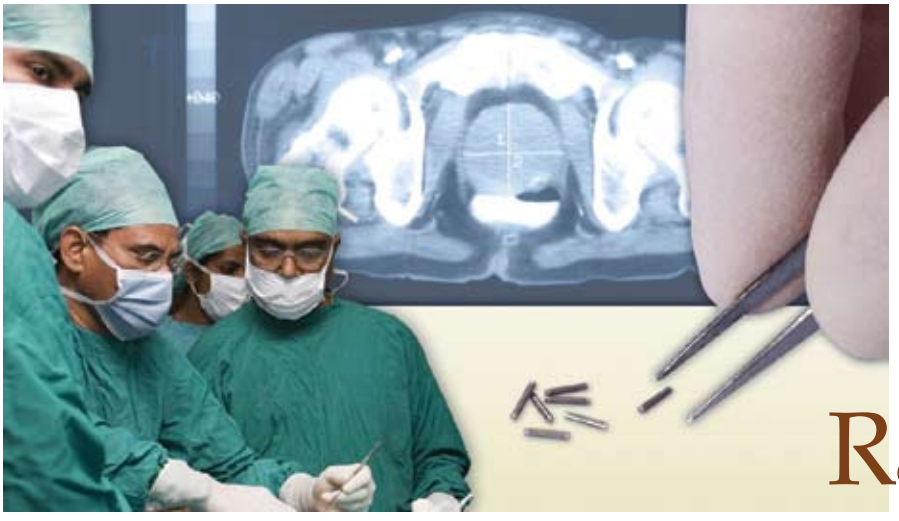


Doctors using cesium-131 radiochemical brachytherapy "seeds," to treat prostate and other cancers. Cesium-131 has a significantly shorter half-life than the two other isotopes commonly used for brachytherapy, allowing faster delivery of therapeutic radiation to the prostate gland, reduced incidence of common brachytherapy side effects, and lower probability of cancer cell survival.

Radioisotopes: The Medical Lifesavers That Congress Is Suppressing

by Christine Craig

The cost of the U.S. policy restricting radioisotope production and use can be measured in human lives lost. Reviewed here is the history of radioisotope suppression, and the promise of new research with alpha emitters.

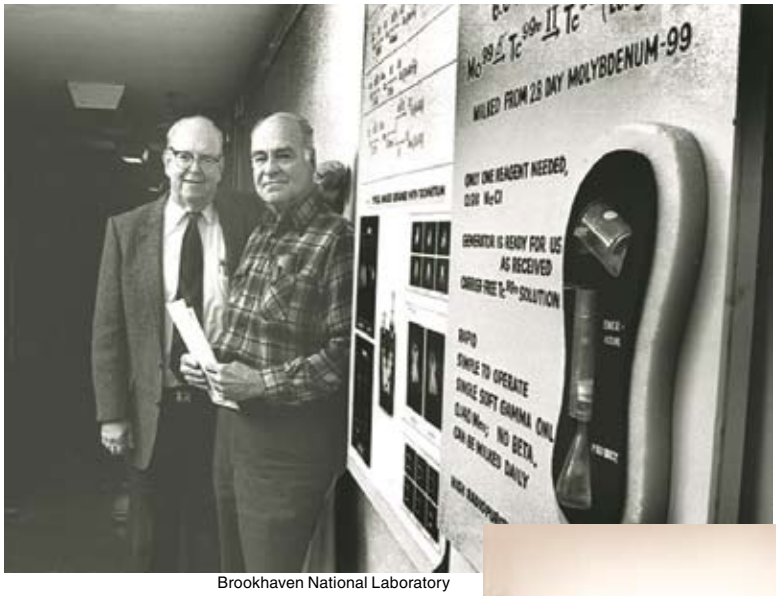
Part I

U.S. Radioisotope Production and Use

The use of radioisotopes for the diagnosis and treatment of disease is now a vital part of modern medical practice. Aside from a few simple treatments for mild infections, it is difficult to imagine a modern medical diagnosis and treatment strategy that does not involve the use of radioisotopes. The industry is huge, and becoming larger as new technologies are discovered and developed. But this growing industry rests on shaky foundations, leaving many areas of the industry susceptible to sudden collapse, and putting potentially millions of patients at risk worldwide.

The most vulnerable link is the production and supply lines of the medical radioisotope most in demand throughout the world, technetium-99m. This man-made isotope was created 50 years ago at the Atomic Energy Commission's Brookhaven National Laboratory in New York, by scientists Walter Tucker and Margaret Greene, while they were working on refining another radioisotope, iodine-132. Tucker and Greene developed the first molybdenum-99/technetium-99m generator, and Powell Richards, also of Brookhaven, fostered its development for medical purposes. But in 1966, the laboratory bowed out of production, leaving the playing field open to two private companies, Mallinckrodt and Union Carbide. At the time, Brookhaven could not keep up with demand for the versatile isotope!

Therein lies the tale. The U.S. Atomic Energy Commission, which ran the Brookhaven laboratory, left the technology to industry, and industry left the country with the technology, leaving the United States with no domestic source for an isotope that is used in more than 30 million diagnostic procedures each year worldwide, and almost 20 million procedures in the United States alone. Now the United States relies on other countries, and specifically Canada, for all of its technetium-99m needs, even though we are the major consumer of such diagnostic procedures worldwide. This folly of globalization has left our nation in an extremely precarious position regarding technetium-99m



Brookhaven National Laboratory

Walter Tucker and Powell Richards, radioisotope pioneers at Brookhaven National Laboratory. Tucker, working with Margaret Greene, created the first molybdenum-99/technetium-99m generator (right). Richards fostered its development for medicine.

In 1998, Mallinckrodt dedicated its new medical building in Petten, the Netherlands, to Richards, installing a bronze plaque with his prophetic words about the isotope: "Technetium-99m should be a useful research tool; it combines a short half-life and unique radiation characteristics. The absence of beta radiation reduces the amount of damage to biological systems usually associated with radioisotopes."

supply, as the last two years have dramatically shown.

Technetium-99m: An Unstable Supply

More than 80 percent of almost 23 million radiopharmaceutical injections given in the United States yearly use technetium-99m (Tc-99m), derived solely from foreign sources, mostly from the Chalk River reactor in Canada and the High Flux Reactor (HFR) in Petten, the Netherlands (see Table 1). Tc-99m is a daughter product of molybdenum-99 (Mo-99), a radioisotope produced as a fission product of highly enriched U-235 targets placed in the reactors.

Without warning, on Nov. 17, 2007, the Chalk River National Research Universal (NRU) reactor was shut down by Atomic Energy of Canada, Ltd., at the request of the Canadian Nuclear Safety Commission. At issue was not a malfunction or a dire safety problem threatening to harm the community, but a long-standing dysfunctional relationship between the operator, Atomic Energy of Canada, and the regulator, the Nuclear Safety Commission, regarding some mandated safety upgrades to the reactor. After the Parliament intervened with emergency legislation, the reactor went back on line in mid-December 2007. In the meanwhile, thousands of medical patients had been prevented from having imaging tests because of the shortage of Mo-99.

Chalk River is a small 1950s vintage research reactor, which has only 5 percent of the power of Canada's CANDU commercial power reactors. Yet it supplies more than 50 percent of the world's Mo-99, the raw material for Tc-99m, which is used for more than 85 percent of the world's medical nuclear imaging procedures.

