The A-Bomb, 50 Years Later:
The Evolution of Nuclear Medicine

Fifty years ago this month, two atomic bombs were dropped on Japan, killing thousands of civilians and ushering in a quick and final end to World War II. The beginning of the postwar era signaled the birth of nuclear medicine as it is widely applied today. In fact, the same nuclear reactor that produced elements for the A-bomb project was turned over for the mass production of radionuclides for medicine and industry.

The link between the A-bomb and nuclear medicine, however, has always been a sensitive subject among nuclear physicians whose patients may associate radionuclide injections with mushroom clouds. Although this link is not justified, the government's interest in developing nuclear technology following World War II did have a significant impact on nuclear medicine: On the upside, millions of federal dollars were funneled into the production of radionuclides for research and medicine. On the downside, Congress established the Atomic Energy Commission (AEC)— which later became the Nuclear Regulatory Commission (NRC)—to oversee safety issues, making nuclear medicine the only medical field regulated by a federal agency.

In the wake of the Hiroshima and Nagasaki bombings, the U.S. government began to invest heavily in its nuclear program. Nuclear medicine stood to gain from these postwar policies, but it also suffered some setbacks.

As nuclear medicine evolved in the early postwar years, the government was there every step of the way offering the encouragement of a proud parent while at the same time setting up stricter and stricter rules like a parent afraid to let go. Similar to the government's investment in the space program, which resulted in spinoff knowledge and technology, its support of nuclear advances was the primary factor that shaped nuclear medicine into what it is today.

First Nuclear Reactor Holds the Key

When Italian physicist Enrico Fermi produced the first nuclear fission reaction in 1942, the race to build the atomic bomb had begun. Researchers using the 60-inch cyclotron at the University of California, Berkeley went underground to produce plutonium; in September of 1942, the Manhattan Engineering District (a.k.a. the Manhattan Project) at the University of Chicago was activated. One year later, the Manhattan Project yielded the first nuclear reactor for the production of plutonium.

"The wartime rush for the U.S. to build the A-bomb before the Germans greatly accelerated the building of the reactor," said Myron Pollycove, MD, a visiting medical fellow at the NRC. If not for this, Pollycove believes, the first nuclear reactor probably would not have been built until about 10 years later. Others contend that the motivation to build the A-bomb had an even greater effect. "The U.S. government would never have built a nuclear reactor during peacetime," said SNM historian Milliard Croll, MD. "If not for the development of the bomb, we never would have seen the widespread application of radioisotopes for medical purposes."

Once the technology for building a nuclear reactor was in place, a second reactor was built at Oak Ridge National Laboratory in Tennessee. During the early 1940s, the Graphite Reactor at Oak Ridge made large amounts of plutonium which was then transported to Los Alamos National Laboratory in New Mexico where the A-bombs were built. "Being involved in the bomb project was an intense experience," said Nobel Prize winner Glenn T. Seaborg, PhD, who worked on the Manhattan Project and is currently associate director-at-large at the Lawrence Berkeley Laboratory in Berkeley, CA. "We worked six days a weeks and evenings, but we were very determined to make the bomb before Hitler."

With the dropping of the A-bombs and the ending of the war, the Oak Ridge reactor was kept up and running for another purpose: to make radionuclides for medicine and research. On August 1, 1946, President Truman signed the Atomic Energy Act of 1946, creating the AEC to pursue the peaceful uses of nuclear technology. This relinquished the military's hold over isotopes and dispelled the secrecy surrounding the Manhattan Project. The very next day, the first shipments from Oak Ridge of carbon-

14 were sent immediately to at least 30 locations, including the University of Chicago, the University of Pennsylvania and the University of California.

The publicity surrounding the shipments was tremendous and centered on nuclear medicine finding a cure for cancer. This dream was fueled by a widely heralded paper published a few months later in the *Journal of the American Medical Association,* in which an endocrinologist reported a complete disappearance of hyperactive thyroid metastases after administering radioiodine to the patient. "The AEC commissioners knew they now had two jobs: to stockpile bombs behind closed doors and to pour money into cancer research out in the open," wrote Marshall Brucer, MD, in *The Heritage of Nuclear Medicine* (Society of Nuclear Medicine, 1979).

"Some people hoped the technology that grew out of nuclear physics wouldn't work, but the fact is that this technology is now an integral part of modern nuclear medicine. Now that the cold war is over, we have the opportunity to put this knowledge to use in the best areas."—Joseph McKibben, PhD, who worked at Los Alamoson developing the particle accelerators used to measure fissure cross-sections of ^{235}U for the A-bomb

Open Purses for Peacetime Efforts

With money rolling in from the government, Oak Ridge initially provided radioisotope supplies for free to universities, hospitals and industries. "The AEC was giving out millions of dollars, and the medical applications of radioisotopes was one of the hottest areas," said Darrell W. McIndoe, MD, a nuclear physician at St. Joseph's Hospital in Towson, MD, who previously worked at Oak Ridge. The field of nuclear medicine was a new frontier supported by the U.S. government and the press.

