Takuo Aoyagi, inventor of pulse oximetry: the great scientist passed away three years ago, in the middle of the first wave of COVID-19 pandemic

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Antoine-Laurent de Lavoisier (1743-1794), the recognized father of modern chemistry, was the discoverer of both oxygen and hydrogen, as well as the first scientist to understand the importance of oxygen in animal respiration. Following his discoveries, researchers have tried to measure oxygenation of both blood and tissues for the next two centuries.

The embryo of this research has been pursued in the work of Johann Lambert, a Swiss scientist active in mathematics, physics (optics), philosophy, and astronomy. He published in 1760 his *Photometria*, in which he formulated the law stating that absorbance of light by a material sample is directly proportional to its thickness. Approximately one century later the German physicist and chemist August Beer completed the Lambert's principles by adding that absorbance is proportional to the concentrations of the attenuating components in the material sample. The Lambert-Beer law, ascribing the attenuation of light to the properties of the material through which the light is traveling, was definitively formulated.

A fundamental new step forward was made in 1864 when the German physiologist and chemist Felix Hoppe-Seyler published an article describing crystalized hemoglobin, also coining this word to describe the oxygen-carrying pigment he had found in blood. Thereafter, the British physicist and mathematician George G. Stokes, having read the Hoppe-Seyler's article, applied himself to the question of the changing color of blood in the body. He found that the twin-peak absorption of hemoglobin disappeared as blood became deoxygenated and was replaced by a single peak: the red-colored solution of hemoglobin became purple, demonstrating that hemoglobin exists in two states, oxygenated and deoxygenated.

The World War II played an important role in the development of oximetry, since fatal crashes of high-altitude fighter pilots deriving from hypoxia-induced loss of consciousness represented a catastrophic problem, thus spurring research toward in vivo oximetry, in order to warn pilots to wear their oxygen masks. The German physician Karl Matthes developed in 1939 a two-wavelength oximeter using an ear probe, and in the following year J.R. Squire, in London, partially solved the problem of background light absorption by using pneumatic pressure to squeeze the blood from the web space of the hand to allow for calculation of the baseline absorbance without blood. Based on these two experiences, the American physiologist Glenn Millikan developed an ear oximeter that, when matched against arterial blood gas analysis, showed an accuracy ranging from 3% to 8%. He also coined the word "oximeter". The device was further improved in 1949 by the American physiologist Earl Wood, who changed the color filters.

The definitive step away, nevertheless, was made in Japan. In 1971 the electronic engineer Takuo Aoyagi (Figure 1) attended a lecture of Yoshio Ogino, the founder of Nihon Kohden Corporation. Aoyagi was deeply impressed by the words: «A skilled physician can treat only a limited number of patients. But an excellent medical instrument can treat countless patients in the world». Few months later, Aoyagi was working for Nihon Kohden, trying to develop a high-accuracy noninvasive dye densitometer for cardiac output measurement. Aoyagi's words: «My new idea was to adopt the principle of Wood's earpiece oximeter to improve the accuracy of previous earpiece dye densitometers». In fact, in Wood's oximeter, the blood in the ear is expelled pneumatically before the measurement, and light transmitted through the blood is measured, storing the value as a reference. Next, the blood is readmitted to the ear. After that, the optical density of the blood is calculated continuously against the reference value. Two light wavelengths, red and infrared, are used, and the ratio of the optical densities at the two wavelengths is calculated and converted to oxygen saturation (SaO_2) by using an empirical calibration curve. For the new dye densitometry method, Aoyagi adopted ICG (indocyanine-green) dye. The initial maneuver was the same as with Wood's oximeter. He used two wavelengths, 805nm and 900nm, to maximize dye sensitivity and to minimize SaO2 sensitivity. The ratio of the two optical densities was calculated to obtain a dye curve, that was expected to correspond to dye concentrations in the blood.

Aoyagi shortly after realized that both the pulsating and non-pulsating portions of the optical densities of the blood in tissue

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must have same information regarding blood color. The theory was then developed as follows: i) if the optical density of the pulsating portion is measured at two appropriate wavelengths and the ratio of the optical densities is obtained, the result must be equivalent to Wood's ratio; ii) this way, the arterial blood is selectively measured, and the venous blood does not affect the measurement; as such, the probe site is not restricted to the ear; iii) in this method, the reference for optical density calculation is set for each pulse.

Aoyagi presented his results at the Japan Society of Medical Electronics and Biological Engineering (MEBE) meeting, in October 1973, and in January 1974 he sent the paper presenting his invention.[1-3] The device was quickly marketed as Oximeter OLV-5100 (Figure 2).

Figure 1. Takuo Aoyagi (1936-2020). Freely available from the internet.

Figure 2. The first pulse oximeter, OLV-5100, patented by Takuo Aoyagi and produced by Nihon Kohden in 1974. Freely available from the internet.

After that, two different companies developed their own oximeters. Firstly, Minolta presented, in 1977, the Oximet-1471 (it should be remembered that in 1969 the astronauts Neil Armstrong and Buzz Aldrin, the first humans on the moon, carried on Apollo 11 a high-resolution exposure meter by Minolta), and subsequently Nellcor presented his N-100 in 1983. Far from being envious, Aoyagi in 2003 wrote: «I thank deeply Minolta and Nellcor. Without them, the idea of pulse oximetry would have been buried».

Introduction of pulse oximetry in operating room coincided with a 90% reduction in anesthesia-related fatalities, and, by 1987, the standard of care for the administration of a general anesthetic in the U.S. included pulse oximetry. From the operating room, the use of pulse oximetry rapidly spread throughout the hospital, especially to Intensive Care Units, and Emergency Departments. In the following years it also spread outside the hospital, firstly in the ambulances and, enormously with COVID-19 pandemics, in everybody's domestic environment. Moreover, pulse oximetry was of great value in the Neonatal Units where the children do not thrive with inadequate oxygenation, but – on the other hand - too much oxygen concentration can lead to vision impairment or blindness from retinopathy of prematurity. As such, pulse oximetry should be considered one of the most important technological advancements in monitoring patients in several clinical situations, most of which of outstanding importance in Emergency Medicine.

Aoyagi received the Medal with Purple Ribbon from the Emperor of Japan in 2002, and was nominated for Nobel prize in 2013, but he did not receive it. Shortly after, in 2015, he was awarded by the Institute of Electrical and Electronics Engineers (IEEE) with the "Medal for Innovation in Healthcare Technology", being the first Japanese to be awarded this way.[4]

Takuo Aoyagi passed away on April 18th, 2020, at the age of 84, in the middle of the catastrophic first wave of COVID-19. The contribution of pulse oximetry to the worldwide management of the pandemic is incalculable.

References

1. Aoyagi T. Pulse oximetry: its invention, theory, and future. J Anesth 2003;17:259-266
2. Severinghaus JW. Takuo Aoyagi: discovery of pulse oximetry. Anesth Analg 2007;105:S1-S4
3. Van Meter A, Williams U, Zavala A, et al. Beat to beat: a measured look at the history of pulse oximetry. J Anesth Hist 2017;3:24-26
4. Miyasaka K, Shelley K, Takahashi S, et al. Tribute to Dr. Takuo Aoyagi, inventor of pulse oximetry. J Anesth 2021; 35:671-709