The NRU is now at the end of its useful life, and MDS Nordion, the corporation with the monopoly on Canadian molybdenum production and distribution, at least had the foresight to plan ahead. The company worked for decades to get two new isotope reactors up and running at the Chalk River site. The two reactors, MAPLE 1 and 2, were to have replaced the aging NRU, allowing Canada and Nordion to continue to dominate the medical isotope market for decades to come. Unfortunately, after numerous setbacks in the design, construction, and financing of the two reactors, MDS Nordion and the Atomic Energy Commission

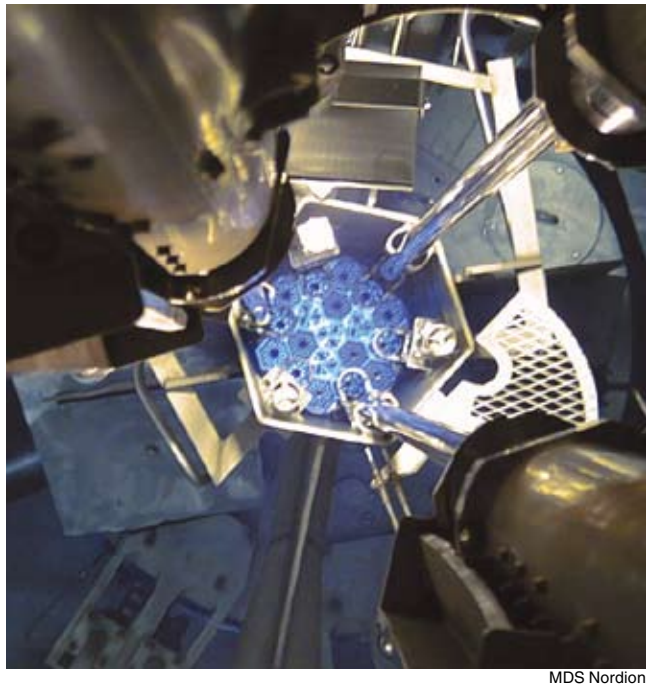
Table 1
MAJOR ISOTOPE PRODUCING REACTORS

Year Nuclear Reactor	Built	Product Country	% World Distributor	Present Mo-99	Status
National Research Universal (NRU)	1957	Chalk River, Canada	MDS-Nordion	40	Offline until May 2010
High Flux Reactor (HFR)	1961	Petten, Netherlands	Covidien IRE	20 10	Offline until August 2010
South African Fundamental Atomic Reactor Installation 1 (SAFARI-1)	1965	Pelindaba, South Africa	NTP	10	Online
Belgian Reactor 2 (BR2)	1961	Mol, Belgium	Covidien IRE	5 4	Online
OSIRIS	1964	Saclay, France	IRE	3	Online

Padraic Ryan

The Chalk River nuclear complex in Canada.

Inside the NRU Reactor at Chalk River, Canada, where MDS Nordion irradiates HEU targets to produce medical isotopes.



MDS Nordion

The Maple 1 reactor at low power.

announced in April 2008 that the already constructed reactors would be mothballed. The NRU has been approved to operate until 2015. After that, unless the MAPLE reactors are resuscitated, Canada will be without a Mo-99 nuclear reactor production facility.

Since that 2007 shutdown, the medical world has been hit with new shortages, as one or more of the five main Mo-99-producing reactors have gone off line for maintenance or repairs in the last year-and-a-half. In May 2009, the NRU was again taken off line for repairs after it leaked tritium from coolant pipes. It remains offline today, its start-up date now pushed back to at least May 2010. And now, the High Flux Reactor (HFR) in the Netherlands has just gone offline until at least August 2010 to repair its leaking pipes. This leaves the world without the two most productive Mo-99 producers for at least three months, and perhaps much longer.

A Sad History

Until 1989, the 5-megawatt Sterling Forest reactor run by Cintichem (Union Carbide, et al.) in Tuxedo Park, N.Y., was irradiating U-235 targets to generate Mo-99. The reactor sprang a leak, and instead of fixing it, the company sold its technology

to the U.S. Department of Energy. In return, it was allowed to decommission the reactor, leaving the DOE to do the cleanup. That is how the United States came to be without a domestic source of Mo-99. It was cheaper for Union Carbide, Mallinckrodt, et al. to move to Europe and use willing government-subsidized reactors for their Mo-99 production.

The DOE sabotage did not stop there. Now the DOE, under a directive from Congress, is preparing to eliminate the supply of the uranium-233 feedstock, which decays to produce valuable alpha-emitting isotopes.

Uranium-233 (U-233) is not at present a naturally occurring isotope of uranium. It is purely a product of the ingenuity of mankind in the nuclear age, a product of the still-nascent *isotope economy*[1] that began a century ago with discoveries that led to the realization that elements were not fixed and unchanging primary substances, but were themselves composed of transmutable subspecies, differing in the number of neutrons within the nucleus.

All of the U-233 now on our planet was created artificially by breeder reactors in nuclear weapons programs and in nuclear fuels research, by bombarding thorium-232 (Th-232) with neutrons (Figure 1). Neutron capture leads, through the short-lived intermediates thorium-233 and protactinium-233, to U-233, a fissile isotope with a half-life of 160,000 years.

Uranium-233 also decays naturally to thorium-229, a precious medical isotope. It takes 160,000 years to generate 1 kilogram of Th-229, the daughter product, from a 2-kg source of U-233. Since, to date, U-233 decay has been virtually the only source of Th-229 on our planet, and the oldest U-233 is less than 60 years old, it is obvious that Th-229 is a scarce commodity, indeed, a rare jewel of incalculable worth. And yet, the U.S. Department of Energy has set in motion plans to dispose of both the mother and daughter products.

The 45-megawatt High Flux Reactor at Petten.

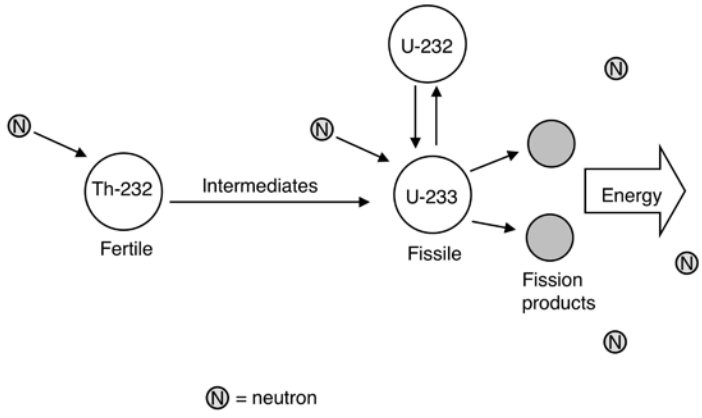


Figure 1
SIMPLIFIED DIAGRAM OF THE THORIUM FUEL CYCLE
The neutron trigger to start the thorium cycle can come from the fissioning of conventional nuclear fuels, or an accelerator. When neutrons hit the fertile thorium-232, it decays to the fissile U-233; a neutron striking the U-233 leads to fission products, more neutrons, and a lot of energy. (Not shown is the short-lived intermediate stage of protactinium-233.)

The Idaho National Laboratory has already shipped a store of 300 kg of aged U-233, mixed within 30 metric tons of Th-232, which originally came from the decommissioned Shippingport light water breeder reactor[2] in Pennsylvania to the Nevada Test Site for burial. The inventory of U-233 at Oak Ridge National Laboratory is also set for burial.[3] The plan is to down-blend it with the non-fissionable U-238 and ship it to New Mexico for storage in the next few years.

These isotopes are being treated as dangerous garbage, which must be disposed of to remove a politically imagined nuclear weapons proliferation threat. The reality is that they are priceless resources. The U-233 bred from Th-232 is not only capable of powering a nuclear reactor to provide needed electricity for our power grid,[4] but its decay product, Th-229, with a half life of 7,340 years, is the source of two short-lived daughter nuclides—actinium-225 (Ac-225) and bismuth-213 (Bi-213)—which are highly prized in the medical field as next-generation treatments for cancer and even HIV and other infectious diseases (Figure 2).

The premature burial plan comes after both the Oak Ridge and Idaho labs had developed highly publicized plans to extract the Th-229 from the U-233 before disposal, for the express purpose of providing a steady supply of Ac-225 and Bi-213 for medical research and clinical trials. But, in the last three years, the DOE, at the behest of Congress, has very quietly pulled the plug on both programs, thus slaughtering the goose that laid the golden egg.

A May 2008 Special Report by the Office of the Inspector General of the Department of Energy,[5] made a strong case that the DOE plan, to dispose of its U-233 stocks without first extracting the accumulated Th-229, was foolish, for it would provide no assurance that sufficient quantities of uranium-233 and its valuable progeny

Alternative Ways To Produce Mo-99

There are at least four separate paths to Mo-99 production, with several possible technologies available for each path. Only the first method has a proven track record. The other methods are under development and investigational.

(1) U-235→Mo-99 (6%) + other fission products (94%)

This can be achieved through fission of high-enriched uranium targets or low-enriched uranium targets in nuclear reactors, or through accelerator-generated neutron fluxes to similar targets. Essentially all Mo-99 is made this way in nuclear reactors, followed by chemical processing of the targets and extraction and purification of the Mo-99 for use in Mo-99/Tc-99m generators.

Although the reactors now producing the bulk of Mo-99 are at the end of their lives, there are several existing reactors that could be brought into service for this task.

