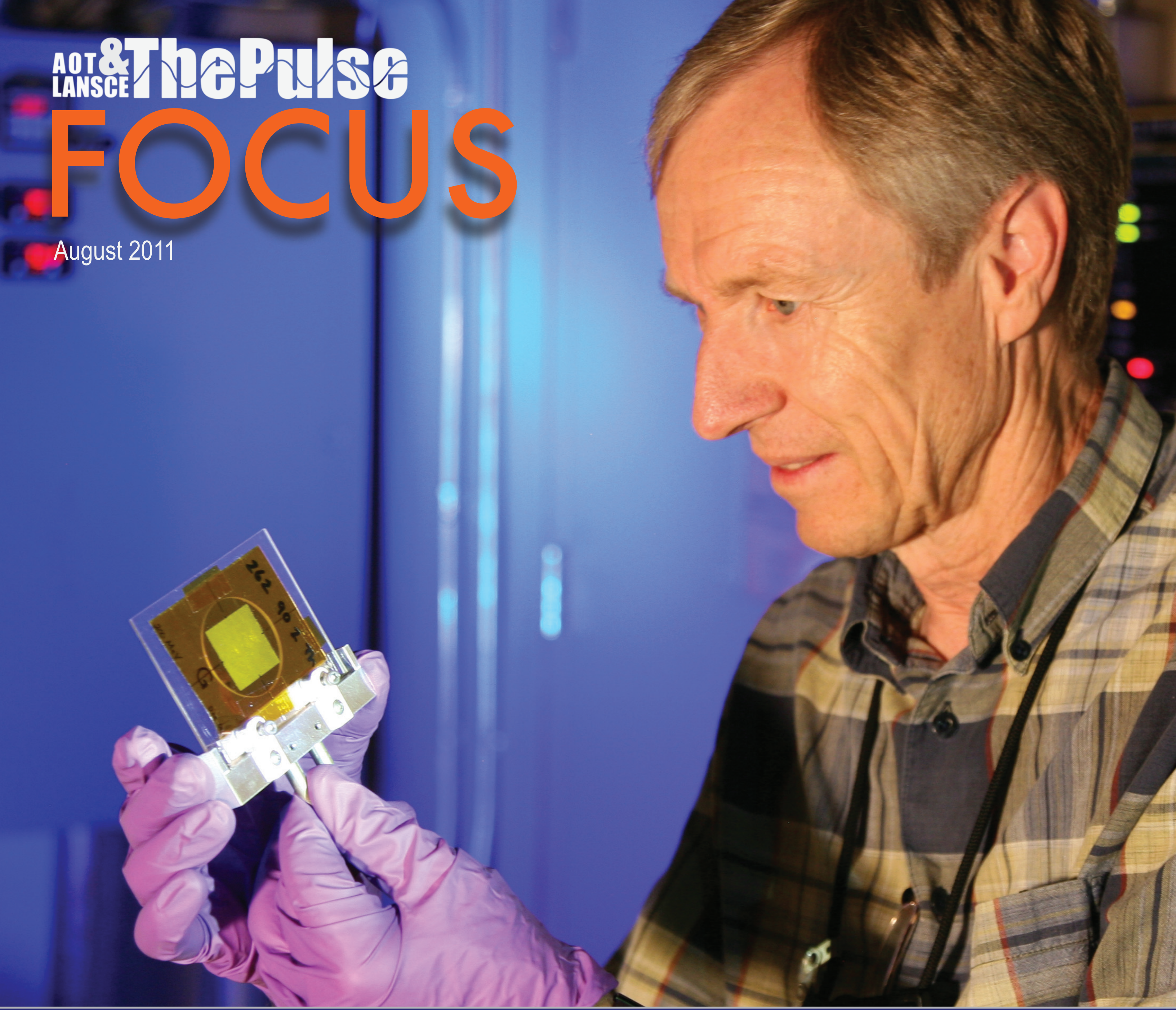
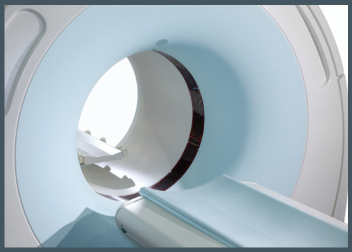
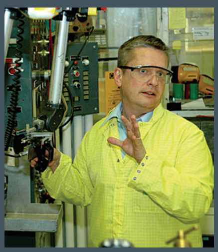
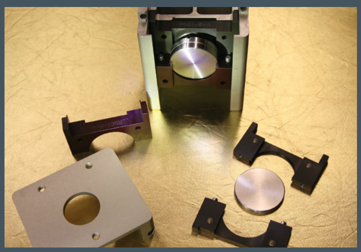
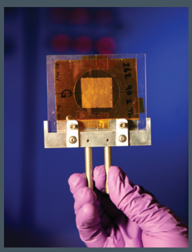
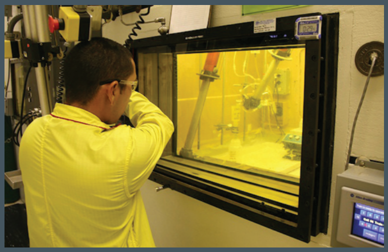
AOT & LANSCE The Pulse

# FOCUS

August 2011



# Isotope Production Facility

Los Alamos NATIONAL LABORATORY

LANSCE

# From Alex's Desk

Colleagues,

I'm pleased to introduce this special issue of the *AOT & LANSCE Pulse* focusing on the Isotope Production Facility (IPF). I find it remarkable that in addition to all the science LANSCE enables for the national and international community, we also host the IPF, where its paramount contribution has lasting effects to a completely different set of customers. In combination with the science produced and the experimental techniques we develop serving national security needs, LANSCE's capabilities are needed now and will be way into the future.

In this issue you will get to know about IPF team members, from how they came to Los Alamos to their vision and the facility's current role in the country and the world. Also described are some of the future plans that take full advantage of LANSCE's scientific and technical environment.

The level of dedication and enthusiasm by the team is palpable. The level of commitment, knowledge, and sense of responsibility by its leadership team is no less than exemplary.

