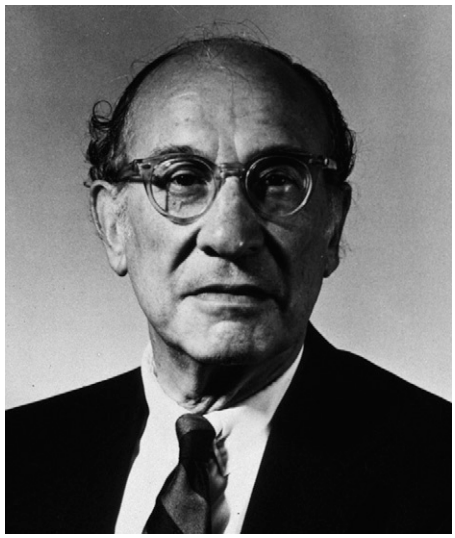
Louis Sokoloff, MD, 1921–2015

Louis Sokoloff, MD, a National Institutes of Health (NIH) researcher recognized for his pioneering work with brain mapping and with PET assessment of metabolic activity, died on July 30 in Washington, DC. He was 93 years old.



Louis Sokoloff, MD

Sokoloff was born in Philadelphia, PA, and completed his undergraduate work in zoology at the University of Pennsylvania (Penn). He received his medical degree from Penn in 1946 as part of the U.S. Army Specialized Training Program's accelerated 3-year course to meet the wartime need for physicians. Sokoloff's internship, which included a concentration in neuropsychiatry, was at Philadelphia General Hospital.

After completing his medical training in 1947, Sokoloff served as head of neuropsychiatry at Kenner Army Hospital at Camp Lee (now Fort Lee), VA. His psychotherapy practice included hundreds of military personnel returning from World War II, and he maintained a dual interest in the benefits of "talk" therapy and in the association of biologic and physiologic processes with specific psychiatric disorders. After discharge from the military in 1949, he returned to Penn as a postdoctoral fellow in the laboratory of Seymour Kety, MD, who, among other foci, was investigating cerebral blood flow (CBF) and cerebral O_2 consumption. In 1948, Kety had coauthored groundbreaking research on the nitrous oxide method for clinical quantitative determination of CBF, and investigations on this and similar topics were in progress when Sokoloff joined the lab. In addition to participation in Kety's ongoing work, Sokoloff became interested in and published on hyperthyroidism and its effects on brain and body metabolism. He also acquired valuable skills in working with radioisotopes, including ^{131}I-trifluoroiodomethane for quantitative autoradiographic assessment of CBF in animals and $^{24}Na^{+}$ for studies in peripheral circulation clearance.

In 1951 Kety was called to Bethesda, MD, to undertake organization of the Intramural Research Programs of the fledgling National Institute of Mental Health (NIMH) and National Institute of Neurological Disorders and Blindness. With the establishment of the NIH Clinical Center and the Section on Cerebral Metabolism of the Laboratory of Neurochemistry at NIMH, Sokoloff joined his mentor at NIMH in 1953. In addition to continuing work on CBF, he partnered with Seymour Kaufman, PhD, in work designed to develop and characterize an appropriate system for protein synthesis for use in exploring the effects of thyroid hormones.

In 1956, when Kety became chief of the Laboratory of Clinical Sciences at NIH, Sokoloff succeeded him as director of activities in the cerebral metabolism laboratory at NIMH. Throughout the 1950s and 1960s, he broadened his interests and expanded collaborations on the relationship between biochemical processes and physiologic function in the brain and nervous system. One ongoing challenge was the lack of a way to measure local metabolic rates in the brains of conscious (unanesthetized) animals. Although he initially worked to resolve this challenge with the ^{131}I-trifluoroiodomethane methods pioneered by Kety and others, Sokoloff soon adapted this approach to use ^{14}C. In the mid-1950s, his team and partners from other NIH labs worked to develop a kinetic model for measuring local cerebral glucose with ^{14}C-glucose, but rapid signal loss made experiments challenging. In 1957 he learned about early investigations with 2-deoxyglucose (DG) and its glycolysis-blocking characteristics and, as he recalled in a memoir, was "intrigued" but filed this information away for future use.

It was not until 1967, working with Martin Reivich, MD, from Penn, that Sokoloff and his team collaborated on reviving the idea of quantitative autoradiography, this time using ^{14}C-DG. Initial studies were conducted with brain slices in vivo, with results published in 1971. During a 1968 sabbatical at the Collège de France (Paris) Sokoloff studied enzyme kinetics. On returning to NIMH, he worked with his laboratory members to develop a new enzyme kinetic model for the autoradiographic DG method for measuring local cerebral glucose utilization. These studies, which included research in nonhuman primates, were presented in 1974.