- The two new Canadian Maple reactors, built specifically to produce Mo-99, were completed but mothballed in 2008 because of design flaws. These could be resuscitated if experts put their heads together. The Maple reactors could probably supply the world's present needs and then some, even if converted from high-enriched to low-enriched fuel and targets.
- Another reactor capable of the high neutron fluxes required to produce Mo-99 is the Fast Flux Test Facility in Hanford, Washington. Although in perfect working order, the FFTF was killed by the Bush Administration in 2005, and is now in cold standby, awaiting a final DOE decision about what to do with it. It could be brought online to produce Mo-99 and many other medical isotopes.
- There are several other reactors at the national labs that could also be used. Further, university research reactors, such as the MURR at the University of Missouri, could be retrofitted to produce Mo-99 as well.

New Systems Under Development

Several novel systems are being developed to deliver the neutron flux necessary to fission uranium to Mo-99, including accelerator-driven systems and liquid reactor systems.

- Babcock & Wilcox of Lynchburg, Va. has received Federal funding to help it bring online several aqueous homogeneous reactors, each with a reactor vessel the size of a 50-gallon drum. The reactor has no fuel rods, but is a solution of low-enriched uranium nitrate or sulfate able to cycle from the reactor through tubing and back to the reactor. Some of this solution would be run through columns able to bind the Mo-99, leaving the rest of the liquid to return to the reactor. This Mo-99 would then be purified and made into Mo-99/Tc-99m generators.
- Several companies, including Advanced Medical Isotopes Corp. (AMIC) of Kennewick, Wash., are testing small linear accelerators capable of producing a particle beam (proton or electron) which can be run through various primary targets which will generate a neutron flux to a uranium target, fissioning the uranium to Mo-99 and other products as above. AMIC's machine is small and designed to be situated near a medical facility.

The linear accelerator (linac) at the Australian Synchrotron in Clayton, Victoria.

TRIUMF Depicted here is the method of electron-accelerator-driven photofission to produce Mo-99.

AccSys Technology, Inc.

AMIC (Advanced Medical Isotopes Corp.) has selected this proton linear accelerator (PULSAR) manufactured by AccSys Technology, Inc. for the production of positron emitting isotopes.

(2) U-238→Mo-99 (6%) + other fission products (94%)

- TRIUMF, a consortium of universities and other institutions in Vancouver, Canada, is pursuing a plan to use photo fission (fission produced by an electron particle accelerator bombarding mercury or tungsten targets to produce a neutron flux) of natural uranium targets to produce Mo-99.

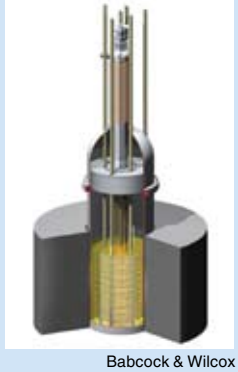
(3) Mo-98→Mo-99

The naturally occurring, (~24%) long-lived isotope of molybdenum can be transmuted through neutron capture to produce Mo-99, using either neutrons from a nuclear reactor, or neutrons generated by particle accelerators. Small producers in several countries already use this method for indigenous use.

- CERN, the European Organization for Nuclear Research laboratory in Switzerland, has a plan to produce enough Mo-99 to supply present world needs. CERN would use a proton accelerator (1-megawatt beam) with Adiabatic Resonance Crossing to create a flux of neutrons equivalent to that of a research reactor, which would produce Mo-99 from Mo-98 targets by neutron capture.

(4) Mo-100→Mo-99

The naturally occurring (~10%) long-lived isotope of molybdenum can be transmuted into Mo-99 by an electron accelerator, which irradiates secondary targets that produce high-energy photons. These photons then bombard the secondary Mo-100 target, dislodging a neutron to produce Mo-99.



Babcock & Wilcox

The Babcock & Wilcox design for an aqueous homogenous reactor to produce Mo-99.

isotopes will be available to support U.S. medical and scientific research needs. The report noted:

- The Department is the only domestic producer of progeny isotopes from uranium-233 and current production is insufficient to meet medical and scientific research needs. Once the planned disposal of uranium-233 is complete, the Department will not have the means to increase isotope production to meet the dramatic projections of future needs for actinium and bismuth;
- At present, no viable alternative methods of production of actinium and bismuth have been demonstrated or proven; and,
- Uranium-233 also is used to support other Department missions such as the National Nuclear Security Administration's Test Readiness Program.

The report concluded:

Should the Department elect to proceed as planned, it may dispose of a national resource that is irreplaceable. The potential for isotopes produced from uranium-233 to help save the lives of thousands of American cancer patients is widely accepted, and one top Departmental official estimated that isotope production from ORNL stocks alone could be used to treat about 6,000 patients annually. While we are sensitive to the complex public policy implications associated with this matter, including significant budgetary issues, we believe that the Department should explore alternatives for ensuring a stable domestic supply of the important isotopes produced from uranium-233.

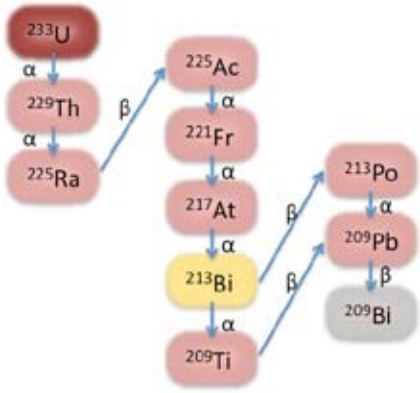


Figure 2
WHAT CONGRESS IS WASTING: THE URANIUM-233 DECAY CHAIN
Uranium-233 is fissionable and can be used to power reactors. Its decay product thorium-229, with a half life of 7,340 years, is the source of two particularly valuable short-lived daughter nuclides—actinium-225 (Ac-225) and bismuth-213 (Bi-213). These are prized in the medical field as next-generation treatments for cancer and even HIV and other infectious diseases.

DOE

The first Shippingport Spent Fuel Canister (SSFC) being welded for storage in underground vaults at the Canister Storage Building, where they will stay until permanent burial—instead of being used to produce radioisotopes.

Thorium Sabotage at Oak Ridge

Oak Ridge National Laboratory, which pioneered in the production of radioisotopes after World War II, has been a storage depot for U-233 supplies for more than 30 years. This includes U-233 produced in the ORNL molten salt breeder reactor, which was shut down in the mid 1970s. In 1995, funding was awarded to the Nuclear Science and Technology Division at ORNL to facilitate extracting the accumulated thorium-229 from the breeder reactor waste tanks in Building 3019A at the Radiochemical Development facility (Figure 3). Previously, the thorium extraction had been funded with internal laboratory funds only, including by selling one third of the waste sludge to a Dutch pharmaceuti-

DOE

The last shipment of Spent Nuclear Fuel From the Oak Ridge National Laboratory to the Idaho National Laboratory (INL) in 2003, where it was being stored until its "final disposal." Its valuable radionuclides are now lost to use.

Figure 3
WHERE THE TREASURE WAS STORED: BUILDING 3019A AT ORNL
Building 3019A at Oak Ridge National Laboratory stored the breeder reactor spent fuel tanks, from which thorium-229 could be extracted. To save maintenance costs, the DOE proposed closing the building and sending the contents to a burial ground, after extracting the Th-229. But Congress reversed this plan in 2006, cutting the funds to carry it out, committing all the material to burial without extracting the valuable Th-229.

cal company, PharmActinium, Inc., for its radioisotope production.[6]

Over the years, much of the thorium had precipitated out of solution onto neutron-absorbing boron-glass rings (Raschig rings) within the tanks, and was easily extracted, then purified. From these initial supplies came the first actinium-225 and bismuth-213 for medical research. In fact, Oak Ridge scientists from the Life Sciences Division, using these supplies, were part of the groundbreaking research demonstrating the potent cancer-killing potential of alpha-emitting isotopes when coupled with an effective targetting mechanism.

That initial thorium extracted from waste, plus additional small quantities of thorium extracted from samples which have been pulled out for examination from containers stored in Building 3019A throughout the years, amounts to 150 millicuries (mCi), or about three-quarters of a gram, from which can be extracted, or "milked," 100 mCi of Ac-225 every 60 days. Without additional sources of Th-229, or new technologies for creating the daughter isotopes Ac-225/Bi-213, research will be severely limited by the existing meager supplies of extracted thorium. The present Oak Ridge Th-229 supplies would yield quantities of daughter nuclides sufficient to treat only about 100 patients per year.

The stored remaining stock of U-233 at ORNL—some 450 kg within some 1,400 kg of uranium-containing materials—presently contains about 37 remaining grams of Th-229 as a decay product. An additional amount (perhaps 69 grams) of Th-229, as mentioned above, was stored until recently within the Shippingport fuel rods at the Idaho National Laboratory. This has since been carted off to the dump at the Nevada Test Site, leaving ORNL as the sole domestic supplier of daughter nuclides from U-233.