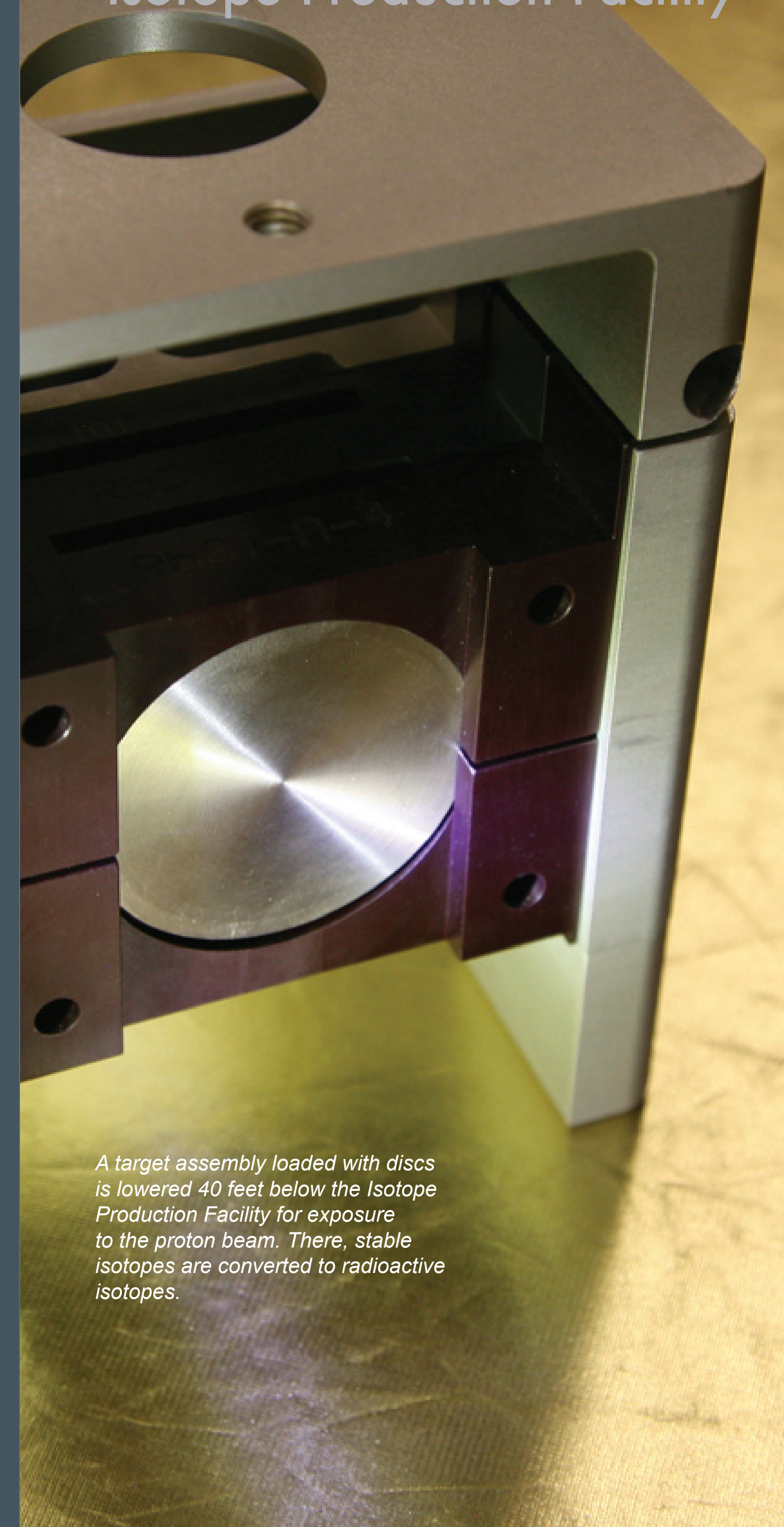
LANSCE Deputy Division Leader Alex Lacerda

*Cover: In an effort to carve out more time for research and development, nuclear physicist F. Meiring Nortier performs early experiments on actinium-225, a promising isotope for cancer treatment, at a specially developed 200-MeV beam in the Blue Room of the Weapons Neutron Research facility. Through ingenuity such as this, the Los Alamos isotope program is able to take on more research projects, while keeping pace with production commitments for the nuclear medicine industry.*

AOT & LANSCE The Pulse

# FOCUS

## Isotope Production Facility



*A target assembly loaded with discs is lowered 40 feet below the Isotope Production Facility for exposure to the proton beam. There, stable isotopes are converted to radioactive isotopes.*



## Profiles

Los Alamos isotope program

# Forging new paths for research and development

Radioisotope production at Los Alamos is entering a new era.

Now under the U.S. Department of Energy's Office of Science Office of Nuclear Physics, the program has new leadership, a revitalized mission, and the promise of new power as the result of a five-year modernization project at the Los Alamos Neutron Science Center (LANSCE).

On the horizon could be new radioactive isotopes available that hold untapped possibilities for advances in nuclear medicine, threat reduction, nuclear power, industry, environment studies, and basic research including space, astrophysics, and nuclear physics.

As charged by its sponsor, the Los Alamos National Laboratory (LANL) isotope program must balance beam time for isotope production with fundamental isotope research and development (R&D). This includes projects focused on developing new isotope lines, novel isotope production techniques, and the information and ability to support the isotopes and nuclear physics communities.

"LANL has proposed 25 percent of beam time for R&D, and under the auspices of the Office of Science, we are aiming for that target," said Don Rej, associate program director of the Office of Science Programs at Los Alamos.

The revitalized mission puts new demands on facilities, people, and finances. "That's where we're looking at clever solutions," he said.

Today, the Isotope Production Facility (IPF) operates somewhat like a pharmaceutical manufacturing business with an unforgiving delivery schedule. And while the isotope program might sound like a production enterprise, there's an important distinction: no profit is made.

According to Chemistry Division Leader Gene Peterson, a guiding force behind construction of the IPF, the original intent was for the facility to be flexible enough to support both a production mission and a research-and-development mission "hand in hand." "Production has expanded beyond my wildest dreams–and that's a double-edged sword," he said.

Los Alamos has produced isotopes since the 1970s, but not until the IPF began full operations in 2005, was the Los Alamos program reliable enough to be a national player. In just a short time, spurred on by the shutdown of a Canadian nuclear reactor and a sharp rise in the number of positron emission tomography (PET) procedures scheduled by cardiologists, the production mission consumed most of the beam time. That continues to be the case today.

With the demand for medical isotopes being one of the fastest growing markets, the commercial health care industry and medical researchers are looking to national laboratories to provide a stable supply of isotopes.

Cranking out two products–strontium-82 for cardiac perfusion imaging and germanium-68 for calibrating PET scanners–took up more than 90 percent of the IPF's available beam time last year. Private industry, at this time, cannot step in to manufacture these isotopes because production costs are still too high and investors aren't willing to take the risk. As a result, the Laboratory continues this service for the nation.

In this new era, the Los Alamos isotope program is at a crossroads. Commercial production needs to be kept in full swing for the health care industry, while scientists explore other isotopes central to the Laboratory's mission of solving basic science and national security challenges. How can one be done without compromising the other?

Due to national shortages of these two isotopes, the Los Alamos isotope program has focused on filling orders for the commercial medical sector at an ever-increasing pace, with little room left for R&D. In 2010, only 64 hours out of a total of 3,500 hours of IPF beam time went to isotope research projects. The lion's share was slotted for commercial production.

Realizing the goal of 25 percent R&D will be "years in the making," Rej said.

In the short term, the Los Alamos isotope program cannot reduce the production of strontium-82 and germanium-68 to make more time for research and development.

In the long term, the program might produce and distribute a different set of isotopes, but a whole lot of factors will determine that course.

## SETTING THE STAGE

To customers worldwide, the National Isotope Production and Applications Program supplies stable isotopes and reactor/accelerator-produced isotopes for a variety of applications. The national program, created by Congress in the late 1980s, was first located in the Office of Nuclear Energy, but in 2009 the program moved to the Office of Science.

The Department of Energy relies on two accelerators–at Brookhaven National Laboratory and at Los Alamos. Their schedules are interlocked, so that when one is down, the other facility is up. Los Alamos is the nation's leading producer of high-energy accelerator-produced isotopes because the IPF has a higher current proton beam.

"No other site in the U.S. operates at the power levels that IPF is capable of," said Kevin John, manager of the Los Alamos isotope program.

*Matt Quintana uses remote manipulator arms to handle target discs that contain newly formed radioactive isotopes.*

### Isotope program oversight

The Office of Nuclear Physics, one of six program offices, has administered the nation's isotope program for the Office of Science since 2009.

The national isotope program has three main objectives:

- Produce and distribute radioactive and stable isotopes that are in short supply, as well as associated by-products, surplus materials, and related isotope services.
- Maintain the infrastructure required to produce and supply isotope products and related services.
- Conduct R&D on new and improved isotope production and processing techniques.

Cleo Naranjo unloads an IPF-irradiated target at the TA-48 hot cells.

In 2010, the national program made 391 isotope shipments (224 radioactive, 167 stable) to customers around the world. Los Alamos supplied more than half of the radioactive isotopes.

## INVESTING IN FACILITIES

LANSCE is powered by an 800-million-electron-volt (MeV) linear proton accelerator (LINAC) that stretches a half-mile long and straddles one of the Laboratory's mesas. Through its national user program, scientists come from all over the world to use its beam current.

From June through December–the period of time when the beam is turned on–LANSCE accelerates protons to 85 percent the speed of light. As protons strike a metal target, neutrons are produced by spallation. During the spallation nuclear reaction, particles are spewed from the target nucleus, resulting in an element with an altered mass number and atomic number.