Although radionuclides for medicine were available before World War II from the Berkeley cyclotrons, only small quantities could be made and only at a high cost. The Oak Ridge reactor enabled scientists to produce the radioactive compounds inexpensively and in vast amounts. "There was a great deal of ego satisfaction and excitement in being involved with transforming A-bomb research into medical use to save human lives," said Ralph Kniseley, MD, who served as the associate chairman of medical distribution at Oak Ridge Associated Universities in the 1950s and 60s. "Those of us in nuclear medicine knew we were going to have some wonderful tools."

This enthusiasm resonated throughout the medical field and spurred Oak Ridge to begin training the first physicians in the practice of nuclear medicine. "Under the AEC's sponsorship, we trained about 150 to 200 physicians a year from the mid-1950s to the late 1960s," said Kniseley who headed the training program. "We taught trainees about the safe handling and measuring of radioisotopes as well as how to use them for therapeutic and diagnostic purposes." The course was only a month long, but Kniseley points out that nuclear medicine was much simpler back then. "In the early years, we didn't even have scintillation counters." What's more, only a handful of radioisotopes had been developed for medical applications, namely iodine-131 for thyroid disorders, chromium for labeling red blood cells, potassium-32 for leukemia and cobalt for megaloblastic anemia.

Public Fear of Anything "Nuclear"

Besides providing money for research and the availability of nuclear reactors, the post-World War II climate had another effect on nuclear medicine's early beginnings: It created a public fear of radiation. As newspapers began to report on an increase in leukemia and other cancers among bombing victims in the late 1950s, Americans became more and more frightened of radiation and its potential ill effects. "The reality is only a very small percentage of deaths from the A-bomb were caused by radiation fallout," said Pollycove. "Most victims died from the impact of the explosion, yet it was the cancer that stuck in people's minds." Americans' fears, however, were also based closer to home as residents of Utah and Nevada brought lawsuits contending that the above-ground nuclear weapons tests performed at the Nevada test site was increasing the incidence of cancer in their towns. The "cancer" label became affixed not only to nuclear weaponry but to everything associated with the nuclear age from power plants to nuclear medicine.

Fortunately, the images of mushroom clouds have faded somewhat from people's minds. "When I started practicing in the 1950s, there was a lot more fear of radiation among the American public than there is today," said Croll. Part of the problem was that scientists— knowing there was no justification for people's fears—simply brushed off the concerns instead of dealing with them and explaining why there was minimal risk. "Today patients are a lot better educated concerning radiation partly because physicians have become better communicators."

"The general population would like to run in the opposite direction when encountering radioactive substances. They don't realize the capabilities we have with nuclear medicine could not have started without the discoveries made with radioactive materials." – Raemer Schreiber who worked at Los Alamos on the core of the A-bomb dropped on Nagasaki

The fears of yesterday, however, are still leaving their imprint today. In response to concerns about radiation, health policy organizations, such as the International Commission for Radiation Protection (ICRP) and the Biological Effects of Ionizing Radiation (BEIR) Commission, were formed in the years following World War II to ensure that both the U.S. and other countries did not expose their citizens to unsafe levels of radiation. These groups have recommended setting such low permissible levels of radiation exposure that the standards are nearly impossible to meet, according to Pollycove. Yet, the NRC and other federal agencies often base their rules on these recommendations. Moreover, the BEIR Commission and other groups have developed their standards for radiation risk on data from A-bomb survivors and the linear dose hypothesis, which assumes that health effects increase as the radiation dose rises from zero. "When the linear dose hypothesis was introduced around 1960, all we had was data from Nagasaki and Hiroshima where bombing victims were exposed to super high levels of radiation," said Pollycove. It was assumed that if a short-term high exposure to radiation caused cancer then a longer term exposure to low levels of radiation must raise a person's risk as well. Several studies have since found that low doses of radiation may repair breaks in the DNA and may lower the risk of carcinogenesis. Thus, he asserts, there may be no justification for the low standards.

What effect does this have on the practice of nuclear medicine? For one thing, it slows the process of selecting sites for low-level radioactive waste disposal. In addition, "the ridiculously low permissible levels that are now in place forces the NRC to enact strict misadministration rules," said Pollycove. Thus, physicians and researchers must report spills and disposal mishaps of radioactive wastes that involve harmless amounts of radiation.

The Cold War Ends, the Budget War Begins

The ending of the arms race between the U.S. and Russia may help nuclear medicine step out of the shadow of the nuclear weapons program. In theory, the technologies used to accelerate particles for defense purposes can now be directed to medical applications, and the money spent on war machines can be diverted to basic research. What seems to be happening, however, is exactly the opposite. "When the Department of Energy (DOE) was spending billions on military programs, it could spin off a mere $35 million a year for its medical isotope program," said Pollycove. "Now that the DOE's budget is being slashed, there may not be any overflow of funds for nuclear medicine programs."

The 30 national physics laboratories run by the DOE are currently in a state of flux. "Most of the isotope producing facilities were constructed for weapons-related projects," said Emory Collins, program manager for the isotope program at Oak Ridge. "As these projects have been shut down, our ability to make radioisotopes for medical research has become more and more difficult." When the cyclotrons were already in use for defense contracts, they could be kept running for research projects at a relatively low cost. Now that military projects won't defray the costs, producing isotopes will become much more expensive, according to Collins.