If the 37-grams of Th-229 accumulated in the U-233 in Building 3019A were extracted, the number of patients who could be treated would be 50-fold greater than at present, and no new technology would even be necessary. This would give the medical research community enough ammunition to proceed expeditiously with its alpha immunotherapy research, backed by the security of a greater-than-7,000-year baseline supply of Th-229, continuously generating the Ac-225 and Bi-213 needed for cancer therapies.

One Step Forward —and Two Steps Back

In 1996, the DOE held a workshop on Alpha-Emitters for Medical Therapy, in Denver. According to the report on the workshop:

> A major consensus was the need for focussing research and development on two promising alpha-emitters: astatine-211 (^{211}At) and bismuth-213 (^{213}Bi). The latter is being currently supplied from abroad and has been linked to a specific monoclonal antibody against tumor cells being prepared for the first clinical trial, phase I, at the Memorial Sloan Kettering Cancer Center in New York, N.Y.[7]

From where abroad was the Bi-213 coming? The former Soviet Union was the only other generator of enough cold-war U-233 to possibly extract significant amounts of Th-229 for medical treatment. However, it was the Institute of Transuranium Elements in Karlsruhe, Germany, that was providing the Bi-213 for the U.S. cancer trials, using thorium-229 received from ORNL!

According to the report: "Preclinical studies with ^{213}Bi have been completed using a 20 mCi actinium-bismuth generator from Karlsruhe, Germany produced from ^{229}Th recovered at a DOE facility." This thorium-229 stock was received from Pharmactinium, Inc., the same company that had purchased some of the breeder reactor waste sludge from ORNL in 1994. The irony of a foreign institute providing a U.S.-derived isotope to the U.S. researchers was not lost on the workshop participants, who concluded:

> A more rapid development of α-emitters should be a national effort by the DOE. This demands *short-term actions for immediate development*, and longer term commitments over the next few years. DOE could provide absolutely essential support for the necessary basic research. This should include radionuclide availability for these projects, and the studies in radiobiology, radiochemistry, dosimetry and toxicity required for designing clinical trial protocols.

In January 2001, the DOE finally got moving on the project to extract the thorium-229 from the U-233 stored at ORNL, as

a DOE report states:

> On January 8, 2001, former Under Secretary of Energy Moniz signed Excess Material Deposition Decision Memorandum No. 2, which established the path forward for managing the U-233 stored at ORNL. Specifically, this memorandum determined that there is no programmic use for the U-233 currently in storage at ORNL other than as a possible source of medical isotopes. The memorandum directed that a Request for Proposals (RFP) be issued that will require a contractor to:
>
> • Process the U-233 to extract Th-229 for use as a source of medical isotopes;
>
> • Further process the U-233 to eliminate current concerns regarding criticality, stability in storage, and provision of safeguards and security; and
>
> • Remove the U-233 material from Building 3019A, allowing the building to be deactivated.[8]

The DOE had decided to kill two birds with one stone. Eager to get rid of the expensive security burden of continuing to store the U-233 in Building 3019A, the Department determined that the uranium was not necessary for any DOE programs, and that millions of dollars in security and radiation protection services could be saved each year if the U-233 were down-blended with the non-fissionable U-238—to remove any danger of criticality accidents or theft by nuclear terrorists—and carted off to a suitable storage repository in New Mexico. Building 3019A was to be shut down.

To put a positive spin on this trashing of a national treasure and to gain proponents for the project, the DOE incorporated into its U-233 disposal plans a concomitant thorium-229 extraction phase, which would salvage the valuable isotope before down-blending the uranium. The DOE put out a proposal, conducted an environmental impact study, and hired a consortium of companies called Isotek[9] to design, manage, and carry out the project. The consortium carried out the design phase of their task in good faith, and its extensive and interesting work was outlined in a paper detailing its efforts and planned future activities (Figure 4).[10]

But by 2006, the DOE was forced to change its plan to extract the Th-229 from the U-233 before processing for disposal (Figure 5). Congress had decided against the isotope extraction, and had provided no funding for the project. A DOE report states:

> In the November 2005, Conference Report for the Energy and Water Development and Related Agencies Appropriations Act for Fiscal Year (FY) 2006, the conferees provided no funding for the Medical Isotope Production and Building 3019 Complex Shutdown project. The conferees' action directed DOE to terminate promptly the Medical Isotope Production and Building 3019 Complex Shutdown project. Per DOE's recommendation, the responsibility for the disposition of the ^{233}U was transferred to the Environmental Management (EM) program. The conferees provided FY 2006 funds in the Defense EM appropriation for the disposition of the material stored in the Building 3019 Complex and directed the Department to provide a report within 60 days detailing a path forward for managing the material.[11,12]

The new directive, needless to say, had dropped all plans to extract the valuable Th-229 from the "waste" U-233.

Nuclear scientists and medical researchers were outraged by Congress and the DOE's double-cross on Th-229 extraction. In the public comment section of the DOE's 2007 Environmental Impact Report on the revised plan, Dr. Rose Boll of the Department of Chemistry at the University of Tennessee, who had worked with ORNL for years on Ac-225/Bi-213 isotope development for medicine, made the following statement:

> Please include in the actions of this process, the separation of the Th-229 from the ^{233}U. The increased cost in the overall process for the recovery of the Th-229 from the ^{233}U is minimal (1-5%).
>
> The Th-229 isotope is being used for medical treatment and research with very promising results. Th-229 exists in limited quantities in our world. The

Congress Throws Away $100 Billion Per Gram

The magnitude of waste of resources demanded by Congress in the name of saving money, by cutting out "1-5%" of the cost, can be calculated in dollar terms. The present value of Ac-225, the daughter isotope of Th-229, is roughly $2.5 million per Ci. The yield of Ac-225 from present stocks (~.75 g) of Th-229, based on a 60-day campaign cycle of extracting the Ac-225 from the Th-229 by present ORNL techniques, is about 100 mCi per campaign. That comes to 600 mCi per year, with a value of $1.5 million.

The estimated additional Th-229 available from processing the U-233 (now considered waste and slated for burial) is 37 g—50 times the present stock. This 50-fold greater quantity of Th-229 would yield 30 Ci of Ac-225 every year, rain or shine, for many thousands of years.* That comes to around $75 million per year, in perpetuity, from slightly over an ounce of parent Th-229.

The quantity of Ac-225 required to produce this $75 million, given a specific activity for Ac-225 of 58,000 Ci per gram, can be calculated to be about 0.0005 g, which comes to a "specific value" for Ac-225 of almost $150 billion per gram!

Here's the catch: Use it or lose it; with a half-life of just 10 days, and daughter products very short-lived, though valuable as well, if you put that Ac-225 in a bank vault instead of to immediate use, you soon end up with nothing but a tiny pile of Bi-209 worth just pennies per gram.

* R.A. Boll, D. Malkemus, S. Mirzadeh, "Production of actinium-225 for alpha particle mediated radioimmunotherapy," *Applied Radiation and Isotopes*, Vol. 62 (2005), pp. 667-679.

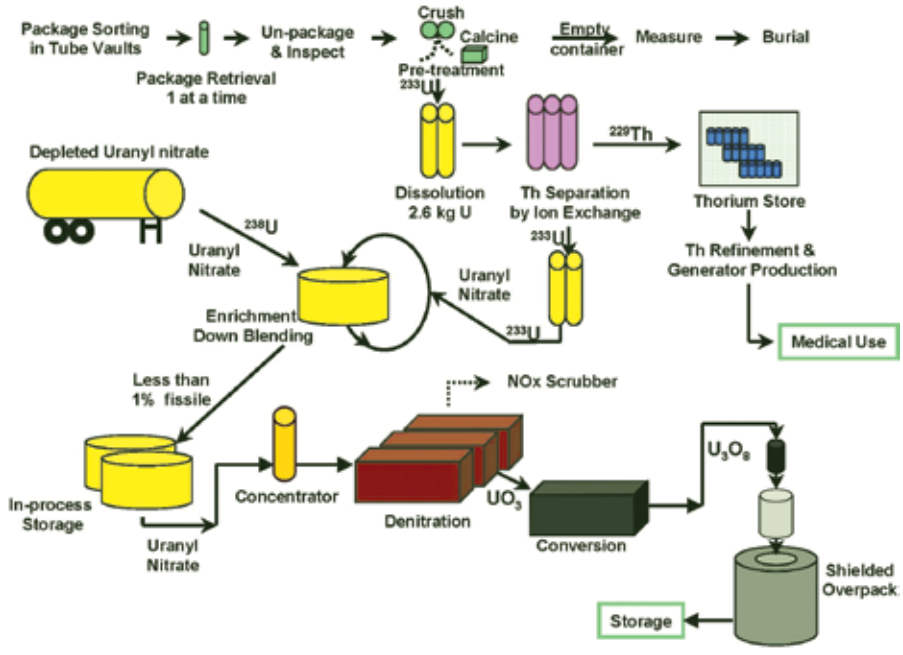


Figure 4
DOE PLAN FOR SHUTTING DOWN BUILDING 3019A—2004
In this plan, the thorium-229 was scheduled to be separated out from the U-233 before the U-233 was treated and sent for burial.