The linear accelerator is used for a wide variety of experiments, and today it serves five facilities. The IPF, located near the front end of the beam line and tapped off at 100 MeV, is one of those. It must compete against a host of other interests for beam time.

Built in 1972 to perform medium energy physics experiments supporting civilian and national security research, LANSCE has been showing its age. Equipment breakdowns and antiquated power supplies threatened to compromise the kind of work that could be done there–including isotope production.

Then, in a vote of confidence for LANSCE, the National Nuclear Security Administration made a big commitment to shore up Los Alamos's signature experimental science facility. The LINAC Risk Mitigation Project, which started in fiscal year 2010 and will continue at least five years, dedicates about $20 million a year to revving up the Laboratory's signature experimental facility.

"The LINAC Risk Mitigation Project will modernize major components of the linear accelerator and will increase the reliability to all programs fed by the LANSCE accelerator," said LANSCE Deputy Division Leader Alex Lacerda. "It will also increase the operations hours per year."

As a result, the IPF will get up to 4,500 hours a year of beam time. That's an additional 1,000 hours of beam per year. "We're going to get a lot more beam at a higher level of reliability," John said.

While LANSCE is upgraded, the IPF will undergo much-needed maintenance work. Meanwhile, other critical facilities are benefiting now from shiny new parts. In 2011, the Los Alamos isotope program received $1.3 million in funding to upgrade the hot cell facility. With new remote manipulators, touch screen displays, and motor-driven train components, as well as refurbished lead-shielded windows, it's now a smoother operation.

After irradiation at IPF, isotopes undergo a chemical separation and purification process at the hot cell facility. Though a formidable structure with thick concrete walls, the hot cell facility is more than 50 years old. "We are very grateful for the investment in our facilities," John said.

Besides improving existing facilities, Los Alamos also expects to add a new capability in this decade. The Materials Test Station (MTS), a project for the DOE Office of Nuclear Energy, will be added onto LANSCE.

Many years ago, the U.S. lost its fast neutron spectrum radiation capability. Now, with MTS, it's being reinstated, Rej said.

The main purpose of MTS will be to aid the development of new nuclear fuels that destroy long-lived constituents of high-level nuclear waste. But, if the Department of Energy agrees, the new facility could become another hotbed of isotope production, especially suitable for research work.

The LANSCE accelerator will deliver 1 megawatt of proton beam power to the MTS. Simultaneously, the accelerator will deliver beam power to all other existing facilities at LANSCE, including IPF. Targets could be placed in the intense 800-MeV proton beam directed to MTS, as well as in the high flux of fast and slow neutrons that will be generated in the MTS. Reactors, in particular thermal reactors, are best suited to produce neutron-rich isotopes through neutron capture reactions. In general, they are less well suited to produce neutron-poor isotopes. Because of the unique mix of both neutrons and protons available in MTS, it can produce both neutron-rich and -poor isotopes.

## BUILDING A NEW TEAM

With the constant demands of the IPF, nuclear physicist Meiring Nortier, of Inorganic Isotope and Actinide Chemistry (C-IIAC), may not have had the time to do groundbreaking production work on actinium-225 on his own. U.S. Army Lt. Col. John Weidner, a graduate researcher from the University of Wisconsin, helped him run the experiments.

"It could very well be the leading isotope produced here," Nortier said of actinium-225. In targeted alpha therapy, the radioactive drug would be used to kill off cancer one cell at a time, with no damage to surrounding healthy cells (please see page 9 ). The promising isotope is entering clinical trials with leukemia patients, even as the nation is looking for a place where greater quantities of the isotope can be manufactured. The IPF hopes to step up to the task.

Meeting the manufacturing demands of the Los Alamos isotope program today takes 75 workers. Pulling together the right people to do research and development means rethinking existing resources, while also utilizing new talent. With special funding from the Office of Science, Los Alamos is fostering new collaborations with universities and other production facilities.

"We have had a very successful interaction with the Missouri University Research Reactor team, as part of a collaborative project to cross-train students, postdocs, and staff in the details of accelerator and reactor production of isotopes," John said. "This effort has resulted in the program's first postdoc in over 10 years."

Michael Fassbender, a C-IIAC radiochemist, worked with the University of Missouri team to develop a greener chemical separation process for use in generators (please see page 21).

## INGENUITY

Despite new resources and facility improvements, the aim of developing new and unique isotopes could be held back–were it not for ingenuity.

By prototyping targets IPF scientists are able to quickly determine whether certain production paths are viable for large-scale volume of critical isotopes. This approach allows IPF scientists to rapidly screen candidate production pathways without competing with precious beam time.

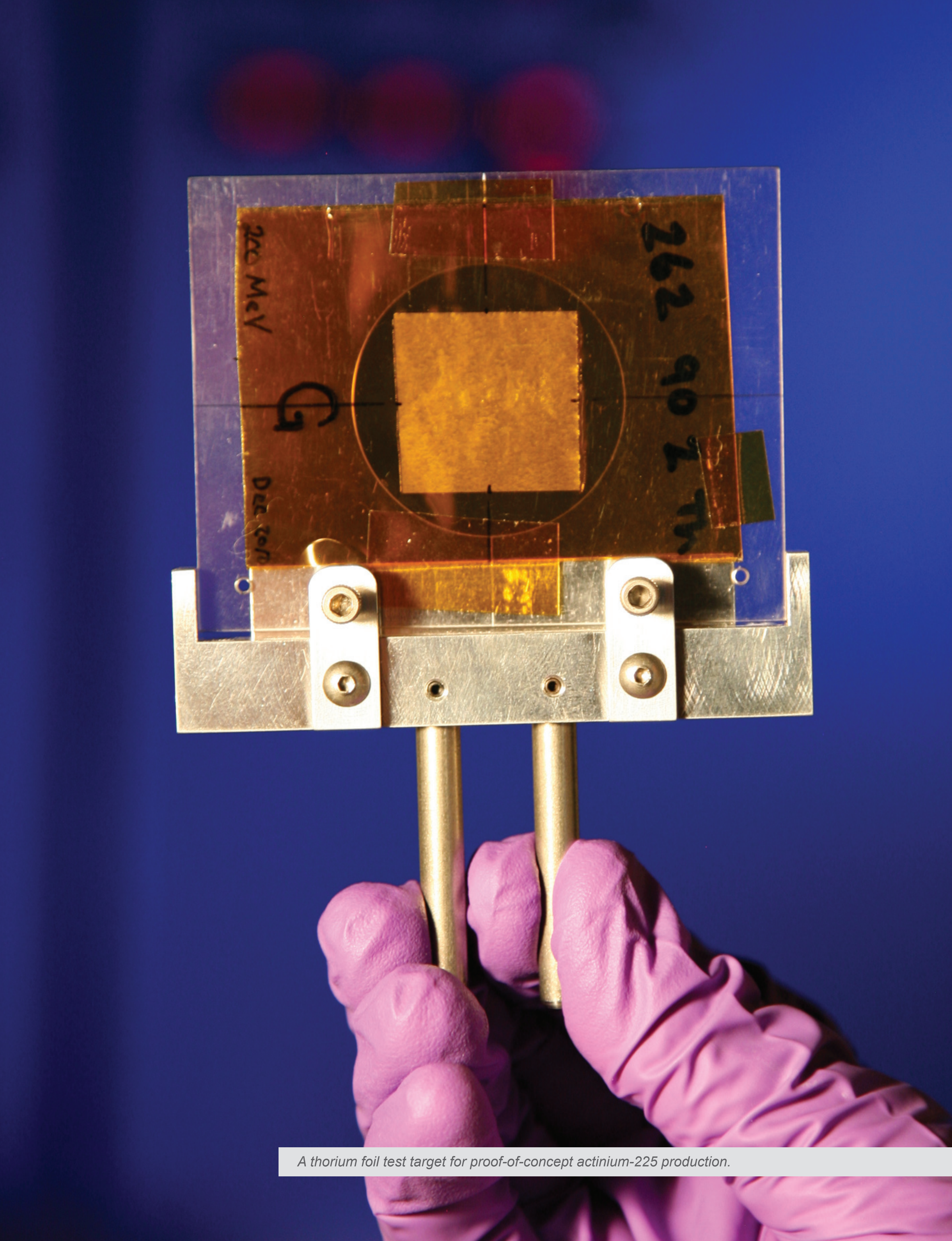
*continued on page 22*

### By the numbers

The Los Alamos Isotope and Applications Program is a leader in developing and producing new and unique isotopes for research and development.

