Takuo Aoyagi, Ph.D., inventor of pulse oximetry, noted the influence of Dr. Yoshio Ogino, Nihon Kohden’s founder, on his work. Ogino said “a skilled physician can treat only a limited number of patients. But an excellent medical instrument can treat countless patients in the world.” The history of Aoyagi’s invention, first described in 1974, illustrates Ogino’s point in a profound and compelling way. In the years after Aoyagi’s breakthrough, practical oximeters for patient monitoring came to market. Their uptake in the developed world was stunningly rapid. Many factors contributed to this uptake even before publication of standards mandating the use of pulse oximetry monitoring. It would now be a rare clinician who would ever anesthetize a patient without this monitor. And decades later, the capacity to monitor patients with this essential tool is spreading to the developing world. The use of Aoyagi’s invention has moved far beyond the operating room—most recently for identifying impending respiratory failure from coronavirus disease 2019 (COVID-19)—and its functionality has been enhanced in many ways. This year, the American Society of Anesthesiologists (ASA) awards posthumous Honorary Membership to Aoyagi to recognize his gift to medicine that has literally touched the lives of billions.

Since at least 1936, the bylaws of the American Society of Anesthesiologists (ASA) have provided for awarding Honorary Membership to nonmembers who have attained outstanding eminence in anesthesiology or related fields. This is a recognition seldom made through ASA’s history, making it all the more notable by its rarity.

In October 2020, the ASA House of Delegates approved the recommendation of the Committee on the Distinguished Service Award (whose purview includes honorary membership) to posthumously confer honorary membership on Dr. Takuo Aoyagi, the Japanese engineer who is widely credited with the discovery of pulse oximetry. In accordance with ASA’s protocol, this honor was presented on October 10, 2021, at the annual meeting of the Society. Profiles of Aoyagi and his work have been previously published by Severinghaus, whose shared interest in oxygenation led to a long association with Aoyagi.1,2 A memorial compendium of short papers on Aoyagi and oximetry, organized by his long-time collaborator Dr. Katsuyuki Miyasaka, recently appeared in the Japanese Society of Anesthesiologists’ English language journal, Journal of Anesthesia. Much of this material is now available at http://www.apsf.org by arrangement with the Anesthesia Patient Safety Foundation.

Takuo Aoyagi (fig. 1) was born February 14, 1936, in Niigata Prefecture, Japan. He graduated from Niigata University with a degree in electrical engineering in 1958, and by 1971 began his nearly 50-year career at Nihon Kohden Corporation (Tokyo, Japan). In 1993, he earned a doctorate degree in engineering from the University of Tokyo with a dissertation on pulse oximetry. He died at age 84 on April 18, 2020, survived by his wife, Yoshiko and three children.3

His work at Nihon Kohden was initially focused on dye-dilution techniques for measuring cardiac output. This technique was complicated by the interference of pulsatile blood flow in measurement of the dye and Aoyagi pursued a mathematical formula to correct for the “noise” in cardiac output measurement.

Noninvasive tools to measure oxygen saturation had been sought for almost a century before Millken’s work in the 1940s and Earl Wood’s adaptation of it for clinical use in anesthesia at the Mayo Clinic in 1949.1 Early ear oximeters heated tissue to enhance circulation and featured a compression bladder to allow measurement and comparison of infrared signals from perfused and unperfused tissue to determine oxygen saturation. Interest in these tools originally came from military aviation and physiology research and they were considered impractical for clinical monitoring. Once skin sensors for transcutaneous oximetry became available1 and the connection of hyperoxia and retinopathy of prematurity was recognized, continuous oxygen saturation monitoring became routine, albeit inconvenient, in the newborn nursery by the 1970s. None of these devices were embraced for operating room use.

An astute observer, Aoyagi recognized the potential application of his cardiac output innovations to earlier work on oximetry. Indeed, his first report4 was titled “Improvement of the Earpiece Oximeter.” Wood had established that the...
ratios of transmission of light at 805 nm and 900 nm in the perfused and ischemic earlobe could yield a measurement of oxygen saturation. Aoyagi determined that the pulsation of blood flow offered the opportunity to measure transmission during arterial pulsation and used the measurement of transmission in venous blood in place of an ischemic measurement. Because the calculation of saturation is derived from the ratios of light transmission, beat-to-beat variation is accommodated in the measurement. Aoyagi’s innovations eliminated the need to heat tissue, compress it, or limit the measurement site to the earlobe. (He selected wavelengths of 630 nm and 900 nm to reduce interference from indocyanine green dye when applied to noninvasive cardiac output measurement, his original research focus.)6 This was the beginning of the era of “pulse oximetry,” in which the pulsatile flow of blood was used to facilitate rather than complicate measurement.