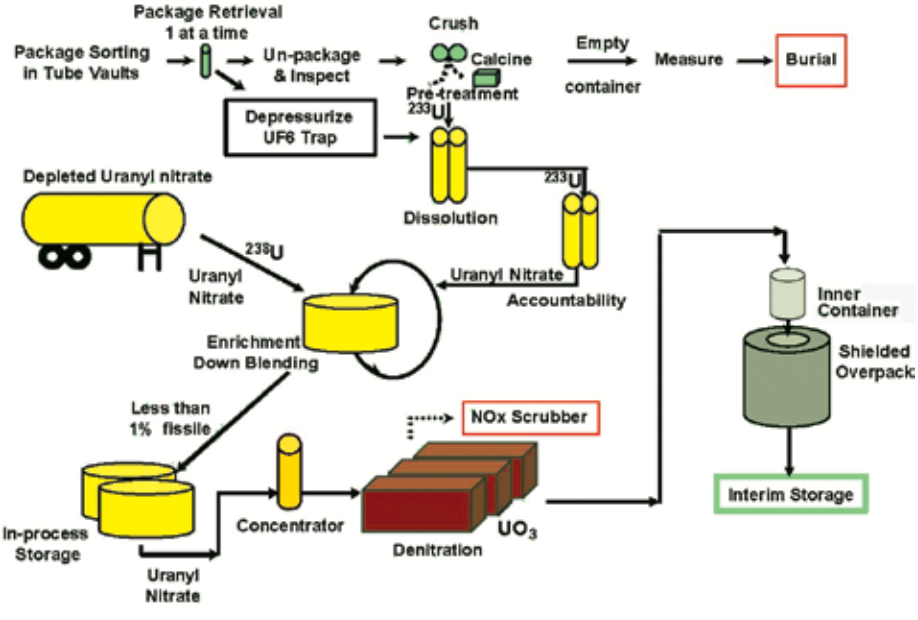


Figure 5
DOE PLAN FOR SHUTTING DOWN BUILDING 3019A—2007
In the revised plan, Congress mandated the shutdown of the U-233 storage facility with no extraction of thorium-229, sending this valuable resource to the dump.

Th-229 that is contained in the ^{233}U at ORNL is high quality material, unmatched in purity and quantity anywhere in the world. For the United States to dispose of the ^{233}U without recovery of the Th-229 would be irresponsible and a major waste of our country's resources.[12]

Since 1990, Congress has mandated that the U.S. isotope program must pay for its isotope production costs through sales of its products and services[13] (a short-sighted "market" approach, the effect of which is to kill technologies and kill people). But even on these terms, an annuity of $75 million from selling the Th-229 would be a tidy nest egg for its projects. The catch is, there has to be a market for the 50-fold greater quantity of Ac-225 that would flood the market if the DOE proceeded with Th-229 extraction. Right now, according to the DOE's own admission, there is not enough Ac-225 available to provide for present medical research, let alone future projects. But in order for the Ac-225 to retain its market value, there must be a large demand for it in the medical field. This requires that the therapeutic value and safety of it and its daughter products for cancer and infectious disease treatment be proven in many clinical trials in order to eventually get Food and Drug Administration approval of the isotopes for human treatment of specific diseases—an expensive and lengthy procedure.

To date, only two radioimmunotherapeutic treatments have been approved by the FDA, and both use beta-emitting isotopes (see box, page 41). Requiring the DOE's Isotope Program to "pay to play" by recouping all costs of production through isotope sales and related services is a very short-sighted policy that has failed in the past, is failing, and will fail in the future.

Part II
Targetted Alpha Radioimmunotherapy

Following the trail blazed by targetted immunotherapy in the last quarter of the 20th Century, a new clinical sub-field has grown and begun to mature: targetted radioimmunotherapy (RIT), which not only holds the potential to add to the effectiveness of cancer treatment, but which also has great potential as a treatment against infectious disease. The only thing standing in the way of this development is the failure of governments, especially the U.S. government, to nurture this promising technology.

Cancer is the second-leading killer of people in the United States (led only by heart disease), killing about 560,000 people per year. The five-year survival rate for all cancers has risen steadily since 1975, from about 50 percent to more than 67 percent today, due largely to earlier diagnosis and better treatments, with radioactive isotopes playing a prominent part in these advances.

Because cancer cells are human cells, almost all treatments to kill cancer cells, including chemotherapeutics and radiation therapy, kill many healthy cells as well. The challenge of cancer treatment is to maximize damage to cancer cells while minimizing damage to healthy tissues; the goal is to cure the disease without killing or maiming the patient. This goal is remarkably hard to achieve, which is why success is measured in five-year survival rates rather than cure rates. Even when no cancer is detectable in the body after treatment, cancer has a tendency to eventually "come back."

In order to surmount these obstacles to successful outcomes in cancer therapy, researchers have increasingly turned their efforts towards highly targetted therapies, capable of seeking out and killing even single cancer cells that are undetectable by present-day diagnostics, while sparing surrounding cells and tissues.

Monoclonal Antibodies Target Cancer Cells

Ever since it became feasible to produce monoclonal antibodies (mAbs) for therapeutic uses more than three decades ago,[14] cancer researchers and clinicians familiar with targetted nuclear medicine have envisioned a time when the power within the nucleus could be harnessed for targetted radioimmunotherapies against cancer cells within the human body—and especially against occult cancers, micrometastases, and minimal residual disease remaining after completion of surgery, chemotherapy, and other treatments (Figure 6).

Even in the early years, researchers in the field considered that short-lived alpha-emitting radioisotopes should, theoretically, be the premier magic bullet to link to specific antibodies targetted to specific antigens, expressed predominantly or solely by target cells such as tumor cells or infectious agents.

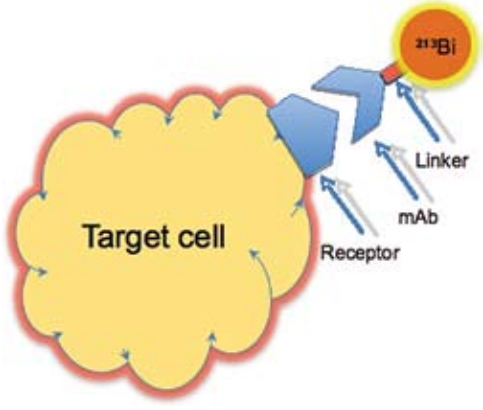


Figure 6(a)
USING RADIOIMMUNOTHERAPY TO TARGET A CELL

Short-lived alpha-emitting radioisotopes like bismuth-213 are linked to specific antibodies (mAb) which are targetted to specific antigens. The linking agent, a chelator, has to attach both to the mAb and the radioisotope. This package is injected into the patient, and the antigen carries the payload to recognized cell receptors, where the radioisotope kills the diseased cells.