In 2010, the DOE national isotope program made 391 shipments: 224 were radioactive isotopes and 167 were stable isotopes.

In 2010, the Los Alamos isotope program made 172 radioactive isotope shipments and refurbished more than 1,300 generators.




A thorium foil test target for proof-of-concept actinium-225 production.

# Gearing up for a promising new weapon against cancer

In the emerging field of treating cancer with radioactive drugs, the National Research Council has made actinium-225 one of its research priorities. Meanwhile, the National Institutes of Health and the Nuclear Science Advisory Committee have identified actinium-225 as a critical isotope that must be manufactured if it is to be studied.

Until now isotopes of the silvery metal were mined from decaying uranium, but the demand for actinium-225 has outstripped the supply available from the nation's uranium stockpile.

Los Alamos scientists are close to determining whether the nation's two accelerators are capable of providing a stable supply of actinium-225 for research efforts and clinical trials. "Preliminary results show great promise for large-scale production at Los Alamos National Laboratory and Brookhaven National Laboratory," physicist Meiring Nortier said. At Los Alamos, both the IPF and the planned MTS have that potential.

Above: John Weidner handling a target assembly in full protective gear.

Using proton beams available at LANSCE and the Blue Room of the Weapons Neutron Research (WNR) facility, scientists successfully produced actinium-225 from thorium-232. In the process, they documented the world's first set of cross section measurements at these high energies for this specific set of nuclear reactions. When published, the data will help isotope production scientists worldwide to fine-tune production parameters for the highest product yield and highest product quality.

Graduate student John Weidner took the lead in executing the experiments and analyzing the data. He helped irradiate thorium-232 foils with 800-MeV protons in the Blue Room, and then transported the foils to the hot cell facility for gamma counting and alpha assay. In other test runs, he used the 100-MeV beam at the IPF and a specially developed 200-MeV beam at WNR.

The researchers, from the Laboratory's theoretical and computational physics, chemistry, and neutron and nuclear science fields, will now shift their focus to production scale-up investigations, including the development of high-power targets and chemical recovery methods.

Targeted alpha therapy, also known as alpha radioimmunotherapy, is a medical treatment that could kill malignant cells without damaging the body's healthy cells. If clinical trials lead to product development, the annual demand for actinium-225 could reach 50,000 millicuries by 2014, according to the Nuclear Science Advisory Committee Isotopes Subcommittee.

Actinium-225 (Ac-225) holds most promise for treating leukemia and other cancers that embody small clusters of cells or individual cells. For the first clinical study testing actinium-225 in people, New York's Memorial Sloan-Kettering Cancer Center and the National Cancer Institute were recruiting participants in 2011. "The antibody HuM195 will be used to deliver Ac-225 directly to leukemia cells throughout the body," according to the study. "Once Ac-225 reaches these cells, it gives off four alpha particles, killing the leukemia cells. Experiments show that actinium-225-HuM195 should be about 1,000 times more potent than bismuth-213-HuM195."

# The making of a radioisotope

For more than 20 years, Los Alamos and Brookhaven National Laboratories have pioneered the production and supported the development of the clinical applications of two isotopes: strontium-82 and germanium-68.

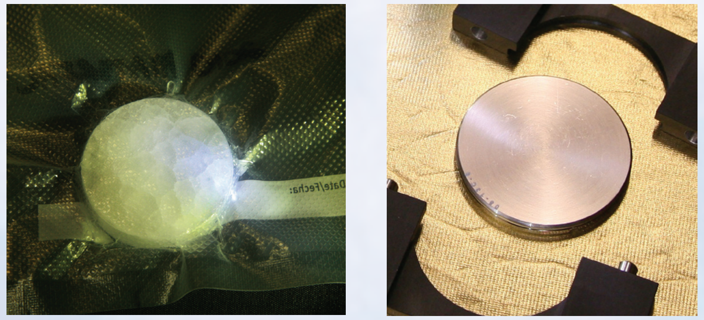
Today, the IPF supplies strontium-82 to companies in North America and Europe for the rubidium-82 generator, which produces a radioactive drug on demand. Hospitals and medical laboratories purchase the generators to support cardiac imaging through PET. The Los Alamos isotope program also manufactures silicon-32, which oceanographic researchers use to study the silicon cycle of marine organisms.

The U.S. Department of Energy's Medical Radioisotope Program developed the generator technology during the 1970s and 1980s, and the technology was transferred to private industry in the late 1980s. The DOE isotope program continues to be one of the main suppliers of the strontium-82 for the generators.

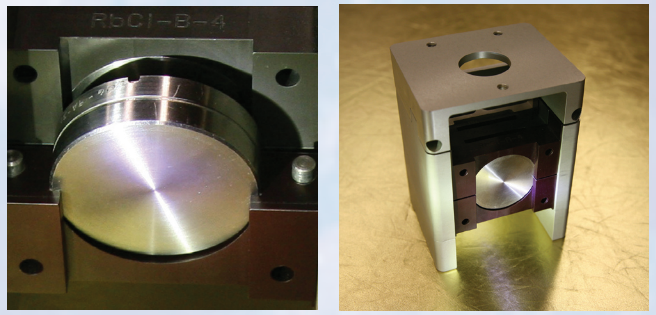
The IPF at LANSCE is one of only five production facilities worldwide capable of manufacturing strontium-82.

Responding to the Department of Energy's call for more strontium-82, the Laboratory accelerated its overall production of the isotope by 350 percent in the past five years. With a team of 20, "I think that's a heck of an accomplishment," said Kevin John, who manages the Los Alamos Isotope Production and Applications Program.

*Background image: Rubidium-chloride granules.*



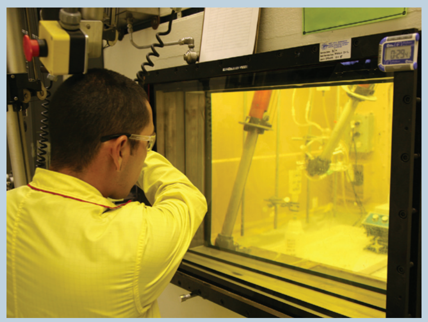
1 Preparing the target: The process starts with a stable isotope. Rubidium-chloride granules, which look like salt, are melted and cast into a solid round shape. The raw material is sealed inside two metal lids, forming a puck-shaped target. Getting the production target qualified, with a certificate of analysis, takes several months.



2 Radiation: Three targets are horizontally stacked in a holder. Forty feet beneath the earth at the IPF, a beam irradiates the targets for 7-14 days. As protons from the LANSCE accelerator slam into the nuclei of the target's atoms, a stable bit of matter (rubidium) is transformed into a radioactive substance (strontium-82).




**3** Purification: The cooled, irradiated targets are trucked in an 8,600-pound lead-shielded container the size of a small refrigerator to the hot cell facility, where the isotopes undergo a process of chemical separation and purification over three days. A crane lifts the container into the "warm corridor" that runs between two rows of hot cells. Only in these heavily shielded rooms with doors on the back and windows on the front can workers using telemanipulators safely view and handle the targets.


From the outside of the hot cells, workers peer through yellow-tinted windows as they extract the strontium-82 from the targets. With a squeeze of remote manipulators to close the mechanical fingers and a push of the buttons to open the mechanical fingers, they perform chemical purification processes to isolate strontium-82 from the target material.