In parallel with these efforts, Sokoloff and his colleagues developed a computerized image-processing system that scanned and digitized ^{14}C-DG autoradiographs and reconstructed the data into colorized displays of brain glucose utilization. Images from these studies, mapping functional neuroanatomic pathways, were reproduced in the popular media in 1978 and spurred intense scientific interest. At Penn, Reivich and David Kuhl, MD, were working with a section scanner that could measure local concentrations of gamma-emitting isotopes in cross-sections of human brain

using external scintillation counting (a prototype of the Mark IV scanner). Sokoloff, along with Reivich and Kuhl, reached out to Alfred Wolf, PhD, from the Brookhaven National Laboratory (Upton, NY) for assistance with identifying and synthesizing a longer-lived isotope for brain imaging. Wolf's team synthesized ^{18}F-FDG, as reported by a combined Penn, Brookhaven, University of California at Los Angeles (UCLA), and NIH team in 1979. Michael Phelps, PhD, and Edward Hoffman, PhD, at UCLA, adapted ^{18}F-FDG for use with their PET technology. Throughout this period of intense and pioneering investigation into functional imaging, Sokoloff served as a bridge among researchers at different institutions and with varying approaches to instrumentation development.

Sokoloff, who retired from the Laboratory for Cerebral Metabolism in 1999 and remained at NIH as an emeritus scientist, was a past president of the American Society for Neurochemistry and the Association for Research in Nervous and Mental Disease. With his NIH colleagues and coinvestigators from across the United States he published hundreds of peer-reviewed articles. In 1981 Sokoloff received the Albert Lasker Clinical Medical Research Award from the Albert and Mary Lasker Foundation, which emphasized the importance of his brain mapping techniques in driving new and innovative methods for assessing brain function. In acknowledging his achievements, the award committee cited Sokoloff for "developing a pioneering method which enables scientists to visualize the simultaneous biochemical activity of an entire network of neural pathways in the brain and central nervous system. This new method maps and measures their functioning, both as a whole and in localized areas, under both normal and abnormal conditions," adding that "Dr. Sokoloff's brilliant contributions constitute a prime example of a bridge that leads from basic laboratory research to clinical application that can benefit literally millions of people everywhere." Sokoloff also contributed detailed and insightful obituaries of his noted colleagues, including Kety and Kaufman, to the scientific literature.

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normal/routine working environment and tasks. The patient's normal/routine living arrangements. The planned changes to the patient's normal/routine behaviors during the treatment period (have friend or family member accompany the patient or spend time with patient, change in living arrangements, etc.). Financial considerations that will affect the patient's preference on early or delayed release. Discussion to evaluate patient's ability to understand and follow instructions. Discussion to evaluate patient's willingness to follow instructions. Discussion to evaluate the level of disruption to patient routine lifestyle, if released, and the ability of the patient to make and follow the changes, if released." NRC is calling for providers to offer descriptions of policies and procedures as well as for patient input on optimal timing for discussions about release.

Guidance for Released Patients. NRC staff has been directed to develop "standardized guidance for licensees to provide to their patients that would help to reduce the variability of instructions provided to patients and eliminate some of the uncertainty regarding the type of information that is provided to the patient." The request for information noted that "While the NRC currently prefers to develop performance-based guidance (articulating objectives but not telling licensees how to reach those objectives), prescriptive guidance (i.e., very detailed and specific) may be necessary to reduce uncertainty and provide confidence that regulatory requirements are met. If the standardized guidance is performance-based, it would need to provide individual patients with the 'tools' needed to follow the objectives in the guidance and protect others." NRC is calling for copies of guidance documents currently in use that effectively address these and other topics/issues: What ''tools'' (or methods/means) can the patient use to protect others once released? Are both oral and written information presented in the patient's native language and presented in a manner understandable to both the patient and physician (licensee)? Does the medical facility/licensee have access to an interpreting service to make sure that oral and written information and instructions are understood? How are instructions personalized to the individual patient? Does the medical facility explain how to limit the exposures to others (especially to young children and pregnant women)?

Brochure for Nationwide Use. The NRC is also seeking to identify an existing brochure that offers clear guidance on the release of patients treated with ^{131}I.

Responses and comments can be submitted at http://www.regulations.gov (search for Docket ID NRC–2015–0020) or by mail to Cindy Bladey, Office of Administration, Mail Stop: OWFN–12–H08, U.S. Nuclear Regulatory Commission, Washington, DC 20555–0001.