Both Aoyagi6 and Hirokazu Ogino, Nihon Kohden chief executive,7 recognized that the company ultimately failed to pursue development of a device based on Aoyagi’s research, even after a Japanese patent was sought. Their introduction of a clinical monitor (OLV 5100) was a commercial disappointment, and Aoyagi and the company ceased work on pulse oximetry for a decade beginning in 1975. In the interim, several other companies adopted and improved upon the design and functionality of the pulse oximeter, largely propelled by availability of the new light-emitting diode technology. Minolta Camera (Tokyo, Japan), Ohmeda (Madison, Wisconsin), and Biox (Jiangsu, China) became early leaders in enhancing and commercializing pulse oximetry. Nellcor (Mansfield, Massachusetts) was founded by Stanford anesthesiologist Dr. William New and engineers Jim Corenmann and Jack Lloyd in 1981 to create a practical device for operating room monitoring based on their own experience and consultations with clinicians worldwide.7 The Nellcor N-100 came to market in about 1983 and quickly dominated the U.S. marketplace. Their device embodied what we would now call “user-centered design”7 with an elegant user interface, finger probe, and introduction of the variable pitch audible saturation signal.

In a very few years, pulse oximeters were ubiquitous in the operating rooms of the United States and other high-income countries. Many believe that their rapid adoption was the result of a mandate in the ASA’s Standards for Basic Intraoperative Monitoring. In fact, these standards were not amended to mandate quantitative monitoring of oxygenation until late 1989,10,11 by which time the uptake of the devices had been enormous. ASA Past-President and Anesthesia Patient Safety Foundation founder Ellison C. Pierce, Jr. commented that “…projecting current trends, it is likely that by the end of 1988, enough oximeters will have been sold for there to be one in every operating room in the country.”12 In this context, one must marvel at the events of the years 1984 to 1988 preceding the mandate. Figure 2 reflects the prevalence of oximetry and capnometry in the claims examined under the ASA Closed Claims Project.13 These may not be representative of U.S. anesthesia practice generally, but the nearly vertical trendline between 1985 and 1988 tells us that anesthesiologists were not waiting for the ASA mandate to require the monitors, nor were they waiting for a randomized controlled trial of their efficacy. The trajectory of introduction of oximetry into anesthesia practice contrasts with the typical S-shaped curve of diffusion of innovation in health care.14 In the New Yorker magazine, surgeon and author Atul Gawande contrasted the stunningly rapid spread of general anesthesia after Morton’s public demonstration with the plodding uptake of surgical antisepsis in the 19th century,15 characterizing the former as a “fast idea” and the latter as a “slow idea.” Experience with pulse oximetry in the 1980s firmly establishes it as a “fast idea.”

The practice of anesthesiology was fertile for this transformation. The specialty was under public scrutiny for its safety record as evidenced by the 1982 ABC News broadcast “The Deep Sleep: 6,000 Will Die or Suffer Brain Damage.” Anesthesiologists knew this to be true, as it was hard to be clinically active and unfamiliar with a case of unrecognized esophageal intubation resulting in death or cerebral anoxia. According to the leading insurer’s risk manager, in Massachusetts alone, 10 to 15 lawsuits for such tragedies were
filed annually during the years preceding adoption of quantitative respiratory monitoring (verbal communication, March 23, 2021, with Maureen Mondor, R.N., Vice President, Professional Education, ProMutual Group [retired], Hyannis, Massachusetts). These events became cloaked with a degree of hopeless inevitability, casting a dark shadow over the practice of anesthesiology, until suddenly there was a method of preventing them through monitoring with oximetry and capnography. What was known as qualitative monitoring of oxygenation, i.e., observing cyanosis in skin or mucous membranes and the hue of blood in the surgical field, was known to be unreliable but, in the absence of a better method, had been relied upon nonetheless. The author recalls dutifully noting in the anesthesia record (where we now record oxygen saturation) “BRB” signifying that there was “bright red blood” in the surgical field.