This highly desirable isotope is now a clear residue inside a glass flask. "It's there at the bottom, but you can't see it," said Matthew Quintana, one of the operators. Up to 10,000 cardiac patients benefit from the material extracted from a single target.

**4**

Pharmaceutical delivery: Shipments vary based on the type of isotope and customer requirements, but in most cases the product is loaded into a sealed vial and placed in a heavy lead shield for transport. Customers will use the isotopes produced at IPF for generator technology. In a generator the parent isotope is immobilized on a solid support and the daughter isotope is available on demand for imaging and therapy procedures. The customer, in turn, supplies the radionuclide generator to hospitals and imaging centers for clinical application.

**5** Patient impact: Inside the generator, long-lived strontium-82 converts to short-lived rubidium-82 through radioactive decay. The rubidium is eluted from the generator for PET scans. A patient's heart muscle absorbs the rubidium-82. The rubidium decays by emitting positrons, which combine with electrons to produce gamma rays that are detected by the scanner. Cardiologists interpret that information to determine the condition of the patient's heart.

*PET-CT scan image of human heart.*

This isotope was used for scan procedures impacting nearly 20,000 patients every month in 2010.

# Aiming to make a better target

Manufacturing an isotope is much more involved than sticking a target in front of an accelerator beam. Scientists, engineers, and technicians must overcome a myriad of complex challenges, including those related to separation chemistry, the physics of beam interaction with materials, and the transportation of radioactive material.

"That know-how is a very rare skill set," said Don Rej, a liaison between the U.S. Department of Energy's Office of Science and the Los Alamos Isotope Production and Applications Program.

For the IPF, increasing production yields is paramount, given competing demands for beam time. To address that issue, nuclear physicist Meiring Nortier and chemical engineer Hong Bach are striving to improve efficiencies by designing tougher production targets.

Targets used to fail routinely—causing clean-up hassles and lost product. But Bach and Nortier have put a stop to target failure. The gains are substantial: If the welded metal containers entrapping the raw material don't leak or crack during irradiation or during the cool-down period, then the IPF can manufacture the same volume of isotopes in a shorter period of time.

Bach and Nortier have gained a better understanding of the physics of beam interactions with targets. Through trial-and-error, they've also learned how to find the right combination of target capsules and target materials, so they don't have to halt production midstream. It's not an exact science. The materials used in making each isotope come with their own idiosyncrasies.

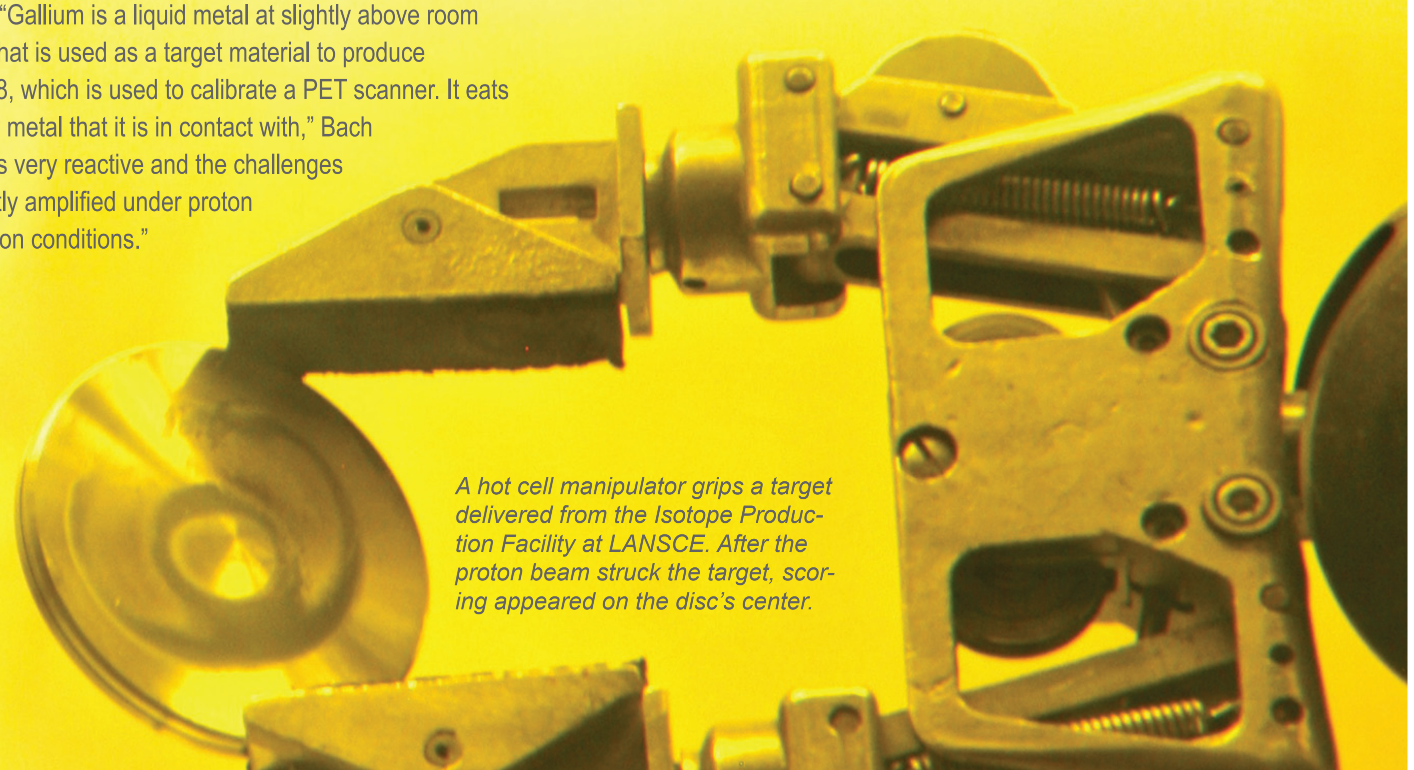
For instance, "Gallium is a liquid metal at slightly above room temperature that is used as a target material to produce germanium-68, which is used to calibrate a PET scanner. It eats through every metal that it is in contact with," Bach explained. "It's very reactive and the challenges are significantly amplified under proton beam irradiation conditions."

Different target materials can result in the production of more strontium-82 product. For example, rubidium metal provides the potential of an overall higher strontium-82 yield. Unlike in the rubidium chloride salt form, rubidium metal has a higher probability to interact with protons during irradiation. Therefore, more strontium-82 can be made per proton inside each target. In fact, rubidium metal is used at other production sites (iThemba in South Africa, INR in Russia, TRIUMF, in Canada). IPF is presently exploring ways to use this extremely reactive metal at the high beam currents provided by IPF.

As the IPF gears up to manufacture different isotopes, the risk of target failure is ongoing. By borrowing imaging techniques used in nondestructive weapons testing, Bach is designing a set of diagnostic tests for each stage of isotope production that will help shed light on why targets fail. "No one else has done this except the LANL isotope program," she said.

The Los Alamos isotope program is also taking stock of its full capabilities. At the IPF, the beam energy is set at 100 MeV and cannot be changed. In principle, however, the beam currents could be increased significantly. The IPF runs an average beam current of 226 microamps, but it is capable of 450 microamps. To take advantage of this, Nortier is developing new production targets suitable for higher beam currents.

If Nortier and Bach succeed in designing a new generation of targets, the IPF can operate at higher beam currents and therefore manufacture more isotopes in less time, opening up more time for isotope research and development.

