A MEDICAL FIELD ARISING FROM THE ATOMIC AGE

U. S. Department of Energy Office of Science Nuclear Medicine Program

1929

Ernest O. Lawrence invents cyclotron

At the University of California's Radiation Laboratory in Berkeley (later to become Lawrence Berkeley National Laboratory), the cyclotron produces the first medically useful radionuclides (iodine-131, thallium-201, technetium-99m, carbon-14, and gallium-67). For this invention, Lawrence receives the Nobel Prize in Physics in 1939.

1946

First delivery of a medical radionuclide to a hospital

Reactor-produced radionuclides from Oak Ridge become available for medical research. Eugene P. Wigner (in dark suit), director of BER research and development at Oak Ridge, delivers lead-lined container of carbon-14 to Barnard Free Skin and Cancer Hospital in St. Louis. Wigner receives the Nobel Prize in 1963 for his research on the structure of the atom and its nucleus.

1951

Benedict Cassen invents rectilinear scanner

Cassen and other BER scientists at the University of California, Los Angeles, build a scanner that provides images of a thyroid gland based on distribution of an iodine radiotracer, the start of imaging in nuclear medicine.

1952

Hal Anger invents gamma camera

In Berkeley, California, Anger and his BER colleagues introduce a revolutionary new technique for radionuclide imaging. The gamma camera becomes the "workhorse" of nuclear medicine for the next 50 years.

1953

Birth of positron imaging

Gordon Brownell at Massachusetts Institute of Technology constructs the first detector device to exploit positron-electron annihilation as an imaging tool, creating a precursor of future PET scanners.

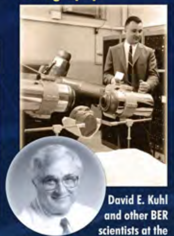
1958

Invention of Technetium-99m generator

BER scientists at Brookhaven (Walter Tucker, Powell Richards, and colleagues) invent a generator system that will make Tc-99m the most widely used radionuclide in hospitals worldwide for millions of nuclear medicine patients each year.

1959

Beginning of emission-computed tomography



David E. Kuhl and other BER scientists at the University of Pennsylvania build the Mark II scanner, ancestor to today's CT and SPECT scanners.

1961

Development of "headshrinker," PET forerunner

James S. Robertson, a BER scientist at Brookhaven, develops the "headshrinker," a direct forerunner of PET.

1973

Thallium-201 for medical use

BER scientists at Brookhaven (Elliot Lebowitz, Harold Atkins, and colleagues) develop a faster, more efficient method for producing thallium-201, leading to nuclear stress testing as a routine scan for heart imaging. By the 1990s, doctors will use thallium-201 about a million times a year, accounting for 13% of all nuclear medicine scans.

1974

First PET camera for human studies

Following several prototypes, Michael E. Phelps, Edward Hoffman, and Michel M. Ter-Pogossian at Washington University, with DOE and National Institutes of Health support, build the PETT III to use advanced algorithms for computing three-dimensional images.

1976

Development of fluorine-18 FDG for PET

Alfred P. Wolf (right), Joanna S. Fowler (not shown), Tatsuo Ido (middle), and other BER colleagues at Brookhaven develop and synthesize fluorine-18 fluorodeoxyglucose (FDG), a form of radiolabeled sugar, for PET imaging of glucose metabolism.

First shipment of fluorine-18 FDG to a hospital

Brookhaven sends F-18 FDG, a PET radiotracer, to the University of Pennsylvania, also a BER research site.

1980

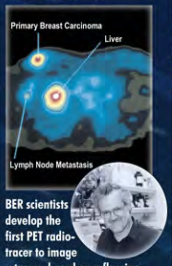
Iodine-131 MIBG for diagnosing and treating rare childhood cancers

Scientist producing radioisotopes

Donald Wieland and other BER scientists at the University of Michigan develop new radiopharmaceutical.

1984

PET image of estrogen receptors in breast tumor



BER scientists develop the first PET radiotracer to image a tumor, based on a fluorine-18-labeled carrier molecule (fluoroestradiol) that targets a specific hormone receptor of the cell. Developers are Michael J. Welch (Washington University, St. Louis) and John A. Katzenellenbogen (University of Illinois, Urbana-Champaign).

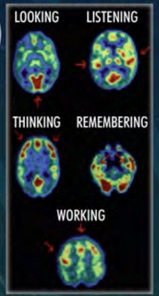
1986

World's highest-resolution PET scanner

BER scientists led by Thomas F. Budinger (left) design more advanced PET imaging systems.

1987

PET scans show different patterns of glucose (sugar) metabolism related to performing various mental tasks



At UCLA, fluorine-18 FDG PET studies, supported by BER, show different patterns of glucose (sugar) metabolism in the brain during five tasks:

1. Looking at scenery
2. Listening to a mystery story with music
3. Thinking by counting backwards from 100 by 7s
4. Remembering objects previously memorized
5. Working by touching the thumb consecutively to the four fingers

Scientist producing medical kit for diagnostic nuclear medicine procedures for imaging body organs

1998

Enrico Fermi Award from DOE

Michael E. Phelps, a BER scientist now at UCLA, receives DOE Presidential award for his 1970s work as one of the developers of the first PET camera built for human studies at Washington University, St. Louis.

