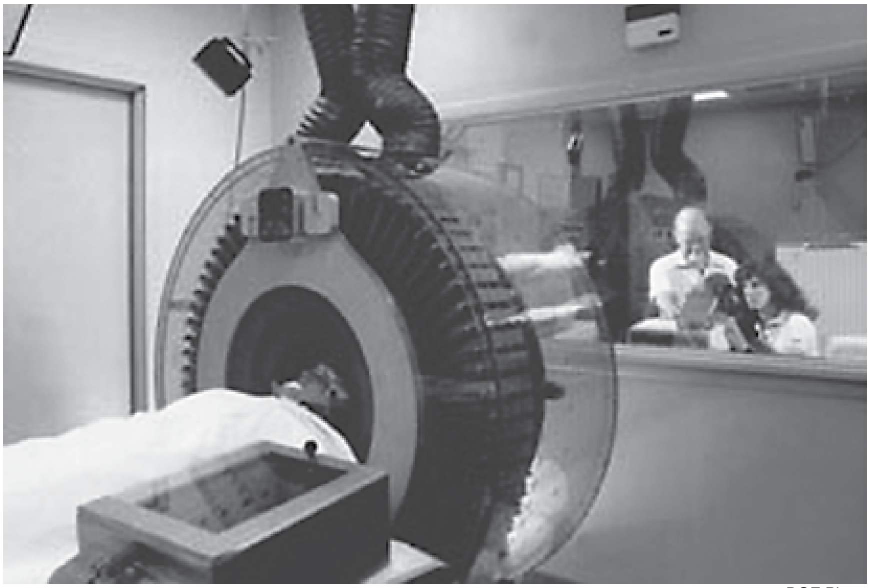
Medical Isotopes in the 21st Century

by Robert E. Schenter, Ph.D.

Radioactive isotopes should and will play a major role in the advancement of 21st Century medicine. These medical isotopes are currently showing outstanding results in both diagnostic and therapeutic medical applications, which should continue to expand for application for essentially all the major diseases (cancer, heart, Alzheimer's, arthritis, etc.) for the rest of this century. There have also been promising research results in killing the HIV virus with medical isotopes.

This paper briefly presents examples of these developments and their future promise for two forms of cancer (breast and liver), Alzheimer's disease, and HIV. The promise of treatment with radioactive isotopes can be seen from one patient who was told, "You have three months to live" four years ago. Now, as a result of treatment with the medical isotope yttrium-90, applied using what are called Y90 microspheres, the patient not only is alive, but works out with a personal trainer every other day, and is living life to the fullest.

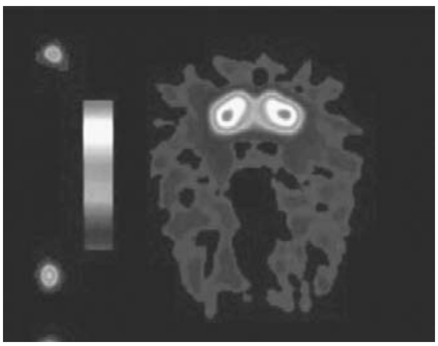


DOE Photo

Brookhaven National Laboratory scientists preparing for a Positron Emission Tomography (PET) scan of a patient. The PET technology uses the radioisotope fluorine-18 in combination with glucose (together called FDG or fluorodeoxyglucose). Cancer tumors overutilize glucose, and the PET scan identifies the metabolic difference between normal tissue and the tumor, thus identifying tumors.

Introduction

Diagnostic and therapeutic medical isotope applications have made major advances for the past 50 years, and these advances should accelerate as we continue through the 21st Century. In the United States, and probably in the rest of the world, the aging of the World War II Baby Boomers will create an exponentially increasing demand for the medical application of these isotopes, as people live longer and acquire the diseases of aging.



DOE Photo

This PET scan shows the chemical uptake in a monkey's brain, to test the effectiveness of a Parkinson's disease treatment. The research is being carried out by the Lawrence Berkeley National Laboratory in collaboration with Somatix Therapy Corporation. By restoring levels of important brain chemicals in animals, the hope is to develop a similar treatment for human Parkinson's patients.

Dr. Robert E. Schenter is one of the leading U.S. experts on fission reactor production of isotopes. Based on his 39 years as an expert on neutron cross-section and decay data information, he has become a world authority on isotope production. Now the chief science officer of the Advanced Medical Isotope Corporation, Schenter previously worked as the site director and deputy site director in the Isotope Program Office at the Westinghouse Hanford Company (WHC) and the Pacific Northwest National Laboratory (PNNL). In 1991, he was responsible for the relief of a world shortage of gadolinium-153, which is used in instruments for early detection of osteoporosis. He also defined the project and directed the production in the Fast Flux Test Facility (FFTF) in Richland, Washington.

