^{18}FDG: Breakthrough for Chemistry, Medicine

Most widely used radiotracer for brain imaging, cancer diagnosis

Seminal achievement

Synthesis of ^{18}FDG, the most widely used radiotracer for brain imaging and cancer diagnosis.

From discovery to diagnosis

^{18}FDG positron emission tomography (PET) and computed tomography (CT) have opened a window for research and diagnosis of a wide range of diseases and conditions, including:

- drug and alcohol addiction
- obesity and eating disorders
- attention deficit hyperactivity disorder (ADHD)
- neurodegenerative diseases such as Alzheimer's
- lung, breast, and other cancers
- epilepsy
- coronary artery disease

Key scientists for first synthesis and imaging studies

- Joanna S. Fowler, Alfred P. Wolf, Tatsuo Ido, Vito Casella, Chung Nan Wan — Brookhaven National Laboratory
- Louis Sokoloff — National Institutes of Health
- Martin Reivich, David Kuhl, Abass Alavi, Joel Greenberg, Michael Phelps — University of Pennsylvania

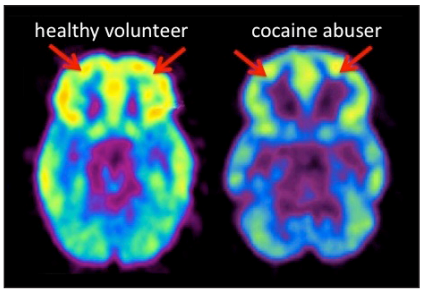
Additional Brookhaven roles

Brookhaven Lab scientists were also involved in: the early development of PET technology, including an earlier predecessor to the PET scanner; advances in ^{11}C and ^{18}F chemistry; determination of the ^{18}F excitation functions; and the development of rapid chemical synthesis methods.

www.bnl.gov/medical/RCIBI/

Early ^{18}FDG synthesis apparatus

Researchers at the U.S. Department of Energy's Brookhaven National Laboratory were pioneers in the development of radioactively "tagged" molecules to trace biological function in living beings. The first, ^{18}FDG or 2-deoxy-2-[^{18}F]fluoro-D-glucose, is a stand-in for glucose, the body's main source of energy. It was first synthesized by Brookhaven chemists in 1976, and is now the most widely used radiotracer for brain imaging and cancer diagnosis.



^{18}FDG brain scans reveal reduced metabolic activity in cocaine abusers vs. healthy subjects.

^{18}FDG and PET

Incorporating ^{18}F, a radioactive form of fluorine, into FDG made it possible to trace the location, concentration, and pharmacokinetics of glucose in living tissue. When injected into the bloodstream, ^{18}FDG travels to wherever glucose (energy) is needed. As the radioactive ^{18}F atoms decay, they emit particles called positrons, identical to electrons but opposite in charge. The positrons and ordinary electrons annihilate, producing back-to-back gamma rays, which can be picked up by the circular array of detectors of a positron emission tomography (PET) scanner. The signals identify the position of the original ^{18}F atom, and create pictures of its location within the body.

"Seeing" chemistry

Because ^{18}FDG is so similar to glucose, its concentration can serve as a key indicator of brain function. This groundbreaking technique opened a window to the exploration of a wide range of neurological and psychiatric diseases, including the effects of addictive drugs.

^{18}FDG PET imaging has also emerged as an essential component of cancer diagnosis. Because tumor cells have high demand for glucose, ^{18}FDG PET scans can pick out these "hot spots" from surrounding healthy tissue, even before anatomical changes are detected. PET can also help monitor patients' response to treatment.

^{18}FDG is now the standard radiotracer used for PET neuroimaging and cancer diagnosis, with more than 1.5 million ^{18}FDG PET scans performed annually. It is produced commercially at regional radiopharmacies and distributed to hospitals throughout the world.

Pathway to discovery

The method used to develop ^{18}FDG grew out of the need of the Atomic Energy Commission, the original federal agency supporting Brookhaven, to understand the basic chemistry of radioactive atoms. With extensive expertise in organic synthesis and radiochemistry, Brookhaven chemists performed the key chemical synthesis, first using ^{14}C, and later, ^{18}F. Collaborators from the National Institutes of Health confirmed that the ^{18}F substitution did not otherwise alter the parent molecule. Samples of ^{18}FDG were soon sent to the University of Pennsylvania, where colleagues first used the tracer to map brain glucose metabolism in humans.

Though ^{18}F has a short "half life" of 110 minutes—the time it takes half the atoms to decay into non-radioactive form—this was sufficient time to transport the molecule and perform the seminal tests. The short half-life makes synthesis challenging; compounds must be made and injected quickly to generate useful data. Amounts used are extremely small, so patients undergoing ^{18}FDG PET scans receive a very low radiation dose.

(10-12)