Special Article

Infrared Measurement of Carbon Dioxide in the Human Breath: "Breathe-Through" Devices from Tyndall to the Present Day

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The ability to measure carbon dioxide (CO_2) in the breath of a patient or capnometry, is one of the fundamental technological advances of modern medicine. I will chronicle the evolution and commercialization of mainstream capnometry based upon infrared measurement of CO_2 in the breath using information from the historical record and personal interviews with many of the developers.

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The ability to measure carbon dioxide (CO_2) in the breath of a patient is one of the fundamental technological advances of modern medicine. The partial pressure of CO_2 in arterial blood indicates the balance between CO_2 production and elimination and provides invaluable insights into metabolism and cardiopulmonary pathophysiology. Measurement of CO_2 in arterial blood is difficult, whereas monitoring CO_2 in the breath provides a convenient, continuous and noninvasive estimate or trend of arterial CO_2. The clinical motivations for measuring CO_2 in the breath of a patient are myriad. For patients dependent upon mechanical ventilatory support, exhaled CO_2 monitoring insures the integrity of the airway, helps to guide ventilator settings and has dramatically enhanced the safety of this life-sustaining therapy. CO_2 monitoring also allows us to monitor the severity of pulmonary disease and the adequacy of the circulation. Measuring both oxygen consumption and CO_2 production is useful to evaluate the metabolism of both critically ill patients and elite athletes.

The CO_2 molecule's asymmetric and polyatomic nature causes it to strongly absorb light in the infrared (IR) part of the spectrum. The concentration of CO_2 in a gas sample can therefore be measured by shining IR light on the sample, and comparing the intensity of light that passes through the sample with the original light intensity.[a] The light intensity is reduced as it passes through the sample in proportion to the concentration of CO_2 present. Translating this theoretical knowledge into the inexpensive, reliable clinical capnometers used daily throughout the world has required almost two centuries and countless human-years of work.

Not only is it convenient that CO_2 strongly absorbs light in a specific portion of the IR range, the technology for creating and transmitting the light through a contained gas sample and detecting the transmitted IR light has enabled real-time respiratory gas monitoring. The "essentials" of nearly all IR gas analyzers are (a) a source[b] of IR radiation with an emission spectrum that includes the absorption bands of the gases to be measured; (b) a sample cell fitted with windows "possessing" suitable transmission properties; (c) an optical or gas filter to limit the wavelength range measured by the detector; (d) a means, either physical in the form of a rotating chopper disk or electronic circuit, to modulate the IR radiation from the source; and (e) a detector, based on either a thermal or photonic mechanism,[c] to convert the IR radiation into an electrical signal. All of these essentials are generally inexpensive and readily available in modern times but that has not always been the case. Integrating these essential aspects for gas measurement into the functional monitors we use today has not been a trivial task.

This review presents the history of the IR analysis of exhaled CO_2 measurement. Although the early history is a matter of public record, the more recent history is based, in part, on the author's experience at Novametrix, where he has worked as a scientist since 1994.

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Conflict of Interest: Dr. Jaffe is employed by Respironics, Inc.

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[a] In a number of devices, the intensity of light that is transmitted is compared at two wavelengths, one at which CO_2 strongly absorbs and another at which CO_2 does not absorb.

[b] The most commonly used type of IR source acts as a blackbody radiator which when heated to moderate temperatures radiates IR energy.

[c] The solid-state devices usually used to detect IR radation include lead salt photoconductors (e.g. lead selenide) and thermopiles.