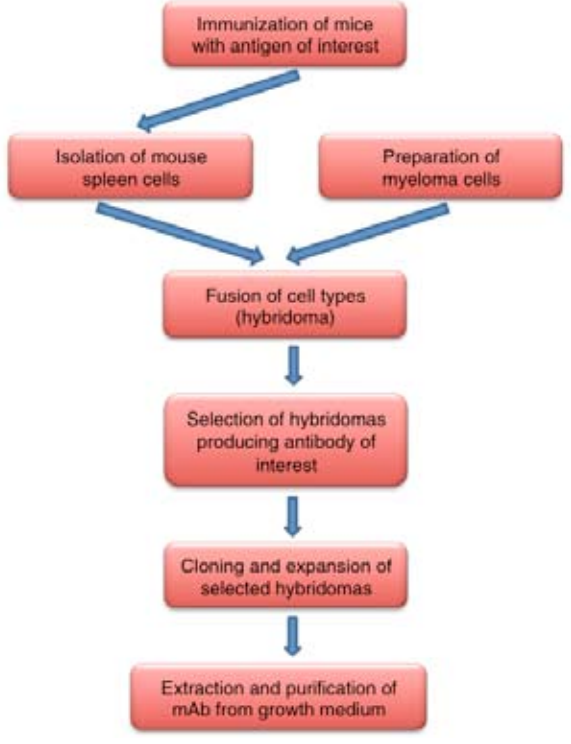


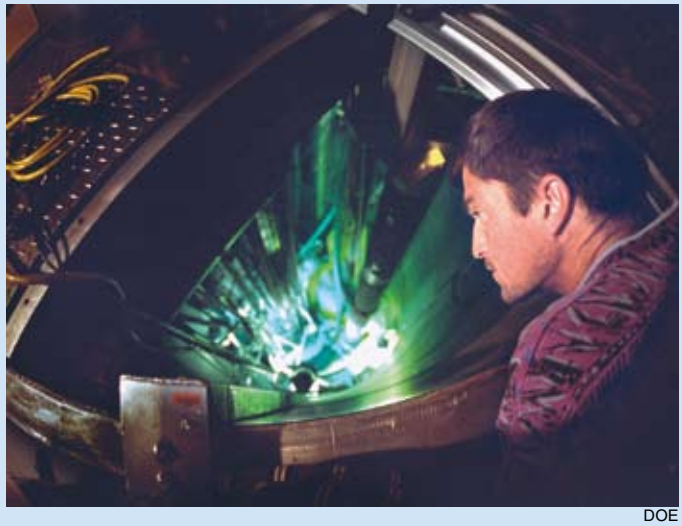
Figure 6(b)
MONOCLONAL ANTIBODY PRODUCTION

Over the past 40 years, researchers have developed a variety of monoclonal antibodies, which now can be used as carriers to target radioisotope receptors specific to particular cells or tissues.

U.S. Reactors That Could Produce Radioisotopes

INL

The Idaho National Laboratory's Advanced Test Reactor during its installation. The ATR is a pressurized water test reactor that operates at low pressure and low temperature. New equipment is being installed that will allow the ATR to produce medical isotopes.



DOE

Looking into the Annular Core Research Reactor (ACRR), a water-moderated pool-type research reactor capable of pulse and steady-state operations, which is currently used for defense purposes. The reactor was modified in the 1990s to allow for the production of Mo-99, but the DOE dropped the project. To use the reactor for Mo-99 production would require the DOE to reassign its mission from Defense Program uses to medical isotope production, at an estimated cost of $10 to $50 million.

DOE

The 400-megawatt Fast Flux Test Facility (FFTF) began full-power operation in 1982, under the management of Westinghouse Hanford. For 10 years it operated flawlessly. It tested materials and fuel components for fast breeder and fusion reactors under actual operating conditions, it transmuted high-level nuclear waste, it tested space nuclear fuel systems, and it produced 60 special isotopes for life-saving medical use and for industry. The DOE shut it down in 1993, stating that there was no "long-term mission" to justify its operating costs (about $100 million per year).

Successful development of such a weapon required, however, the development and maturation of several prerequisite medical technologies, which have been largely perfected in the intervening years. The most important technologies enabling the advancement of targetted radioimmunotherapy were of course those making possible a library of monoclonal antibodies (mAb) and mAb protein fragments in the commercial quantities and purity necessary to be utilized as vectors to target receptors specific to certain cells or tissues in an organism. These technologies, after 40 years, are now beginning to mature.[15]

Once the vector technologies were in place, the problem became one of weaponizing the mAbs to make them more potent killers of the target cells. Initially it was thought that mAbs alone could cause the destruction of cancer cells by binding to spe-

Memorial Sloan Kettering Cancer Center

David A. Scheinberg (left), a pioneer in research with monoclonal antibodies in the 1980s and in using alpha-emitting radioisotopes to target cancer cells. With him (from left) are Andrew Zelenetz and Joseph Jurcic.

cific surface receptors expressed on the cells to signal the body's own immune system to attack and destroy the target cells. The results of that approach often proved disappointing for various reasons, one of which was that the monoclonal antibody—produced from a hybridoma of a mouse antibody-secreting cell and an immortalized myeloma cell—was itself soon targetted for destruction by the body's immune system.

Researchers soon began to develop methods of attaching "payloads" to the mAb vectors using linking molecules. These linking agents had to be bifunctional, with one moiety able to attach to the mAb, and the other capable of binding the payload. The linking agents had to be as diverse as the payloads, which included drugs, toxins, fluorescent molecules, and radioactive isotopes. The molecules developed to attach such payloads to the mAb vectors were chelators modified by linkers of various sorts to be bifunctional.

Chelators (from the Greek word for claw) are molecules able to chemically bind one or several small molecules or atoms such as metal ions. The most well-known chelator to the layman is EDTA (ethylenediaminetetraacetic acid), used to bind metal cations such as Ca^{2+} and Fe^{3+}. EDTA has been around since the 1930s, and is ubiquitous in our society. Since its characterization, however, many other chelators with useful binding qualities have been discovered. Two of the most common of these used to bind radionuclide payloads to mAbs are known as DOTA (1,4,7,10-tetraazacyclododecane-1,4,7,10-tetraacetic acid), and DTPA (diethylenetriaminepentaacetic acid).

Once the payload could be bound tightly to the mAb by chelation or other techniques, the formulation could be injected into the patient's blood stream or into a localized compartment of the body, where the antibody could freely bind to recognized cell receptors, carrying the payload to its destination.

An Early Proof of Principle Study

In 1982, David A. Scheinberg, Mette Strand, and Otto A. Gansow,[16] used a bifunctional metal chelator, 1-(p-carboxymethoxybenzyl) EDTA, conjugated to the monoclonal antibody (mAb) 103A, targetting the Rauscher leukemia virus (RLV) envelope glycoprotein (gp70), which is copiously expressed in mouse leukemic spleen cells 12 days after infection by the virus. Being bifunctional, the unconjugated side of the chelator is designed to carry a radioisotope payload piggyback on the antibody straight to the diseased cell, where the antibody will attach strongly to the antigen.

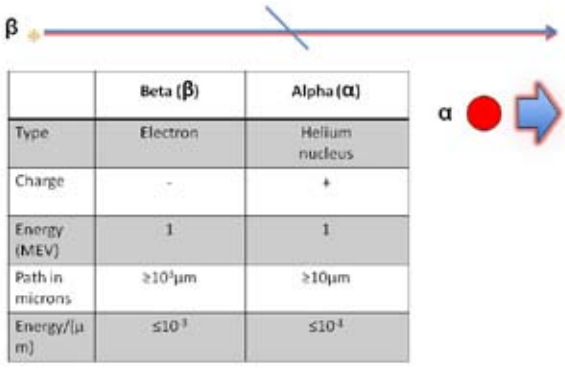
In the Scheinberg et al. research, the isotope targetting the cell was the radiometal indium-111 (In-111), a gamma-emitting radionuclide with a half-life of 67.9 hours. The purpose of the targetting was to explore the specificity and quality of imaging of the leukemic cells in the mouse spleen, using an external gamma camera to record the gamma photons released from the targetted celles as the isotope decayed by electron

BEXXAR® and Zevalin®: Prolonging Life

At present, there are only two targetted radioimmunotherapy drugs approved for treating human disease, and neither of them is an alpha emitter. The two drugs are Zevalin® and BEXXAR®, which were approved by the FDA in 2002 and 2003 respectively. Both are approved for the same limited indications of the same disease: CD20-positive (that is, bearing the CD20 targetting antigen) follicular non-Hodgkin's lymphoma which is refractory to chemotherapy. Zevalin® consists of a monoclonal antibody linked to the radioactive beta-emitting isotope yttrium-90 and targetting the antigen CD20 expressed on both malignant and normal B cells. BEXXAR® binds iodine-131, a beta- and gamma-emitter, to a mouse-derived antibody targetting the same antigen.

These drugs have shown promise in treating non-Hodgkin's lymphoma and prolonging life, often with less toxicity than traditional chemotherapeutic modalities. The main drawback to the drugs is the dose-limiting bone marrow suppression, which results from the target antigen CD20 being expressed on both diseased and non-diseased B cells. Since the beta particles emitted from the antigen/antibody complex are both energetically weak, and have a long path length in comparison to alpha particles, it takes a large number of them to ensure a kill. The bone marrow suppression factor thus limits the effectiveness of the drugs.

Furthermore, the I-131 also emits a gamma ray, which makes the patient a radioactive source, although it does allow easy imaging of the I-131 uptake by the patient. Lastly, any I-131 that is freed from its complex targets the thyroid, making it imperative to saturate the thyroid before, during, and for some time after the procedure, to limit thyroid damage.