Just as respiratory monitors practical for clinical use emerged, there were professional liability carriers collapsing and/or dramatically escalating premiums, creating a “medical malpractice crisis” of availability and affordability. While most leaders in organized medicine emphasized tort reform as the remedy, Dr. Pierce stood out as one who acknowledged the imperative to address known preventable patient harm. Particularly when these carriers were physician-owned mutual companies, the opportunity to utilize conditional premium discounts to incentivize use of the monitors was eagerly embraced. In the environment described, user-friendly monitors “sold themselves,” providing critical information with minimal user effort, promising to improve patient outcomes and, ultimately, the cost of liability insurance, too. Jeffrey Cooper, a founder of the Anesthesia Patient Safety Foundation, points to many of these drivers as contributing to the explosive uptake of oximetry with none singularly responsible.

This phenomenon is all the more remarkable considering that then, as now, the clinical outcomes data to support use of pulse oximetry are largely absent. Indeed, as recently as 2014, the Cochrane Database of Systematic reviews “found no evidence that pulse oximetry affects the outcome of anesthesia for patients.” ASA’s Closed Claims project similarly concluded that “the significant decrease in the proportion of claims for death or permanent brain damage from 1975 to 2000 seems to be unrelated to a marked increase in the proportion of claims where pulse oximetry and end-tidal carbon dioxide monitoring were used.” These findings are notably in contrast with an earlier ASA Closed Claims report in which review of more than 1,000 claims led to the conclusion that “these two technologies (pulse oximetry and capnometry) were considered potentially preventative in 93% of the preventable mishaps.”

Neither of these analyses constitute a randomized trial, but a Danish randomized trial with 20,000 patients documented substantial improvements in practice related to use of oximetry, but was underpowered to demonstrate different outcomes with and without oximetry. There have certainly been skeptics of oximetry-driven improved outcomes but in Massachusetts, after the rapid uptake of monitoring accelerated by a liability premium discount, the tragic annual cadence of aforementioned catastrophic cases disappeared (verbal communication with Maureen Mondor, R.N. [retired], Hyannis, Massachusetts).
Mondor, R.N.) and this change was reflected in premium reductions in Massachusetts and similarly throughout the nation.20 There will never be another randomized controlled study to determine the impact of these monitors on patient outcomes but, in the author’s opinion, it would be similarly impossible to find an anesthesiologist with access to the devices who would anesthetize a patient without them. Some of this is due, as in the classic diffusion of innovation model, to peer-to-peer influence of early adopters and some from influential thought leaders in the specialty.26 Oximeters have joined parachutes27 as devices understood to be essential in the absence of a randomized trial.

Since its introduction to operating room practice, this technology has continued to improve and the applications of oximetry likewise expand. Today, there is virtually no corner of a healthcare facility in which oximeters are not found; applications beyond the hospital also abound. Adaptations of Aoyagi’s technology pioneered by Masimo addressed measurement pitfalls from movement and low perfusion.7 These advances facilitated application of oximetry to home monitoring for sleep apnea28 and for surveillance of respiratory depression related to opioid administration,29 though the latter application is limited when supplemental oxygen administration confounds detection of hypoventilation.30,31 Derivation of important physiologic parameters, such as shunt, arterial impedance, and intravascular volume from the pulse oximeter waveform are emerging practices in critical care.32 Oximeters utilizing additional wavelengths can now provide noninvasive monitoring of hemoglobin and dyshemoglobins, including carboxyhemoglobin.33