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MAJOR PET ISOTOPES AND THEIR APPLICATIONS

Isotope	Half-Life	Diagnostic Applications
Bromine-76	16.0h	Anti-Carcinoembryonic Antigens, Anti-CEA Antibodies, DNA Studies, Nerves of the Heart, Quantitative Imaging
Carbon-11	20.3m	Cancers: Chest, Chronic Lymphocytic, Glioblastoma, Liver, Multiple Myeloma, Prostate, Urinary Tract
		Diseases: Alzheimer's, Brain, Epilepsy, Heart, Parkinson's
		Alcohol Addiction, Amphetamine Release, Drug Addiction, Neuropsychiatric, Nicotine Dependence, Pain Processing, Schizophrenia, Small Animal Imaging, Tobacco Addiction
Copper-62	9.74m	Cerebral and Myocardial Perfusion, Colorectal Cancer, Human Biodistribution, Liver Cancer, Renal Blood Flow, Renal Injury
Copper-64	12.70h	Cancers: Cervical, Colon, Colorectal, Lymphoma, Melanoma, Pancreatic, Prostate
		Diseases: Angiogeneses, Brain, Hypoxia, Parkinson's, Wilson's
		Stem Cell Research
Fluorine-18	1.83h	Cancers: Adrenal Gland, Anal, Bone, Bone Marrow Transplants, Bowel, Breast, Cervical, Chest, Colorectal, Esophageal, Gastric, Head and Neck, Hodgkin's Disease, Laryngeal, Leukemia, Liver, Lung (NSCLC), Lung(SCLC), Melanoma, Multiple Myeloma, non-Hodgkin's Lymphoma, Osseous, Ovarian, Pancreatic, Prostate, Rectal, Rhabdomjo Sarcoma, Squamous Cell, Thyroid, Urinary, Vocal Cord
		Diseases: Alcohol Addiction, Alzheimer's, Anorexia, Atherosclerosis, Brain, Depression, Diabetes, Heart, Herpes, HIV, Hypoxia, Infection, Liver, Muscle, Kennedy's Narcolepsy, Lung Inflammation, Osteomyelitis, Parkinson's, Pneumonia, Ulcerative Colitis, Schizophrenia, Tourette's Syndrome
		Infection: Pen-Prosthetic, Hip-Prosthetic, Joint-Prosthetic
		Small Animal Imaging, Chemotherapy Research
Gallium-68	1.13h	Breast Cancer, Heart Imaging, Immunoscintigraphy, Molecular Imaging, Neuroendrocrine Tumors, Pancreatic Cancer
Iodine-124	4.18d	Apoptosis, Cancer Biotherapy, Glioma, Heart Disease, Mediastinal Micrometastates, Scouting of Therapeutic Radioimmunoconjugates, Thyroid Cancer
Iron-52	8.28h	Anemia, Human Bone Marrow
Nitrogen-13	9.97m	Ammonia Dog Studies, Coronary Artery Disease, Diabetes, Gamma Camera, Heart Disease, Imaging of Heart, Pancreas and Liver, Lupus Erythematosus, Myocardial Perfusion, Pulmonary Ventilation
Oxygen-15	122.s	Acute Brain Injury, Arterial Blood Flow, Brain Cancer, Oxygen Utilization, Brain Studies, Cerebral Blood Volume, Cerebral Responses, Coronary Artery Vasospasm, Coronary Reserve, Heart Disease, Ischemic Stroke Disease, Kinetics of Oxygen, Liver Cancer, Myocardial Viability, Oxygen Metabolism, Pain Control, Venous Ulceration
Rubidium-82	1.26m	Heart Disease, Myocardial Perfusion, Sarcoidosis
Yttrium-86	14.74h	Distribution of Y90, Lung Cancer, Melanoma, Renal Cell Carcinoma
Zirconium-89	3.27d	Brain Tumors, Head and Neck Cancers, non-Hodgkin's Lymphoma

Source: Dr. Robert E. Schenter, Ph.D.

A good example of this increase in demand is the explosion in the diagnostic application of Positron Emission Tomography (PET) for essentially all major diseases.