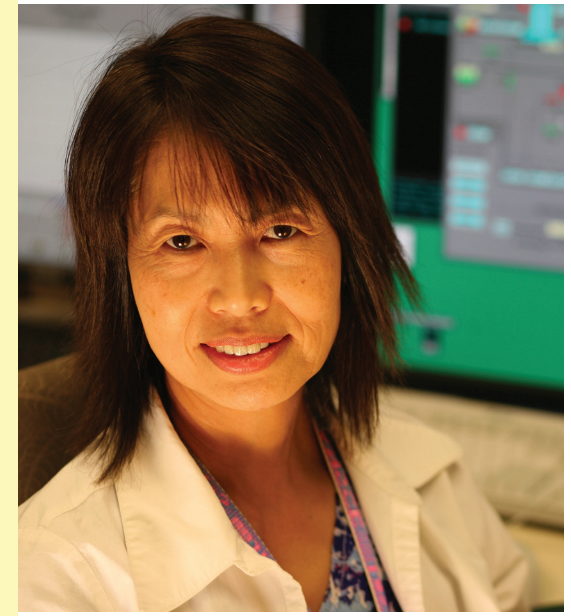


*A hot cell manipulator grips a target delivered from the Isotope Production Facility at LANSCE. After the proton beam struck the target, scoring appeared on the disc's center.*



# Hong Bach

## Devising new tools for old problems



As a child growing up in the war-torn countryside of Vietnam, Hong Bach thought she wanted to be a medical doctor. But when she embarked on a new life in Madison, Wisc., she opted instead for chemical engineering.

After spending 25 years in many programs at Los Alamos, she now is happily re-connected with her interest in the medical field. Her latest assignment is experimental area manager of the Laboratory's IPF.

When Bach took the job in 2007, the facility was in its second year of full operation and facing a slew of production challenges. Too often, production targets cracked under the blast of the accelerated proton beam, and the isotope inside–which could serve thousands of patients–had to be thrown away. "This is my passion when I came to the program," said Bach, of C-IIAC. "I saw a lot of need for improvement–to nail down the source of failure."

Bach considers it quite an accomplishment that last year not a single target failed. "This is one of the fun ones–a big challenge to solve–because the technology is not there," she said, referring to production targets.

Not since 1988, when Bach was a graduate research assistant at Los Alamos, had she worked with isotope separation. Now, as the one charged with overseeing the Laboratory's isotope production plant, Bach is immersed in the field. "With the medical isotopes program, I have a heart in it," she said. And in response to rising demands from the nuclear medicine industry, Bach has ratcheted up and fine-tuned the production process for radioactive isotopes.

Bach's office building abuts LANSCE, a linear accelerator that flings protons at nearly the speed of light. Targets are located underground, at the accelerator's front end. If something goes wrong, immediate action is necessary. Bach and the IPF team rotate being on call around the clock.

"The IPF is a highly complex facility to run," said C-IIAC Deputy Group Leader Felicia Taw, noting the need for coordination with radiation protection, facility operations, and accelerator operations. "The fact that Hong is a very well-organized, meticulous individual helps her excel in this position."

Bach is one of three chemical engineers in her group. She's responsible for production strategy and experimental planning, equipment repair after radiation damage, target packaging and transportation, beam authorizing and receiving, radiation protection, waste service, environmental protection, industrial hygiene, and facility infrastructure and support.

Her early work with stable isotopes and her later work with tritium in the Los Alamos weapons program help her solve the isotope program's most vexing problems. Collaborating with Thomas Claytor and James Hunter of Applied Engineering Technology, Bach devised a new tool that uses ultrasonic technology developed at Los Alamos to capture pictures of the raw isotope material and the target before it is irradiated. Bach's next project is to take pictures of the target in the hot cell, after it has been irradiated over extended periods of time. "To send sound waves into the hot cell facility to evaluate highly proton-activated targets is an engineering challenge," she said. "So we're working on that."

Armed with better information from those images, Bach hopes to be able to identify flaws before they become critical and, in turn, reduce potential losses of targets due to a catastrophic failure.

# Eva Birnbaum

### Keeping cool under pressure

A year ago, Eva Birnbaum slid into the hot seat when she became team leader of the Los Alamos isotope program, stepping up the production and purification of radioactive isotopes for research applications and the commercial health care market. In her career as a chemist, it is a fascinating new world.

"One amazing thing about this job is you know at the end of the day your product is going to help a lot of people," she said. Every time a small box containing a glass bottle with a microscopic amount of isotope is shipped, Birnbaum and her 20-member team have helped hundreds of heart patients. If isotopes aren't manufactured and shipped on time, patients might not get their diagnostic tests on time.

"Last year, we were 100 percent on time," Birnbaum said, noting that the isotope program always had a good record but demand increased substantially last year. "What the team has delivered is really incredible."

"I think the biggest challenge is trying to get the pieces to fit together for us to get our product out the door," said Birnbaum, of C-IIAC. "Our schedule is pretty much unforgiving."

Research technician Glenn Wiuff, who helps keep the complex hot cell facilities operational, said Birnbaum is the best team leader he has worked for. She keeps in touch daily with the team members, holds people accountable for their tasks, and takes charge, he said. "I don't know how she does it," Wiuff said. "We call her Wonder Woman."

Before she became team leader for the isotope program, Birnbaum devised new ways to mitigate beryllium and uranium contamination, and she also served as chief science officer for a local start-up company. Now, Birnbaum's analytical strengths and her regulatory knowledge come into play in the isotope program.

"Things that are very easy on the bench become very complicated in the hot cell," Birnbaum said.

Isotope targets are zapped by a proton beam at the IPF and then trucked to the hot cell facility. Upon arrival, the targets are intensely "hot," or radioactive. Thirteen concrete rooms contain contamination and radiation.

A train—only a little bigger than a model train set and uniquely suited to the hot cell environment—moves flasks of isotopes from cell to cell. Workers, peering through leaded glass windows, remotely direct the mechanical arms that handle the flasks as they perform chemical separations and purify the isotopes.

As the Los Alamos program takes on more research and development work, isotopes for treating cancer may soon be in the hopper.

"I am very motivated about cancer research," said Birnbaum, who lost her mother-in-law and a close friend to the disease. "I would be very proud if I could advance the tools for cancer research and treatment."




# Francois Meiring Nortier

### Pioneering the isotopes of the future

Over the past two decades, from South Africa to New Mexico, Francois Meiring Nortier has helped push the frontiers of nuclear medicine and isotope production. As a nuclear physicist, he has had a hand in planning and operating two of the world's biggest isotope production facilities. He is considered a leading world expert in his field.

"It's a very exciting field to work in," said Nortier, who traveled to the International Atomic Energy Agency's headquarters in Vienna this summer to give advice on medical isotope production.

Born and educated in South Africa, Nortier spent six years designing bombardment facilities and production processes for a government-run accelerator with a 66-MeV proton beam that opened in 1988 near Cape Town.

For 11 years, Nortier led the physics and targetry division of the radioisotope production group. At that time the world's largest producer of radioactive isotopes, the program supplied more than 40 South African hospitals and clinics, while also manufacturing isotopes for export. When Nortier heard that Los Alamos hoped to build an even more powerful isotope production facility, he saw it as a "wonderful opportunity to come here."

Not surprisingly, the Laboratory handpicked Nortier for the job. "It was a real coup attracting Meiring to Los Alamos," said Gene Peterson, who spearheaded the IPF construction project. "Without his expertise we would not have made anywhere near the progress that we have made toward full utilization of the IPF's capabilities."

In 2001, Nortier moved to New Mexico and oversaw commissioning of the newly constructed IPF. Equipped with a 100-MeV proton beam, the IPF holds the distinction of being the world's largest producer of radioactive isotopes. A facility with such production capacity had never before been constructed as a whole, Nortier said.

In the IPF's day-to-day operations, Nortier makes purity and yield projections for isotopes. He also designs targets and target shells, which encapsulate the raw material that is transformed into the desired isotope. The metal targets undergo radiation at the Laboratory's high-intensity proton accelerator–and that's where the isotope is born.

"Meiring had a major role in the conceptual design and operating system of the Isotope Production Facility," said C-IIAC Group Leader David Thorn. "Now he spends more time doing the science and representing (Los Alamos), nationally and internationally, at the request of the program. Maintaining our presence, and knowing what other people are doing, is a big part of our job."

