On October 19 the New York Section of the American Chemical Society announced its designation of the Chemistry Building at the U.S. Department of Energy (DOE) Brookhaven National Laboratory (BNL) (Upton, NY) as a Historic Chemical Landmark. This designation recognizes the importance of $^{18}$F-FDG, originally synthesized at Brookhaven in 1976 for PET scanning. $^{18}$F-FDG is now the world’s most widely used radiotracer for cancer diagnosis, with more than 1.5 million $^{18}$F-FDG PET scans performed annually. “This recognition is a great honor for Brookhaven Lab as a whole and particularly for the chemists who performed this seminal work, including Joanna S. Fowler, PhD, and her colleagues, who continue to explore innovative applications for radiotracer and imaging technologies,” said BNL Director Samuel Aronson, PhD. “The development of $^{18}$F-FDG is also a testament to one of the key strengths of the national laboratories, which bring together scientists from a range of disciplines in an environment that fosters collaborative approaches to address some of our nation’s toughest challenges.”

In a news release, Fowler said, “We were fortunate to have so much expertise in organic synthesis and radiochemistry with short-lived isotopes like $^{18}$F ‘in house’ in Brookhaven’s Chemistry Department—specifically Al Wolf, PhD, Tatsuo Ido, PhD, Vito Casella, PhD, and Chung-Nan Wan, PhD, who worked directly on the $^{18}$F-FDG problem. But we also benefited from the expertise of other scientists at the lab, including other chemists, physicists, and engineers who worked on early detector technology and advanced our understanding of radioactive elements.”

External collaboration was also essential to the $^{18}$F-FDG success story. The original idea of radioactively “tagging” 2-deoxyglucose to create a radiotracer that could be used to image metabolic activity in the brain came from Louis Sokoloff, MD, at the National Institutes of Health (NIH) and Martin Reivich, MD, at the University of Pennsylvania. Sokoloff and Reivich turned to the chemistry experts at Brookhaven to figure out which isotope to use, where to place it on the 2-deoxyglucose molecule, and to develop the complex synthesis technique. The Brookhaven chemistry group had recently pioneered the development of $^{18}$F-labeled elemental fluorine gas. They suggested that this gas could be used to label 2-DG, with the $^{18}$F atom substituting for a hydrogen atom at “position 2” on the molecule. They predicted that this configuration would allow the tracer to mimic the behavior of 2-deoxyglucose. “At first this seemed like an insurmountable challenge,” recalled Fowler.

“Not only did we need to develop a very rapid synthesis from the very reactive fluorine gas, but we had to make enough to make up for radioactive decay for the trip from Brookhaven to Philadelphia, where the imaging would be done. Fortunately, by working at low temperatures and with dilute samples, we were able to ‘tame’ the reactivity.”

After the Brookhaven team synthesized the first samples, NIH collaborators confirmed that the fluorine atom did not otherwise alter the parent molecule. Samples of $^{18}$F-FDG were quickly flown to Pennsylvania, where Reivich and his colleagues first used the tracer to map brain glucose metabolism in humans using the Mark IV scanner developed by David Kuhl, MD. Later, Prantika Som, DVM, ScM, of the Medical Department at Brookhaven, published one of the earliest papers outlining the use of $^{18}$F-FDG in cancer diagnosis. “We couldn’t have done this work or continue what we do today without the combined expertise of chemists, biologists, physicists, and medical doctors and the long-term investment in chemistry and physics by the DOE and its predecessor agencies,” Fowler said.

“Al Wolf, Joanna Fowler, and their colleagues accomplished a tour de force in combining accelerator-based methods for radioactive fluorine production and rapid chemical synthesis to incorporate this isotope into deoxyglucose—and particularly, doing so with the speed required to allow transport to the University of Pennsylvania for experiments to proceed within the several-hour useful lifetime of the tracer,” said Brookhaven Chemistry Department Chair Alex Harris, PhD. “We are very honored to have our Chemistry Building designated as an Historical Chemical Landmark to honor this ground-breaking research.”

BNL chemist Joanna Fowler, PhD, with an early $^{18}$F-FDG synthesis apparatus.
Brookhaven Lab Named Historic Chemical Landmark