At Oak Ridge, for instance, 10 of 15 buildings containing hot cells have been closed recently. Hot cells are shielded facilities that scientists use to purify and extract particular radionuclides and are just as vital to production as reactors and accelerators, contends Collins. The scarcity of hot cells has drastically prolonged the amount of time required for processing an order of, say, tungsten-188 for cancer therapy. "It's much more difficult to operate today," he said. "We have received requests for radioisotopes from medical researchers that we cannot possibly meet."

The development of the atomic bomb and subsequent nuclear weapons program seems to have held a mixed bag for nuclear medicine. Without the World War II development of atomic technologies and postwar funding for peaceful uses of the atom, nuclear medicine never would have progressed as rapidly and, some contend, it may never have come into widespread application at all. Without this initial help, however, the U.S. government may not have developed the strong foothold it now has in nuclear medicine, and the specialty would not be bogged down by federal regulations. Whether nuclear medicine would have been better off with or without the government's interest may be a matter of debate. One thing is for certain, however: The policies established during the decade following World War II will have everlasting effects.

Deborah Kotz

"I was pleased to see that after the war the Oak Ridge nuclear reactor was used for producing large quantities of radioisotopes for medicine and research, which hadn't been possible with the cyclotron. On a personal note, the mass production of ^{131}I saved the life of my mother who suffered from hyperthyroidism." –Glenn T. Seaborg, PhD, who produced plutonium for the Manhattan Project and won the Nobel Prize for his discovery of several radioisotopes including ^{131}I

NEWSLINE

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Nuclear Medicine in Japan

Although nuclear medicine was born in the 1920s when radioactive tracer technology was applied to medicine, its rapid growth occurred in the years directly following World War II. In 1946, civilian institutions began receiving supplies of radioactive compounds for the purpose of a peaceful use of atomic energy. On April 10, 1950, Japan received its first overseas shipment of a reactor-produced radioisotope from America. It was a gift from the American Philosophical Society to Yoshio Nishina, PhD, a famous nuclear scientist who constructed one of three cyclotrons in 1937, all of which were unfortunately destroyed in November 1945 by the U.S. army occupying Japan. The shipments of radioisotopes from Oak Ridge National Laboratory continued and were shared by five research laboratories, including university hospitals where radioactive tracer technology was applied to patients.

Japan Radioisotope Association (JRIA) was founded in 1951 as a nonprofit organization with the purpose of facilitating the use of radioisotopes in Japan; even now, all radioisotopes, including radiopharmaceuticals, must be purchased through JRIA. By conducting periodic nationwide surveys, JRIA has been able to provide reliable and precise statistics related to nuclear medicine in Japan. For example, they have documented that 6600 in vivo procedures and 260,000 radioassay tests were performed in one day in 1992 at 1250 nuclear medicine facilities.

When I started my medical training in 1964 in the Second Department of Internal Medicine at The University of Tokyo, I saw the sign "The Japanese Society of Nuclear Medicine" hanging on the door of the secretariat's office and realized that I had never heard of this medical specialty. Two years later, Professor Hideo Ueda, MD, chairman of the department, invited me to become a member of the radioisotope group in the department. The assignment was based on my first case report of a 63-year-old woman who had died of a thorotrast liver injury caused by an angiography she had received 32 years earlier. While I was in charge of this patient, I learned how to perform whole-body counting for spectrum analysis and microautoradiography on a liver biopsy specimen, which clearly demonstrated a trace of Thallium-232.

From 1969 to 1971, I was a research fellow in nuclear medicine at The Johns Hopkins Hospital under the guidance of Professor Henry N. Wagner, Jr., MD. It was during this time that I became convinced nuclear medicine could serve as a clinical specialty—although it was then still regarded as clinical research in Japan. In 1974 the first World Congress of Nuclear Medicine was organized by Prof. Ueda who served as president and Dr. Ilio who served as secretary general. I worked very hard serving as the secretariat.

Currently, regulations on the use of radioisotopes and radiation are very strict in Japan. In a way, this protects the nuclear medicine specialty since all studies using radioisotopes, even radioassays, must be performed in a licensed restricted area which is under the control of nuclear physicians. Many people in Japan are still very sensitive to and even scared of any kind of radiation. This is unreasonable but understandable as we are the only people in the world who experienced atomic bomb attacks. The strong desire among the Japanese for the abandonment of atomic weapons is alive half a century after the bombings.

The Japanese Society of Nuclear Medicine was founded in 1960 and has promoted nuclear medicine. There are now about 3500 members in the Society. The 35th Annual Meeting of the Japanese Society of Nuclear Medicine will be held this year from October 4 to 6 in Yokohama City. As president of the Society, I would like to welcome all foreign participants who wish to attend the International Session of the Meeting where all presentations and discussions will be held in English for the first time. I hope this trial run will facilitate international communication and provide a good opportunity for overseas participants to be exposed to nuclear medicine in Japan, thus promoting nuclear medicine in this region.

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