	Beta (β)	Alpha (α)
Type	Electron	Helium nucleus
Charge	-	+
Energy (MEV)	1	1
Path in microns	≥10^3µm	≥10µm
Energy/(µm)	≤10^{-3}	≤10^{-1}

Figure 7
COMPARISON OF ALPHA AND BETA EMISSIONS IN SOFT TISSUE

Beta emitters can penetrate into solid tumors, and have a cross-fire effect, but have weaker energies than alpha emitters and longer path lenghts. This means that more disintegrations are required to kill a targetted cell. Alpha-emitters, by contrast, can often kill the target cell with one or just a few hits, and the short path-length of the alpha particle spares surrounding tissues from destruction.

capture to stable cadmium-111. (In-111 is produced from another stable cadmium isotope, Cd-112, by proton bombardment in a cyclotron.)

Their procedure functioned splendidly, producing easily visualized images of the infected spleen area when the 103A mAb was used. Infected spleen cells bound 60 times more radioactivity than non-infected cells. Control infected mice given non-relevant mAbs showed no cell-binding capabilities.

In the discussion section of the 1982 article, the authors speculated that in the future it should be possible to use similar techniques to deliver cytotoxic (lethal) doses of radionuclides to leukemic cells—and that particularly useful might be certain alpha-emitting radionuclides.

This paper not only illustrated an extremely useful technique of using short-lived gamma emitters bound to mAbs to locate and image cancer cells within the body, but also pointed the way forward for techniques to target and kill cancer cells with appropriate particle-emitting radioisotopes. Furthermore, it illustrated the usefulness of mAbs targetting unique receptors (caused by the infection of the transforming virus) expressed on the cancer cells. Variations on these themes have been ubiquitous in subsequent medical literature dealing with cancer treatment.

Targetting Cancer with Radioisotopes

It was not long before researchers in nuclear medicine (including those who authored the paper referenced above) turned their attention to finding and exploiting radioisotopes capable of delivering a therapeutic dose of ionizing radiation specifically to target cells.[17]

Using radionuclides for targetted therapy requires a different sort of radionuclide from those gamma emitters used for targetted imaging. With imaging, the point is to have the emitted high-energy photons travel right through the body to the imaging device. But to treat cancer using targetted radioimmunotherapy, the radionuclide must have a short half-life and a short path length capable of delivering a powerful dose to cells at short range, but sparing nearby non-targetted cells (Figure 7).

Some of the radioisotopes used for early imaging studies, such as lutetium-177, and I-131 were also capable of giving a therapeutic dose of ionizing radiation through electrons emitted during decay. These and other beta emitters, including yttrium-90 (Y-90) were some of the first radionuclides successfully exploited for targetted radioimmunotherapy purposes. Even today, the two beta emitters I-131 and Y-90 are the only radionuclides approved by the FDA (Federal Drug Administration) for use in targetted radioimmunotherapy in the United States (See box, p. 41).

Although beta emitters have some great qualities for targetted therapy, including a cross-fire effect, and the ability to penetrate into solid tumors, their weaker energies and the longer path lengths over which their energies are expended mean that sometimes hundreds or more disintegrations are required to kill one targetted cell, thus requiring more of the radioactive isotope at the target area. Alpha-emitting isotopes, by contrast, can often kill the target cell with one or just a few hits. And the short path-length of the alpha particle spares surrounding tissues from destruction.

These qualities make short-half-life alpha-emitting radioisotopes ideal for going after single cells, micrometastases, and the residual disease remaining after other cancer therapies have been applied.

Problems and Promise of Alpha Isotopes

Alpha radioimmunotherapy has been long envisioned but slow to arrive in clinical usage, to a great degree because many of the most useful radionuclides are so rare and of such short half lives.

However, since the early 1980s, long before the daughter products of U-233 became available through ORNL in the 1990s, a very few short-lived alpha-emitting radioisotopes were already being shown to have therapeutic properties in treating certain cancers in animals. The early researchers working with these isotopes had to pave the way, overcoming numerous hurdles in evaluating the usefulness and safety of these isotopes for medical use. Not only were monoclonal antibody and radioisotope-linker technologies in their infancies, but the dosimetry and fates of the daughter isotopes within animals had not been worked out for the relevant isotopes. Furthermore, the isotopes were in extremely short supply because they were products of military research carried out during the Manhattan Project.

The alpha emitter astatine-211, for example, was first produced at the cyclotron at the University of California at Berkeley in 1940, and only in the 1950s was there the leisure to begin to study its bio-characteristics. As late as 2001, Zalutzky et al. commented regarding still-unsolved problems impeding the medical use of At-211:

Although there is a compelling rationale for initiating

human trials with some of these ^{211}At-labeled compounds, patient studies have been impeded by the lack of methodologies for producing clinically relevant levels of ^{211}At labeled radiopharmaceuticals. There are 2 aspects to this problem. First, cyclotron targetry and ^{211}At purification systems are needed to provide large quantities … in chemical form appropriate for chemical manipulation. Second, labeling and purification procedures are required that are appropriate for high-level syntheses under conditions where radiolytic decomposition may play a role.[18]

These problems are not unique to At-211, but have hampered the development of all the useful alpha-emitting isotopes. Part of the reason that the beta emitters BEXXAR® and Zevalin® are the only two FDA-approved targetted radioimmunotherapy drugs for cancer treatment is that the isotopes I-131 and Y-90 are relatively cheap and plentiful, not because they are necessarily the best isotopes for the job. In order for such treatments to be approved by the FDA for use in human medicine, the safety and effectiveness of the treatments must be proved to a high degree. Such proofs require *in vitro* studies, and large-scale animal studies followed by phase 1, 2, and 3 clinical trials in humans to prove the safety and effectiveness of the therapies. Such lengthy and expensive studies require a large and steady supply of the isotopes in usable form at a reasonable cost.

No private company can be relied upon to provide for such needs because there is no short-term profit in the early days of research and development, and no guarantees of any profit in the medium or long term. Providing adequate medically useful isotopes for research and clinical development is the proper task of governmental institutions funded by governments.[19]

In fact, many of the current research and clinical projects involving alpha-targetted radioimmunotherapy are collaborations between research groups and major government-subsidized alpha-isotope producers. such as the Institute for Transuranium Elements (ITU) in Karlsruhe, Germany, and Oak Ridge National Laboratory in the United States. These are two of the few institutions able to extract from "aged" uranium-233 the minuscule amounts of thorium-229 (Th-229) from which actinium-225 (Ac-225) can be "milked" at intervals for use directly, or as a bismuth-213 (Bi-213) generator. The Karlsruhe ITU got its original stash of aged U-233 from ORNL long ago, and since then has benefitted from producing the Ac-225/Bi-213 generator for medical research efforts throughout the world.

The ITU decided to devote a significant portion of its work to the development of alpha-emitting isotopes for medicine. Specifically, it decided to concentrate on the daughters of U-233 generated from Th-229: Ac-225 and Bi-213. Over the years its researchers have methodically developed the basic science and technologies necessary to provide a reliable, well-characterized delivery system for these alpha-emitting isotopes. They have also collaborated with medical researchers in many countries, providing both the means and know-how to utilize isotopes to study the effects of alpha targetted radioimmunotherapy on cancers and infectious disease.

Some of their collaborations using Bi-213 are listed in Table 2. These studies have allowed researchers to test the effectiveness of this on solid tumors such as malignant melanoma and brain tumors, and also on blood cancers such as leukemia, which form no tumors. The isotopes have even been tested on HIV and the fungal pathogen *Cryptococcus neoformans* in mouse models. Some of these early studies with animals and human volunteers have been very promising, especially those targetting single cells or small clumps of cells. The results with larger solid tumors have been more disappointing, as would be predicted given the short half-lives and short path-length of the alpha-emitters used.

Radioisotopic 'Nano-generator' with a Powerful Punch

One collaborator with both ITU and ORNL, is the laboratory of David A. Scheinberg, the early pioneer who targetted cancer cells with radioisotopes (see above). He has devoted a good portion of his professional career to trying to develop alpha-targetted radioimmunotherapy for cancer treatments at Memorial Sloan Kettering Cancer Center, using Bi-213 alone, and using the parent Ac-225 (half-life 10 days) as a nano-generator able to produce four targetted alpha emissions as it decays to stable Bi-209 (see Table 3).