E.O. Lawrence Award from DOE

Joanna S. Fowler, a BER scientist at Brookhaven, receives award for her innovations in radiopharmaceutical development and their application for imaging brain chemistry and the biological action of various drugs.

CURRENT BER RESEARCH ACCELERATING BIOMEDICAL PROGRESS

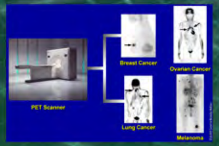
Today, BER investigators are merging new genomic data and resources with advances in chemistry, physics, mathematics, and engineering to develop novel radiopharmaceuticals, sophisticated scanners, and other technologies.

These advances support

- Highly sensitive, noninvasive diagnostic procedures that eliminate the need for exploratory surgeries
- More accurate and effective treatments for cancers and other diseases
- More detailed studies of normal physiology and disease

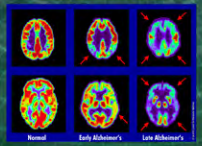
Miniature Mobile PET camer and MRI Scanning Techniques for Brain Imaging in Mice/Rats without Anesthesia

Today, hospitals and clinics perform about 13 million nuclear medicine procedures on patients each year in the United States.



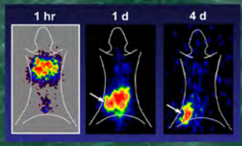
PET Studies of Cancer

As the patient is moved through the scanner, images are made of the whole body or specific organ systems. The tomographic sections shown depict malignant tumors (arrows) in patients with different cancers. PET has been shown to be from 9% to 43% more accurate than conventional anatomical imaging (e.g., X-rays, CT scans, and MRI scans), depending on the particular clinical question, for detecting and staging 19 different cancers, as well in assessing therapeutic responses. Cancers include lung, breast, colorectal, and ovarian, as well as melanoma and lymphoma. According to published clinical studies involving over 26,000 patients, PET scan information changes the treatment chosen in 15% to 50% of patients, depending on the particular clinical question and cancer type. The FDA has approved PET for use in all cancers. Medicare and private insurers have approved PET for use in the cancers listed above plus head, neck, and esophageal cancers, and are now considering approvals for most remaining cancers.



PET Study of Alzheimer's Disease

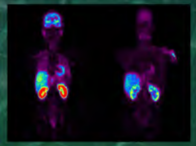
These positron emission tomography (PET) images show the brain of a patient in different stages of Alzheimers disease (AD). The upper row of images depicts the top of the brain, and the lower row images are from about half way down; the top of each image is the front of the brain. Tomography collects data from imaging instruments and creates mathematical cross-sectional slices of the organ. While CT and MRI scans reveal body structure and disease lesions, PET shows images of living chemical and biological processes occurring in the body. In these images, the color scale is proportional to the work being performed by the brain as measured by the rate of glucose metabolism. Red areas reveal the highest rate of glucose metabolism, with decreasing rates through orange, yellow, green, blue, and purple regions. PET has been shown to detect AD with a 93% accuracy about 3.5 years before conventional approaches can diagnose "probable" Alzheimer's.



Targeting of a human EBV lymphoma xenograft with radiolabeled activated T cells

Epstein-Barr virus (EBV) lymphoma can be a complication of bone marrow transplants in which an immune-deficient recipient develops a tumor by outgrowth of host lymphocytes infected with the ubiquitous virus. In some cases the lymphoma can be cured by infusing highly specialized radio-labeled donor T-cells into the recipient.

These photos demonstrate noninvasive tracking of the migration of altered donor T cells in immune-deficient mice bearing human tumor xenografts. After systemic injection into the mice, the modified cells migrate through the lungs, gut, and finally reach the tumor. The T cells selectively accumulate in the tumors and retain their capacity to eliminate just these cells. The technique is informative, nontoxic, and potentially applicable to humans. The group plans to monitor the cells and their migration in humans using PET imaging. DOE supported the development of FIAU and the production of I-124, including cyclotron support.



Smoker vs. Nonsmoker

Using PET, researchers found that smokers have significantly reduced monoamine oxidase B (MAO B) in peripheral organs, particularly in the heart, lungs, and kidneys. MAO B breaks down catecholamines and other physiologically active amines, including those released by nictorine, and its inhibition may contribute to the medical consequences of smoking. The findings also highlight that in addition to the lungs and upper airways, multiple organs in the body are exposed to pharmacologically significant quantities of chemical compounds in tobacco smoke.

Scientist at Oak Ridge National Laboratory examines sample of medicine he developed for potential diagnosis and therapy of cancer.

The Nuclear Medicine Program ended in 1998.