The PET application uses several radioisotopes, which have a whole range of half-lives, predominantly led by fluorine-18. The list of isotopes used with PET and their half-lives and applications is given in the Table.[1]

In the area of therapy, the isotopes of iodine-131 and yttrium-90 are applied very effectively in treating follicular non-Hodgkin's lymphoma. They are used in Food and Drug Administration-approved radiopharmaceuticals called BEXXAR (I-131) and Zevalin (Y-90). This procedure is called radioimmunotherapy, or RIT, where the goal is to kill all the cancer cells without harming the healthy cells. This is also known as cell-directed therapy.

Four additional examples of medical isotope application for both diagnostic and therapeutic procedures are presented below, for two types of cancer (breast and liver), Alzheimer's disease, and HIV.

Examples of Medical Isotope Applications

- *Breast Cancer*

Currently, 40,000 women in the United States die each year as a result of breast cancer. That number could double as the Baby Boomers age. Consequently, better treatments for this devastating disease should be aggressively pursued.

An important method of treating breast cancer is the application of brachytherapy. This procedure involves placing a tiny radioactive seed inside the breast, up against tissues harboring the breast cancer. The radiation is focussed on the breast tumor

Radiological Society of North America

An ultrasound-guided breast brachytherapy procedure, in which a radioactive "seed" is inserted into a tiny balloon, placed at the site of the surgically removed tumor. The seed delivers the prescribed dose of radiation directly to the site where cancer recurrence is most likely, minimizing exposure to healthy tissue in the breast, skin, ribs, lungs, and heart. This outpatient treatment can be for one to five days. No source of radiation remains in the patient's body between treatments or after the procedure is completed.

area, which significantly reduces the destruction of the healthy breast cells.

The isotopes irridium-192 and iodine-125 are used for this application.

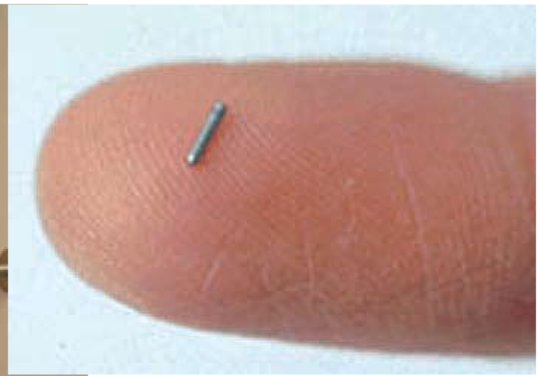
Robert R. Kuske, M.D., a radiation oncologist with Arizona Oncology Services, discussed advantages of Accelerated Partial Breast Irradiation (APBI) at the July 2004 meeting of the Radiological Society of North America (RSNA).[2] APBI combines surgery with brachytherapy as a breast conservation therapy.

- *Liver Cancer*

A medical breakthrough called microsphere brachytherapy is giving new hope to patients with liver cancer.[3] This therapy works by delivering radiation from the medical isotope yttrium-90 through a catheter tube, directly to tumors inside the liver. The yttrium-90 is contained in tiny glass bead microspheres. Several million of these Y-90 microspheres are used in a single treatment.

According to Dr. Andrew Kennedy of Raleigh, N.C., the Y-90 microspheres are delivered into the liver, where they reside permanently in the tumors; and the radiation is designed to penetrate only about one-quarter of an inch into the tissue. So, as the tumor is being destroyed, the nearby normal liver tissue is not being affected. The outpatient procedure takes about one hour.

- *Alzheimer's Disease*



Northshore Medical Accelerator

A similar radioactive treatment is used for prostate cancer. This shows the actual size of a prostate seed implant.

Currently, more than 5 million Americans have Alzheimer's disease. Symptoms vary considerably, but usually begin with a tendency to forget, which becomes so severe that it affects the patient's social life, family life, work, and recreational hobbies. Alzheimer's is the most common form of dementia, and is the result of brain aging.

The two major methods of diagnosing Alzheimer's disease both use medical isotopes: Single Photon Emission Tomography (SPECT) and Positron Emission Tomography (PET).

With SPECT, a small amount of gamma-ray-emitting isotope (for example, technetium-99m or thallium-201) is bound to neuro-specific pharmaceuticals and then injected into a patient's vein, from where it is taken into the brain tissue. The isotope fixes itself onto the brain with proportional flow, emitting a gamma ray which is picked up and detected by a SPECT gamma camera.

PET is a way of getting three-dimensional images or maps of functional processes of the body (see box). For Alzheimer's disease, PET scan images use the isotopes carbon-11 or fluorine-18, to compare normal brain activity to reduced brain activity. A PET scan can show the brain's biological changes attributable to Alzheimer's disease earlier than any other diagnostic test can provide this information. Alzheimer's disease can even be detected several years earlier than the onset of symptoms.[4]

The application of PET for Alzheimer's disease is rapidly spreading in use at medical clinics and hospitals all over the world. There were 25 papers on this presented at the 2006 Society of Nuclear Medicine meeting in San Diego.

