HISTORY OF BLOOD GAS ANALYSIS. VII. PULSE OXIMETRY

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Severinghaus JW, Honda Y. History of blood gas analysis. VII. Pulse oximetry.
J Clin Monit 1987;3:135–138

ABSTRACT. Pulse oximetry is based on a relatively new concept, using the pulsatile variations in optical density of tissues in the red and infrared wavelengths to compute arterial oxygen saturation without need for calibration. The method was invented in 1972 by Takuo Aoyagi, a bioengineer, while he was working on an ear densitometer for recording dye dilution curves. Susumu Nakajima, a surgeon, and his associates first tested the device in patients, reporting it in 1975. A competing device was introduced and also tested and described in Japan. William New and Jack Lloyd recognized the potential importance of pulse oximetry and developed interest among anesthesiologists and others concerned with critical care in the United States. Success brought patent litigation and much competition.

KEY WORDS. Oxygen: saturation. Measurement techniques: oximetry. Blood: gas analysis, history.

Within the last four years, pulse oximetry has become widely used in anesthesiology and many critical-care situations; at least 15 manufacturers are now marketing pulse oximetry instruments. Severinghaus and Astrup's review of the history of oximetry in a preceding issue of this journal [1] contained several errors relating to the origin and development of pulse oximetry. Perhaps because of the difficulty of uncovering original Japanese sources, its origin has been ascribed variously to the anesthesiologist Yoshiya and his colleagues in 1980 [2] or to the surgeon Nakajima and his colleagues in 1975 [1], and the development of the pulse oximeter has been attributed to the wrong company as well. Corrections to and further details of the history of pulse oximetry are presented here.

ORIGIN OF PULSE OXIMETRY

The idea of using pulsatile light variation to measure arterial oxygen saturation was conceived by the Japanese physiological bioengineer Takuo Aoyagi (Fig 1). Aoyagi was born February 14, 1936, in Niigata Prefecture, Japan. In 1958, he was graduated from the Faculty of Engineering at Niigata University, where his speciality was electrical engineering. Initially he worked at the Shimazu Corporation on instrumentation, and in February 1971 he joined the Research Division of Nihon Kohden Corporation, one of Japan's leading medical electronics firms. His research interests have been instrumentation for monitoring fetal heart rate during childbirth, electrical bio-impedance monitoring of ventilation, the phenomenon of airway closure at low lung volume, pulmonary circulation, and cardiac output

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Received Nov 8, 1986. Accepted for publication Nov 21, 1986.

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Fig 1. Takuo Aoyagi.

measurement by dye dilution using an improved earpiece.

In the early 1970s, Aoyagi's research concerned the measurement of cardiac output by dye dilution, a well-developed technology in which light of specified wavelengths is passed through blood, usually as it flows from an artery through an external cuvette, and is detected by photocells. Various investigators had attempted to use ear oximeters for dye measurement to avoid the need for arterial blood sampling. The transmitted light signal was noted to exhibit pulsatile variations, which made it nearly impossible to compute cardiac output accurately from these noninvasive dye dilution curves.

To effectively use the earpiece for dye densitometry, Aoyagi devised a method of cancelling the pulsatile variations by electrically subtracting a pulse signal detected at 900 nm (infrared), where the cardiogreen dye is transparent, from the dye-sensing 630 nm red signal. However, he and his associate noted that this cancellation was fickle (probably due to changes in the oxygen saturation). Fortunately for the discovery of pulse oximetry, the effect of oxygen desaturation increases infrared light transmission while decreasing red light transmission. Therefore, oxygen saturation changes had the best possible chance of "spoiling" his dye dilution curves.

Here is a classic example of the wisdom that "one man's noise is another man's signal." This failure of elimination of pulsatility in the dye curves led directly to pulse oximetry. Aoyagi had long been interested in oximetry and was familiar with the work of Millikan and Wood. He knew that the older oximeters compensated the red light signal with a signal from infrared light at 805 nm, the "isobestic" wavelength, where oxygen has no effect on the optical density of hemoglobin. Fortunately, however, instead of choosing the isobestic 805 nm infrared light, Aoyagi continued to use 900 nm because he hoped to make an earpiece that would have a dual purpose, not only measuring oxygen saturation but also recording dye dilution curves.