As chief scientific investigator for two International Atomic Energy Agency research projects, Nortier helped establish an online database of reliable nuclear data for the international isotope production community.

In his Los Alamos office, Nortier often studies the chart of the nuclides, which lists all the known isotopes. "Not a day goes by without me looking at this thing and figuring out if we can go from this block to that block," he said. Each isotope of an element has the same number of protons, but a different number of neutrons. On the nuclide chart, each isotope is represented by a block shaded in a different color. If Nortier eyes a radioactive isotope in a colored block, he then must pick as a starting point a black block, which represents a stable isotope that is naturally occurring in the environment. Then the question is how to take that stable isotope and get the isotope he wants with just a blast of the beam.

# Kevin John

## Embracing challenges with enthusiasm

Chemist Kevin John has been leader of the Laboratory's isotope production initiative since 2006. His most unforgettable day on the job was when Pittsburgh Steelers Hall of Famer Franco Harris donned a yellow lab coat, goggles, and booties and took a tour of the hot cell facility with him. Harris learned about the Los Alamos isotope program when he met a C-IIAC employee on an airplane. He promptly booked a tour. "It was surreal," said John, who keeps a photograph of Harris, standing by his side, on his file cabinet. "I grew up in western Pennsylvania watching him on T.V. all the time."

Q: Under the U.S. Department of Energy isotope program, you operate a manufacturing business and distribute key ingredients to commercial health care companies, as well as universities and other customers. Why are national laboratories, particularly a national security science laboratory such as Los Alamos, involved in this endeavor?

A: Louis Rosen's vision for LANSCE ensured that the accelerator could operate in such a manner as to satisfy the National Nuclear Security Administration's core mission requirements and provide beam to facilities like IPF. LANSCE is truly a unique and powerful facility. It is one of only two facilities in the U.S. that can provide high-energy (70 MeV and above) proton beam for isotope production. These energies are required to make our core isotopes: strontium-82 (cardiac imaging) and germanium-68 (medical imaging diagnostics). The infrastructure requirements needed to operate and maintain such a facility in the commercial sector make this a daunting undertaking anywhere outside of a national lab.

Q: The Medical Isotope Production Team is a cross-disciplinary group of more than 75 people from 11 different Laboratory divisions and offices. What's an example of their best teamwork?

A: The best example that comes to mind is the recent dedicated operation of LANSCE in January 2011. Due to increasing demand for strontium-82 (used in cardiac imaging), LANL was asked to provide more material.

LANSCE extended its operating schedule for the IPF so that we could irradiate and process targets to meet customer orders. Then, our team at the TA-48 hot cell facility had to work aggressively to process these extra targets.

*continued on page 23*

*Pittsburgh Steelers Hall of Famer Franco Harris and Kevin John near hot cell 13.*



# Don Rej

## Fostering success in new directions

Don Rej is the associate program director for the Laboratory's Office of Science programs, which are governed and funded by the U.S. Department of Energy. The DOE Office of Science is the single largest supporter of basic research in the physical sciences in the United States, providing more than 40 percent of total funding for this area of national importance. The Los Alamos Isotope Production and Applications Program falls under that sponsorship.

Q: In 2009, the U.S. Department of Energy's Office of Science assumed responsibility for the national isotope program, which includes the Los Alamos IPF and the hot cell facility. The Office of Nuclear Physics is now running the isotope program under the Office of Science. What is the vision for the nationwide program?

A: The mission of the Office of Nuclear Physics is to discover, explore, and understand all forms of nuclear matter. As the isotope program sponsor, the Office of Nuclear Physics supports the production, distribution, and development of production techniques for radioactive and stable isotopes that are in short supply and critical to the nation. These isotopes are essential for energy exploration and innovation, medical applications, national security, and basic research.

The vision of an optimized balance of R&D, production, facility stewardship, and industrial partnership is key to meeting this mission. The Office of Nuclear Physics has already commissioned several studies by the Nuclear Science Advisory Committee to identify compelling research opportunities using isotopes, a strategic plan for isotope development and production, and a national isotope long-range plan.

Q: What did that change mean for the IPF at LANSCE, in particular?

A: The change in sponsorship has meant stronger engagement and support, accompanied by higher standards and accountability. Since 2009, the Office of Nuclear Physics has already issued four national competitions for isotope research and production. Los Alamos National Laboratory favorably competed and received funding to start new projects, such as exploring production of alpha particle emitting isotopes for cancer treatment.

Since 2009, the Office of Nuclear Physics also convened three formal peer reviews to judge the science, production, operations, and management at the Los Alamos isotope program. These were serious, multiple-day reviews by distinguished panels that the Office of Nuclear Physics selected from all over the country. Each panel produced a formal report, all of which were highly complimentary to our performance and plans.

Q. Last year, the Laboratory's isotope production team demonstrated technical and operational innovation, which resulted in record amounts of strontium-82 and germanium-68 being delivered to the commercial medical market. Such successes are valued by businesses and manufacturing plants. How does this kind of performance fit into the Office of Science's vision?

A: Very well. Right now, strontium-82 production dominates the national program supply to industry. Meanwhile, the Office of Nuclear Physics's support has enabled us to pursue R&D to explore new

*continued on page 23*

# IPF innovation to benefit star studies

Large quantities of radioactive isotopes, in stringently pure forms, are in short supply in the field of nuclear astrophysics. "There are tons of measurements we can do, but we need samples to advance science," said Aaron Couture, a nuclear physicist who performs neutron capture cross section measurements using the Los Alamos Detector for Advanced Neutron Capture Experiments (DANCE), an instrument with broad applications. "The capability of handling and making samples is being lost."

Couture's passion is to better understand how the elements were formed in the stars, which provides important insight into the dating of the universe. One area of interest, the study of nucleosynthesis in a specific rare-earth region of the stars, requires accurately measured neutron capture cross sections of a range of isotopes, including many based on europium. But current samples, taken 30 years ago from natural sources, are not clean enough. Couture already analyzed them.

The IPF might be able to fill this void. LANSCE, which powers the isotope facility, is one of three accelerator facilities worldwide with the right beam parameters to produce high-purity isotopes in large quantities.

To find out, Couture, nuclear physicist Meiring Nortier, and radiochemist Michael Fassbender propose to manufacture and evaluate the non-naturally occurring europium-152. Instead of using the 100-MeV proton beam of the IPF, the research team would generate a sole-use 40-MeV primary beam in the LANSCE Drift Tube Linac and transport it to the IPF target station. In 2009, Los Alamos scientists established this new 40-MeV capability.

Traditional techniques for creating isotopes cannot produce a europium-152 sample of sufficient purity, and the 40-MeV beam can. To produce europium-152, researchers would irradiate a highly enriched samarium-152 target. Next, the research team would use DANCE as a diagnostic tool to determine the impurities in the sample and as an instrument for measuring neutron capture on the sample. DANCE offers the right combination of neutron flux and detector efficiency required for the measurement. The crowning achievement: Couture would measure actual neutron capture cross sections on pure europium-152, the first ever for a pure form of this isotope.

As scientists try to unravel the mysteries held in the stars, they face a lot of hurdles. Due to the vast uncertainties in stellar mixing, scientists cannot decipher some of the enormously important information that stars of low initial mass hold about nucleosynthesis and structure evolution in the early stages of the universe.

In neutron capture, a neutron smashes up against an atomic nucleus and is absorbed, creating heavier isotopes. This kind of nuclear reaction simulates what happens in the stars; neutron capture is essential to the cosmic nucleosynthesis of heavy elements. In stars, neutron capture can be a slow process or a rapid process. For the Los Alamos research team and the field of astrophysics, the larger ambition is to study nucleosynthesis in the Sm-Eu-Gd region of the stars. There, neutron capture is a slow process.

"How do we end up with the elements we have?" Couture asked. "Basically, everything is made in the stars."