- *HIV*

Twenty-five years from the start of the epidemic, HIV is still an incurable disease. It is clear that something completely different needs to be done to eradicate it, commented Dr. Ekaterina Dadachova of the Albert Einstein College of Medicine in New York City.[5]

Using radioactive antibodies, as is done in many successful cancer treatments, Dr. Dadachova and her colleagues have been doing research directed towards killing HIV-infected cells. This involves treating mice infected with HIV and has been reported in the online journal *PLoS Med*.[6]

Dadachova's team linked radioactive bismuth-213 and rhenium-188 to antibodies designed to stick to two HIV proteins (gp4) and (gp20), displaced on the surface of the infected cells. The initial results reported showed significant killing of HIV cells in the mice, providing support to the concept that radioimmunotherapy could work against HIV/AIDS.

Conclusions

Major medical advances in the 21st Century should occur through the application of medical isotopes. This paper presented several examples of the diagnostic and therapeutic applications of essentially current results and indicate promise for future significant developments.

For more information on the medical isotope/disease connection for the examples presented here and several other examples, please contact the author at 2521 SW Luradel St., Portland, Ore., U.S.A. 97219, or via e-mail: reschenter@comcast.net.

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NUCLEAR MEDICINE

Technologies We Can't Afford to Ignore

by Marjorie Mazel Hecht

Nuclear medicine, the use of radioactive isotopes in diagnosing and treating disease, has a proven track record of saving lives, and saving money, by providing faster and better diagnostic results and cancer treatment with no unpleasant or dangerous side-effects. But although many nuclear medicine techniques were pioneered in the United States, today this country lags behind in research, development, training, and treatment.

In Europe, where nuclear medicine is overtaking standard chemotherapy treatment for certain types of cancer, a patient is more likely to find the most advanced treatment, using radioisotopes.

Every aspect of nuclear medicine is underfunded and underdeveloped here. Most striking is the fact that the United States must import more than 90 percent of the medical radioisotopes used. When you consider that 20 million diagnostic and treatment procedures are performed annually here with radioisotopes, this level of "outsourcing" is staggering.

Eighty percent of the medical radioisotopes used in the United States come from Canada, with the rest coming from Europe and Russia. When Canada's Chalk River reactor, which is dedicated to isotope production, was shut down for a safety upgrade in November 2007, it meant that patients in Canada and elsewhere would have to go without their needed tests and treatment for several weeks. The situation was so dire, that the Canadian Parliament met in an unprecedented special session to mandate the reopening of the reactor and the postponement of the upgrade. The Parliament judged, correctly, that the immediate risk to human lives was far greater than the hypothetical risk for which the reactor was being upgraded. On Dec. 16, 2007, the 50-year-old Chalk River reactor, which supplies half of the world's radioisotopes, went back on line.

The Chalk River event points up the frustrating situation of nuclear medicine in the United States. Both the Congress and the Executive for years have ignored the many government reports advising more Federal funding for nuclear medicine research and facilities for isotope production. Perhaps as the generation of Baby Boomers ages, and suffers from the diseases of aging, their desire for advanced medical treatment will overrule their knee-jerk opposition to anything nuclear, and these programs will get the support they need.

NAS: More Funding Needed

The most recent of a series of scientific reviews of the nuclear medicine situation is a National Academy of Sciences (NAS) report "Advancing Nuclear Medicine Through Innovation," issued in September 2007.[1] This report comprehensively describes the promise of nuclear medicine and concludes: "In spite of these exciting possibilities, deteriorating infrastructure and loss of federal research support are jeopardizing the advancement of nuclear medicine. It is critical to revitalize the field to realize its potential."

But although the NAS report accurately characterizes the present dismal state of U.S. infrastructure in nuclear medicine, its recommendations for isotope production are far too modest. It recommends merely that "a dedicated accelerator and an upgrade to a nuclear reactor should be considered."

The glaring omission in the NAS review is that it never mentions the Fast Flux Test Reactor (FFTF) at Hanford, Washington. This 400-megawatt sodium-cooled fast reactor was designed to test fusion and fission materials, and to produce isotopes. Yet, for no good reason, and despite a lack

1. Committee on State of the Science of Nuclear Medicine, National Research Council, "Advancing Nuclear Medicine Through Innovation" (Washington, D.C.: National Academy Press, September 2007).