Making Fresh Radionuclides with Leftover Gamma Rays

Photons in high-energy probe beams that pass through their intended target can be "reused" for making promising nuclides in nuclear medicine, new experiments show.

By **Charles Day**

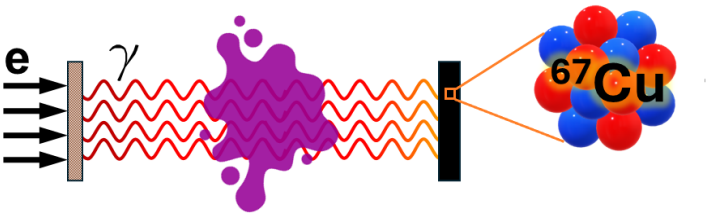
Radioactive nuclides are often used in medicine, as their emissions provide a wide array of energetic particles that can help diagnose and treat diseases. However, a challenge is creating nuclides that are both medically useful and cost-effective. Now Mamad Eslami of the University of York in the UK and his collaborators have demonstrated a new and efficient way to make radionuclides using leftover gamma rays from experiments at electron accelerators [**1**]. Specifically, the team showed that this recycling method could create two copper nuclides, copper-64 and copper-67, the second of which has proved difficult to make in sufficient amounts using previous methods. Medical researchers are especially interested in this pair of nuclides, as they could potentially be administered together to fight cancer—with one nuclide delivering therapeutic radiation and the other providing diagnostic imaging.

Nuclear medicine. Radioisotopes are used in a number of medical procedures, such as PET scans.
Credit: Gorodenkoff/stock.adobe.com

The strategy of combining therapy and diagnosis in one procedure is called theranostics. In nuclear medicine, the therapy side often involves attaching radioactive nuclides to antibodies and injecting them into a patient's bloodstream. When the nuclide-carrying antibodies reach their tumorous target, they latch on, and the locally delivered radiation breaks the DNA of the cancerous cells, killing them. On the diagnosis side, doctors have tools, such as positron emission tomography (PET), which also rely on nuclide–antibody combinations, but to locate tumors, not to kill them. Conceivably, two nuclides—one therapeutic, the other diagnostic—could be yoked to the same antibody, enabling doctors to monitor a treatment as it unfolds. This double yoking is easier if the nuclides have the same chemistry, which occurs when they are isotopes of the same element. Pharmaceutical companies have identified several promising theranostic pairs.

One such pair is that of copper-64 and copper-67. Copper-64 emits positrons, which can pinpoint tumors in PET scans, while copper-67 emits beta particles, which can attack cancerous cells. Both nuclides have clinically convenient half-lives, and their chemistry is well-known—specifically, the propensity of copper to bind to antibodies and other biomolecules has been extensively studied. The potential of copper-64 and copper-67 to treat cancers has been demonstrated in mice [**2**]. The isotopes in that mouse study were produced by bombarding a zinc target with high-energy protons, but the yield of copper-67 was too small—relative to that of copper-64—for theranostic applications.

Eslami and his collaborators have found a way to produce higher yields of copper-67. The method might also have a



Recycling gammas. An electron beam from an accelerator hits a foil, generating gamma rays that can be used to probe a sample (purple). Some of the gamma rays pass through this primary target and typically go to waste. Researchers have shown that these unused gamma rays can be harnessed to create copper-67, a medically useful nuclide.
Credit: M. Eslami/University of York

cost-cutting advantage, since it could piggyback on existing infrastructure. Eslami learned from colleagues that some particle-accelerator experiments run with intense electron beams for long periods and that some of the gamma rays generated by the beams are dumped after passing right through their intended target. Those wasted photons, he realized, could be harnessed.

Eslami and his collaborators tested their idea at the Mainz Microtron, an electron accelerator on the campus of the Johannes Gutenberg University Mainz in Germany. In their experiment, 855-MeV electrons struck a sheet of cobalt-iron-vanadium alloy, producing bremsstrahlung radiation—gamma rays—that subsequently impacted the team's zinc-foil target.

After 2 hours, the researchers measured the amount of copper-67 (and other nuclides) produced in the foil. In current studies with copper-67, patients receive doses whose radioactivity amounts to a few gigabecquerels (GBq), which corresponds to a few billion nuclear decays per second. Eslami and his colleagues found that their proof-of-principle experiment yielded about 0.06 GBq per hour, which implies that producing 4 GBq of copper-67 would take about 5 days. This production time is comparable to how long it takes for a high-flux research reactor to produce 4 GBq of lutetium-177, a nuclide used to treat neuroendocrine tumors and prostrate cancer.

Seeing if useful amounts of copper-67 could be produced was not the researchers' only goal. They also wanted to investigate the potential of producing other useful nuclides in gamma-ray collisions with zinc nuclei. From electron-beam-scattering data, they inferred the gamma-ray spectrum hitting their target. They then compared their radionuclide yields to a popular model of photon–nucleus reactions and found that there were discrepancies, particularly for the high-energy range of gamma rays. "Our data revealed clear gaps in the models," says Eslami. "That's a strong sign that new theory developments are needed in this energy range."

David Rotch leads the medical isotope development group at Oak Ridge National Laboratory in Tennessee. Ten years ago, he and his collaborators made copper-67 by bombarding zinc targets with gamma rays at Argonne National Laboratory in Illinois. They abandoned the project because contamination from natural copper reduced the radioactivity below the levels needed for therapy. But, he says, "The photonuclear production route is an excellent route to produce this isotope."

Charles Day is a Senior Editor for *Physics Magazine.*

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