Aside from patient monitoring uses, oximetry has become a screening tool for congenital heart disease 34 and for recognition of impending respiratory failure.35,36 In austere settings in 116 countries. As we understand the value of oximetry beyond the operating room, the oximetry gap estimated in 2010 for operating rooms alone grows. For example, the value of oximetry for diagnosis and triage of respiratory insufficiency in COVID-19 led Lifebox to rapidly deploy 6,500 oximeters in 43 low-resource countries. The work done by Lifebox and its partners is dramatically amplifying Aoyagi’s impact. Dr. Aoyagi recognized inspiration from the words of Nihon Kohden’s founder, Dr. Yoshio Ogino, who said “a skilled physician can treat only a limited number of patients. But an excellent medical instrument can treat countless patients in the world.”79 The global diffusion of pulse oximetry illustrates Ogino’s point exquisitely. In his later years, Aoyagi received several important recognitions of his work. In 2002, he was awarded the Emperor’s Medal of Honor with Purple Ribbon by the Government of Japan (seen in fig. 1). The Society for Technology in Anesthesia presented him with the Gravenstein Lifetime Achievement Award in 2013, and in 2015, he was the first Japanese recipient a medal awarded by the Institute of Electrical and Electronics Engineers. In 1997, Professor Sten Lindahl, then a member of the committee on the Nobel Prize in Medicine or Physiology, is reported to have addressed the Japanese Society of Pediatric Anesthesiology and publicly stated that Aoyagi’s contributions merited a Nobel Prize.7 Indeed, in 2013, Professor Kirk Shelley was invited to submit a nomination to the Nobel committee and submitted Dr. Aoyagi’s name. He notes that “the Nobel Prize committee has a tradition of recognizing these discrepancies is an important part of understanding the appropriate use of oximetry in making clinical decisions. Whether they can be engineered out of the technology remains to be seen.

Like many other advances in health care, the spread of oximetry to low-resource settings has been slow and sparse; these settings suffer not only from insufficient access to surgical care but also shocking rates of perioperative mortality and morbidity.44 In 2010, it was estimated that 77,000 operating rooms around the world lacked oximetry, the basic physiologic monitor that had become a universal standard of care in high income countries nearly three decades earlier.45 Because of—or despite—this gap, the World Health Organization’s Safe Surgery Saves Lives project included reference to the pulse oximeter in the Safe Surgery Checklist released in 2008.46 Notably, the oximeter is the only piece of equipment cited in the Checklist. Leaders of the Safe Surgery Saves Lives campaign and others recognized the need to close the gap and soon created Lifebox, a global foundation aimed at improving outcomes of surgery in low- and middle-income countries.7 Recognizing the oversized contribution of anesthesia-related mortality to preventable surgical deaths, the first priority for Lifebox was improving anesthesia safety by disseminating oximetry and related training. Since its creation in 2011, Lifebox has distributed more than 26,000 oximeters specifically designed for use in austere settings in 116 countries. As we understand the value of oximetry beyond the operating room, the oximetry gap estimated in 2010 for operating rooms alone grows. For example, the value of oximetry for diagnosis and triage of respiratory insufficiency in COVID-19 led Lifebox to rapidly deploy 6,500 oximeters in 43 low-resource countries. The work done by Lifebox and its partners is dramatically amplifying Aoyagi’s impact. Dr. Aoyagi recognized inspiration from the words of Nihon Kohden’s founder, Dr. Yoshio Ogino, who said “a skilled physician can treat only a limited number of patients. But an excellent medical instrument can treat countless patients in the world.”79 The global diffusion of pulse oximetry illustrates Ogino’s point exquisitely. In his later years, Aoyagi received several important recognitions of his work. In 2002, he was awarded the Emperor’s Medal of Honor with Purple Ribbon by the Government of Japan (seen in fig. 1). The Society for Technology in Anesthesia presented him with the Gravenstein Lifetime Achievement Award in 2013, and in 2015, he was the first Japanese recipient a medal awarded by the Institute of Electrical and Electronics Engineers. In 1997, Professor Sten Lindahl, then a member of the committee on the Nobel Prize in Medicine or Physiology, is reported to have addressed the Japanese Society of Pediatric Anesthesiology and publicly stated that Aoyagi’s contributions merited a Nobel Prize. Indeed, in 2013, Professor Kirk Shelley was invited to submit a nomination to the Nobel committee and submitted Dr. Aoyagi’s name. He notes that “the Nobel Prize committee has a tradition
of awarding significant technical innovation in medicine. Willem Einthoven, in 1924 for his discovery of the electrocardiogram, Allan Cormack with Sir Godfrey Hounsfield, in 1979 for the development of computer assisted tomography and Sir Peter Mansfield, in 2003 for his discoveries concerning magnetic resonance imaging are such examples. I believe Dr. Aoyagi’s discoveries concerning pulse oximetry had achieved that degree of significance.” Aoyagi did not receive that honor in his lifetime but, this year, the ASA posthumously bestows its highest honor for a nonmember in recognition of work that has truly transformed not only the practice of anesthesiology but all of health care, and in doing so has touched the lives of billions.

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Competing Interests
Dr. Hannenberg is a trustee of Lifebox Foundation, Brooklyn, New York.

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