Aoyagi also was aware of the principle of compressing the tissue to set a bloodless zero, first introduced in 1940 by Squire and Goldie [1]. He was well prepared to recognize the opportunity inherent in the noise in his dye dilution curves: to create from it a signal for oxygen measurement. Credit thus belongs to Aoyagi for the idea of measuring only the pulsatile *changes* in light transmission through living tissues to compute the arterial saturation. He realized that these changes of light transmission at all wavelengths would solely be due to pulsatile variations of the intervening arterial blood volume. Thus, the unpredictable absorption of light by tissue, bone, skin, and pigments would be eliminated from analysis. It was this key idea that permitted the development of instrumentation that required no calibration after its initial factory setting, as all human blood has essentially identical optical characteristics in the red and infrared bands used in oximetry.

In early 1973, Susumu Nakajima, a surgeon then working at the Sapporo Minami National Sanatorium, heard about Aoyagi's idea from Aoyagi's supervisor, Y. Sugiyama. Nakajima placed an order with Nihon Kohden for the apparatus, which he wanted to test in patients.

In January 1974, an abstract in Japanese describing the invention, titled "Improvement of the Earpiece Oximeter," was submitted to the Japanese Society of Medical Electronics and Biological Engineering by the developing team of Aoyagi and associates Michio Kishi, Kazuo Yamaguchi, and Shinichi Watanabe of the Second Division of Technology, Nihon Kohden Corporation [3]. The new oximeter used an incandescent lamp with filters at 630 and 900 nm and analog detection of the pulsatile optical signal ratio at these wavelengths. The paper was presented by Aoyagi on April 26, 1974. On March 29, 1974, a patent application titled "Apparatus for Photometric Blood Analysis" was submitted to the Japanese Patent Office by the Nihon Kohden Corporation, naming Aoyagi and Kishi as inventors. The application was publicly disclosed on October 9, 1975 and published on August 2, 1978 (No. 53-26437), and the patent was granted on April 20, 1979 (No. 947714).

On April 24, 1974, a patent application based on a similar idea was submitted by Masaichiro Konishi, who was named as inventor and was working at the Minoruta Camera Company (known in the United States as Minolta). How this competing application arose and whether Aoyagi's idea was discovered and copied has never been established. Konishi's patent application was rejected by the Japanese Patent Office on February 9, 1982. However, Minolta applied for and obtained patent protection in the United States.

DEVELOPMENT OF THE INSTRUMENTATION

The prototype pulse oximeter was made by Aoyagi between September 1973 and March 1974. That instrument was used by Nakajima and his associates Yasuro Hirai, Hiroshi Takase, and Akihiko Kuze at the Sapporo Minami National Sanatorium. Their first publication (reference 97 in Severinghaus and Astrup [1]) included the developers—Takuo Aoyagi, Micho Kishi, and Kazuo Yamaguchi of the Nihon Kohden Corporation—as the fifth, sixth, and seventh authors. The first commercial instrument, the OLV-5100 (Fig 2), was made available in 1975 as an ear oximeter by Aoyagi and his associates. However, Nihon Kohden did not continue to develop or market this instrument and made no effort to patent it abroad.

The Minoruta Camera Company developed their similar device, marketing it as the Oximet MET-1471 in 1977 with a fingertip probe and fiberoptic cables from the instrument. This was the design illustrated as Figure 15 in Severinghaus and Astrup's history [1]. Nakajima and nine associates then tested and used this Minoruta fingertip pulse oximeter and described it in 1979 [4].

SUCCESS, PATENTS, AND SUITS

Several groups began developmental work in pulse oximetry using Aoyagi's idea in the late 1970s. Important advances in the technology were made by the Biox Company of Boulder, Colorado, and were protected by patents. However, limited interest was generated by the development of pulse oximetry during the first 8 to 10 years. Few foresaw its value in anesthesiology, intensive care, and other emergent situations, probably because conventional oximetry had never been convenient enough for these uses. The Hewlett-Packard ear oximeter had been used almost entirely in pulmonary function laboratories and other physiologic environments. Indeed, the initial work on pulse oximetry in the United States by several firms (Minolta, Corning, Biox) considered these types of laboratories to be the probable market.

Credit for the present enormous interest in pulse oximetry belongs to anesthesiologist William New, of Stanford University Medical School, who with engineer Jack Lloyd founded Nellcor Incorporated. New recognized the potential importance of and market for a convenient, accurate oximeter in the operating room and all other hospital and clinic sites where patients are sedated, anesthetized, unconscious, comatose, paralyzed, or in some way limited in their ability to regulate their own oxygen supply.