# Supporting new generator technologies

Radionuclide generators may look as low-tech as a plastic bucket, but the portable devices allow short-lived isotopes to be delivered in the clinic. Just six inches tall, with lead shielding and two thin tubes poking out of the top, it's a well-packaged solution. On demand at hospitals and outpatient imaging centers, medical technologists can extract a powerful radioactive drug that locates tumors or reveals heart disease in patients.

Yet so far, only a few kinds of generators are available.

For radiochemist Michael Fassbender, perfecting this emerging technology has been an ongoing project since 2005. This year, he announced a long-awaited advancement: a process that omits toxic ingredients and, in turn, could make a germanium-68/gallium-68 generator viable. Gallium can be used in PET scans.

On the U.S. market, no generator system for this pair of isotopes exists, and Fassbender's research could help open the doors for U.S. Food and Drug Administration approval. Fassbender's new separation technique also yields a greater amount of germanium-68, he said, because the isotope doesn't become volatile and distill away.

Los Alamos is the biggest germanium-68 supplier "on the face of the Earth" right now, Fassbender said. If a new generator were approved, the Laboratory could manufacture and purify this isotope and then ship it to a company that would package and deliver the generators to health care facilities.

Every generator poses unique challenges. Typically, within each bucket is a parent isotope that languishes slowly and a daughter isotope that vanishes rapidly. The daughter isotope, which is derived from the parent, is used as the active ingredient for imaging. "The challenge for us chemists is to find a clear-cut, rapid, and uncomplicated separation for the parent and the daughter," said Fassbender, who is collaborating with researchers at the University of Missouri, Columbia on yet another generator approach.

For diagnostic purposes, short-lived isotopes are needed to minimize the radiation dose to the patient, yet these last only a few minutes or hours and cannot be transported long distances. Consequently, in the past, health care facilities performing imaging had to be located near a nuclear reactor or cyclotron to obtain suitable isotopes for patient procedures.

Now, with portable generators, imaging centers can be located anywhere with the isotopes they need. With a bucket-sized generator on site, medical technologists can convert a long-life isotope into a short-lived one as needed, just before injecting the isotope into a patient, or feeding it into an imaging machine.

A pharmaceutical-grade germanium-68/gallium-68 isotope generator would offer a host of new options for PET imaging, according to Fassbender. Isotopes such as gallium-68 don't accumulate in a patient's muscle tissue and are necessary for imaging infection sources or cancer tissue, he said. In addition, with half-lives of 271 days and 68 minutes respectively, the germanium-68/gallium-68 would have a longer shelf life than some other commonly used generators with much shorter half lives.

### Isotopes (continued from page 7)

Nortier is already thinking outside the box. In his effort to produce actinium-225, he collaborated with astrophysicist Aaron Couture of Neutron and Nuclear Science, in the Blue Room. Located in the Weapons Neutron Research (WNR) facility–one of the five facilities served by the LANSCE accelerator–the Blue Room allows researchers to expose samples to a direct 800-MeV proton beam. In 1½ days, scientists can do a dozen experiments in the Blue Room. The Blue Room provides complimentary experimental capability to IPF as is operates at beam energies between 200-800 MeV as compared to IPF operating energies of 0-100 MeV.

The Office of Science's oversight has provided opportunities for R&D funding, such as this, which the Los Alamos isotope program has never known before. "We have been funded to pursue a proof-of-concept study on the accelerator-based production of actinium-225," John said. "This has been a highly collaborative project with LANSCE WNR staff."

That's how Nortier and Couture began putting their heads together in the Blue Room.

"Scientific collaboration can have the full support of management, but if the scientists won't talk, it's not going to happen," Lacerda noted. "Already having the scientists talking to each other is a huge step."

Within the three divisions and multiple groups connected to LANSCE is a rare combination of cross-disciplinary expertise–nuclear chemistry, radiochemistry, and physics.

## LOOKING TO THE FUTURE

Forging ahead, the plan at Los Alamos is to divide the isotope program's time and resources between 25 percent R&D and 75 percent production.

"Our vision is to get the cost of production so low for strontium-82 that private industry can take it over," Rej said.

Realistically, that milestone could take 5 to 10 years to accomplish, he added. By then, new isotopes might be ready to fill the slot that strontium-82 leaves, assuming that it can be rolled over to the private sector.

It will take time–as well as technological advancements –to restore the balance of production and R&D envisioned for the IPF. Important strides are already under way. In a series of efforts to engineer more reliable and more robust production targets (please see page 14), the IPF is getting closer to recovering beam time for R&D work, said Chemistry Division's Peterson.

However it plays out, the revitalized mission for the Los Alamos isotope program won't turn the production plant into solely an R&D laboratory.

"Production will always be the main priority–it's the reason IPF exists and is funded," Rej said. "Part of our mission is providing societal benefits to the nation, and I can't think there's a better example of what national laboratories do… And to me, it's Los Alamos at its best."

*For more information about the Los Alamos Isotope Production and Applications Program, please see isotopes.lanl.gov.*

### Kevin John (continued from page 18)

I'm exceptionally proud to be part of the teams at LANSCE and at the hot cell facility. There is a can-do attitude at both sites that is contagious.

Q: The National Isotope Program is now managed by the Office of Science's Office of Nuclear Physics, which wants to see more research and development at its isotope production facilities. How are you preparing for the new direction?

A: Through careful planning and investments we are methodically moving toward a healthy balance between our production mission and our desire to be a world leader in the R&D arena related to production and application of isotopes.

We are looking forward to expanding into other areas of medicine, as well as areas that align with core missions at LANL. In particular, we are pursuing accelerator-based production of actinium-225, which is a promising isotope in the treatment of certain forms of cancer.

From an R&D perspective, I view our efforts as setting the stage for the next production missions with the long-term aim of eventual U.S. commercialization. Our current actinium-225 research effort is a prime example. We anticipate that demand for this isotope will be very high given the current clinical trials, and we are exploring the application of IPF to meet that demand.

We are attempting to push IPF to its full potential by increasing the beam current delivered to our targets. We have recently demonstrated that we can operate IPF up to 350 microamps, but we need to advance our targetry to withstand the extreme thermal and mechanical stresses that higher beam currents present.

### Don Rej (continued from page 19)

isotope generation, such as actinium-225 alpha emitters. The Office of Nuclear Physics also supports technological R&D to further increase our production throughput and yield, and mitigate risks, all of which not only satisfies ever-increasing industrial demand but provides more beam time for research.

Q: Researching new isotopes often involves working with small amounts of material. With increased funding for research-and-development ventures, how are Los Alamos scientists preparing to address changes in scale?

A: The LANSCE IPF is well equipped to support research with one-off low-quantity production, and we already have some exciting work under way since 2009. In addition to the actinium work, the Office of Nuclear Physics is considering our proposals for the production of aluminum, arsenic, cadmium, europium, gadolinium, neptunium, plutonium, and sodium isotopes for a variety of basic and applied research in nuclear physics, national security, and medicine.

We often leverage other existing LANSCE capabilities for cross section measurement provided by the Lead Slowing-Down Spectrometer (LSDS) and the Detector for Advanced Neutron Capture Experiments (DANCE). These other substantial capabilities at LANSCE give us a distinct competitive advantage.

Q: Fostering new collaborations with universities is part of the new direction. Why is that important for the Los Alamos isotope program?

A: Universities are essential for many reasons, such as their outstanding faculty, facilities, student training, workforce development, and recruiting. We have existing partnerships with three universities–the University of Missouri, the University of New Mexico, and the University of Nevada, Las Vegas. We're pursuing new relationships with other universities.



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Published by Experimental Physical Sciences Communications:

Editor-in-Chief: Karen Kippen
Writer: Diana Del Mauro
Photographer, Designer: Robert Kramer
Copy Editor: Francisco Ojeda

To read past issues of *The Pulse*, see lansce.lanl.gov/pulse.shtml.





LALP-11-017

Los Alamos NATIONAL LABORATORY EST. 1943

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