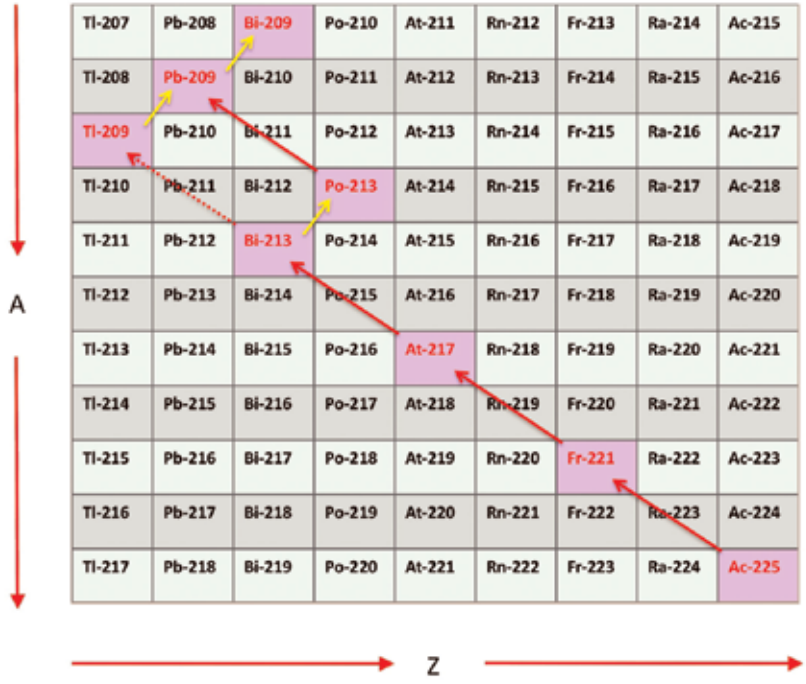
The rationale for using Ac-225 as an alternative to Bi-213 is to capitalize on the potential of delivering over a period of days rather than minutes, four alpha blows to a cancer cell for each atom of Ac-225 delivered to the target—more bang for the buck. Scheinberg's experience with this isotopic nano-generator amply illustrates the potential and problems with alpha targetted radioimmunotherapy.[20]

With a 10-day half-life and four alpha emissions, Ac-225 potentially packs a punch 1,000 times greater than Bi-213 alone, allowing a much lower total radiation dose to the non-targetted tissues and the potential to penetrate solid tumors more effectively. The problems involve the complexity of dealing with the daughter products of Ac-225, which are all different elements with different binding properties to linkers, and different tissue affinities and excretion rates. The fates of these daughters when not bound in the cells, and their effects on non-targetted tissues such as kidney, thyroid, and bone marrow, must be fully ac-

Table 2
SELECTED COLLABORATIONS BETWEEN ITU AND MEDICAL RESEARCHERS

Country	Location	Disease
Australia	Sydney	Malignant melanoma
Belgium	Gent	Chronic leukemia
France	Nantes	Multiple myeloma
Germany	Heidelberg	Lymphoma
	Düsseldorf	Lymphoma
	Munich	Gastric cancer
	Ulm	Acute leukemia
Switzerland	Basel	Brain tumors
United States	New York MSKCC	Acute leukemia
	New York AECM	Infectious diseases

Table 3
Ac-225 AND ITS DAUGHTERS



The parent Ac-225, with a half-life of 10 days, can deliver four alpha blows to a cancer cell for each atom of Ac-225 delivered to the target, as it decays to the stable element bismuth-209.

counted for, even though all the daughters except the stable and relatively benign Bi-209 have short half-lives. The longest-lived of the daughters, Bi-213, becomes the problem child in this system.[21]

For targetting cancer cells with Ac-225 using the Scheinberg, et al. protocol (where the Ac-225 is internalized into the cancer cell after binding), the limiting factor in achieving the maximum therapeutic dose is the accumulation of Bi-213 in the kidneys. Too high a dose can lead to eventual kidney failure. Because the cancer-killing benefits are dose dependent, techniques to lower kidney damage at higher doses must be developed, including using metal chelators in the blood (DMSA, DMSP), or adding molecules which compete with bismuth for kidney binding sites, or using diuretics and forced hydration to increase the patient's excretion rates.

All of these problems are solvable, but to solve the problems and realize the benefits, requires scientific manpower focussed on the research. And that takes plenty of available isotopes, and plenty of funding, without which, these technologies will never make it into clinical usage.

Where Do We Go from Here?

The problem with cancer is that, after all the standard treatments, in almost every case, some cells or colonies are left behind. Not only did the patient's immune system not deal successfully with the original disease, but, after the ravages of chemotherapy and many non-targetted radiation treatments, the patient's body is often left totally unable to mount an immune attack on the remaining cells. From wherever they were sequestered, these cancer cells start to grow and spread. And often these surviving cells are more resistant to repeats of the same treatments. The patient's options narrow and the outlook darkens. In the conventional cancer therapy, more toxic treatments are then tried to knock down the new growth.

If this sounds somewhat like a scenario one might find with highly drug resistant tuberculosis or with HIV/AIDS, that is not coincidence. In many respects, cancer acts like an infectious disease once it has successfully gained entrance to the body. Monoclonal antibody treatments, and the weaponized versions of mAb treatments follow this model, targetting somewhat unique receptors on the cancer cell. The best treatment would be one which successfully flags only cancer cells for destruction by recruiting the body's existing immune system—the original dream of mAb development.

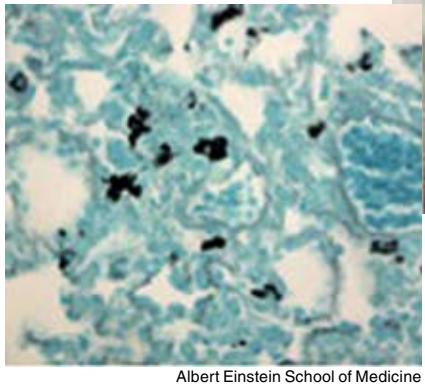
Lacking such recruitment, radioisotopes and other toxins or drugs attached to the mAbs can be used for the destruction. In this scheme, radioimmunotherapy, and especially alpha RIT would be the mop-up crew in the armamentarium of the war on cancer, spreading out locally to heave grenades into remaining enemy enclaves after the carpet bombers have finished. It is for just this purpose that highly targetted immunotherapies are at the leading edge of cancer research.

But, why stop there? Why not use radioimmunotherapy to target diseases like HIV/AIDS? At least one medical research lab is doing just that. Dr. Ekaterina Dadachova and her team at the Albert Einstein School of Medicine have, in collaboration with ITU and others, been testing RIT against the bacterium *Pneumococcus,* HIV/AIDS, and a fungal pathogen, *Cryptococcus neoformans*, in a mouse model. Her lab has also been focussing on the potential for RIT to target the many cancers that are actually the result of infectious disease, such as hepatitis-induced liver cancer and human papilloma-virus-induced cervical cancer. Worldwide, those cancers account for a significant portion of cancer morbidity and mortality.

Using the beta emitter rhenium-188 and the alpha emitter Bi-213, Dadachova's lab has gotten promising results using mAbs targetting the foreign proteins expressed on cells infected with HIV—the very approach used by David Scheinberg way back in 1982 when he targetted the Rauscher leukemia virus receptors in infected mouse spleen cells with mAb-linked In-111, to visualize the infected spleen. The spiral has come full circle at a

higher level. But these are still very preliminary studies—promises, but nothing delivered.[22,23]

To actually get some of these therapies into clinical use, especially in the United States, would require a mandate by Congress, backed by adequate funds, to put medical isotopes on the front burner. The United States has to get back into the isotope business. We have seen the harm to the nation from choosing not to have a domestic source of Tc-99m. When foreign sources shut down, patients in the United States are harmed. But a much greater harm is sustained by the millions of cancer patients treated with old-school methods because we are too cheap, shortsighted, and in some cases deliberately Malthusian, to build the infrastructure to foster new technologies that might prolong the lives of our citizens or cure them outright.



Albert Einstein School of Medicine

Cyryptococcus neoformans *in mouse lung.*

Albert Einstein School of Medicine

Ekaterina Dadachova (center) and her laboratory at Albert Einstein School of Medicine are using radioisotope immunotherapy to target HIV/AIDS, the bacterium Pneumococcus, *and the fungal pathogen Cryptococcus neoformans (inset). Dadachova's lab members are (from left) Ekaterina Revskaya, Ruth Bryan, Zewei Jiang, Robertha Howell, and Andrew Schweitzer.*

For too long, Congress has hidden behind a "free-market" ideological façade, proclaiming that government should not compete with private industry. President Obama even wants to leave space exploration to private industry! We never would have reached the Moon with private funding. And without generous public investment, we will never realize the massive potential benefit waiting to be harvested from the many dozens of short-lived isotopes with useful medical properties. Meanwhile, those with potentially treatable diseases will go on dying.

Footnotes

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