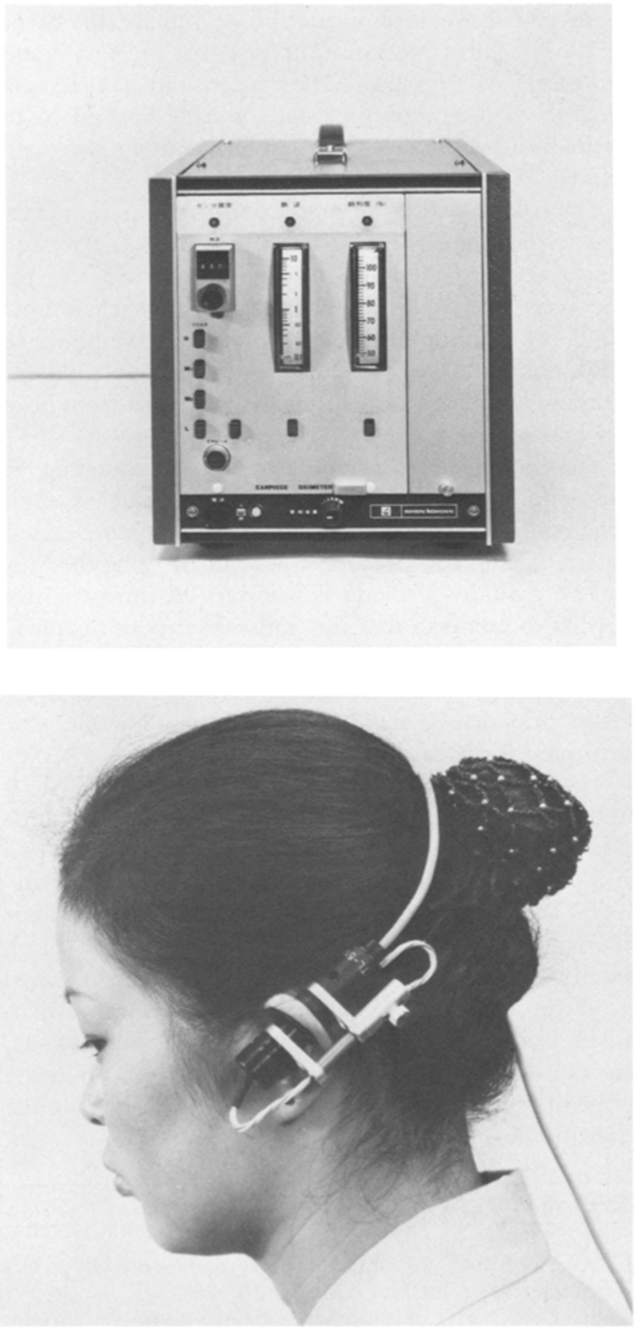

Fig 2. Oximeter OLV-5100.

With the worldwide interest in pulse oximetry has come patent litigation initiated by Ohmeda, the owner of Biox, against Nellcor. The case was recently settled out of court, leaving the Biox patent intact. It remains unclear whether this precedent will be applied to the entire mushrooming industry surrounding pulse oximetry.

The role of patents in medical instrumentation is fascinating and sometimes depressing. The links between innovation and income are tortuous and tenuous; patents were intended to forge an invulnerable chain binding them. But human struggle for achievement finds the weak links and breaks the bond wherever possible. It is a rare inventor who enjoys financial reward from his or her brilliant insight.

The story of the patent litigation surrounding the polarographic oxygen electrode is a classic example. One court determined that the initial oxygen electrode patent was invalid because it did not describe the Stow carbon dioxide electrode as prior art. A third trial was needed to establish that the omission was not evidence of deceit and therefore not basis for triple damages under the Sherman antitrust law. Above all, the careers of the principals, Leland Clark and Ryan Neville, were disrupted for many years.

The winners are usually those who persist in developing and marketing an invention; particularly those who continue to improve and to respond to criticism and suggestion while keeping costs down and quality high. The relationships between users and manufacturers are fragile and especially vulnerable when bright small companies are bought out, moved, mismanaged, neglected, starved, or rejected in their attempts to make a better product. Perhaps in the long run, the best society can do is to acknowledge innovation and honor in print the men and women whose ideas initiate innovations in life-support technology.

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