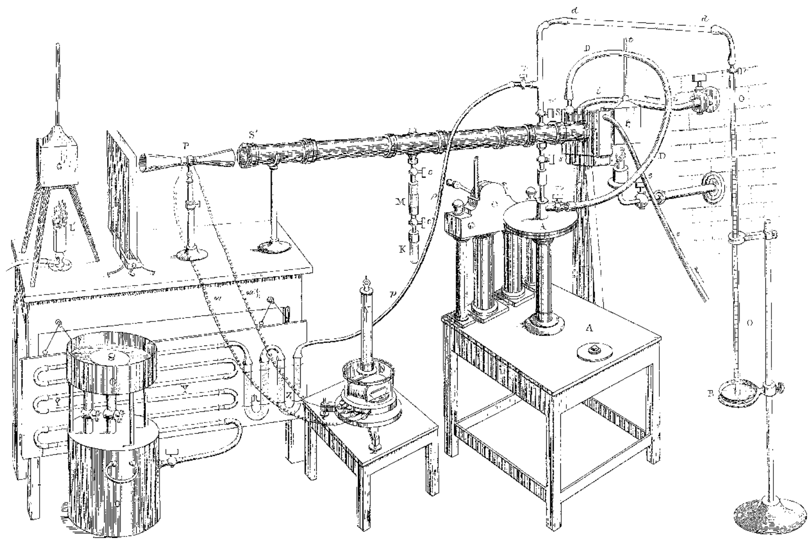

Figure 1. Tyndall's experimental apparatus, shown here consisted of a long tube that he filled with various gases. To contain the gas, the tube was capped with rock salt crystal which is transparent to heat radiation. To create the incident light, a Leslie cube[jj] was heated and emitted radiation that traversed the tube and interacted with the gas before entering one cone of a detector called a differential thermopile. Radiation from a second Leslie cube passed through a screen and entered the other cone. A galvanometer measured the voltage difference between the cones. The intensity of the two sources of radiation entering the two cones could be compared by measuring the deflection of the galvanometer. The difference in the intensity of light detected indicated the absorptive power (concentration) of the gas in the tube (adapted from Tyndall[4]).

Early IR CO_2 Analyzers

One of the earliest IR measurements of CO_2 in the expired human breath was reported by John Tyndall.[1,2] Tyndall (1820–1893) constructed the first ratio spectrophotometer, which he used to measure the absorption of gases and vapors such as water vapor, "carbonic acid" (now known as CO_2), ozone, and hydrocarbons.[3] (Fig. 1). He observed the large differences in the abilities of "perfectly colorless and invisible gases and vapors" to absorb and transmit radiant heat and as such played a pivotal role in elucidating the physics underlying global warming.[5] He reported in his famous Rede Lecture "On Radiation" at Cambridge University perhaps the earliest IR quantitative measurement of CO_2 in the human breath.[d] In the section of the lecture titled "Influence of vibratory period and molecular form-physical analysis of the human breath," he notes:

> The presence of the minutest quantity of carbonic acid[e] may be detected by its action on the rays from the carbonic oxide flame. Carrying, for example, the dried human breath into a tube four feet long, the absorption there effected by the carbonic acid of the breath amounts to 50% of the entire radiation. Radiant heat may indeed be employed as a means of determining practically the amount of carbonic acid expired from the lungs . . . . . The absorption produced by the breath, freed from its moisture, but retaining its carbonic acid, was first determined. Carbonic acid, artificially prepared, was then mixed with dry air in such proportions that the action of the mixture upon the rays of heat was the same as that of the dried breath. The percentage of the former being known immediately gave that of the latter. The same breath, analyzed chemically by Dr. Frankland, and physically by Mr. Barrett, gave the following results:
>
> Percentage of Carbonic Acid in the Human Breath
>
> | Chemical Analysis | Physical Analysis |
> |---|---|
> | 4.66 | 4.56 |
> | 5.33 | 5.22 |
>
> It is thus proved that in the quantity of ethereal motion which it is competent to take up, we have a practical measure of the carbonic acid of the breath, and hence of the combustion going on in the human lungs.[1]

These measurements were made to demonstrate the sensitivity of different molecules to absorb IR radiation depending upon the radiation source. Since human breath had a significantly higher percentage of CO_2 than the atmosphere, it provided an easy source of the gas. Also of interest is the statement of the paradigm dominant in the 1860s of human metabolism by Tyndall that the CO_2 in the lung is a result of the "combustion" (i.e., oxidation) within that organ. It was not until a few years later in the 1870s when it was shown that metabolism occurs in peripheral tissues and that the blood serves to transport the respiratory gases between the tissues and the lung.[f]

In the intervening years between Tyndall's work and the later work of Pfund, Luft, and others, methods to determine CO_2 concentration in the breath based on

[jj]Leslie's cube (named after Sir John Leslie who experimented with radiant heat in 1804) consists of a cubical vessel with different sides - one of highly polished metal, another painted black, and the other two consisting of a dull metal (copper). He showed that radiation was greatest from the black side and negligible from the polished side.

[d]Note that the relationship between emission and absorption spectra was elucidated in the work of Kirchhoff and Bunsen (Kirchhoff G, Bunsen R. Chemical Analysis by Observation of Spectra Annalen der Physik und der Chemie (Poggendorff) (1860), 110:161–189.) it was not until later improvements in instrumentation allowed quantification and visualization of the absorption spectra of CO_2.

[e]Carbonic acid-Carbon dioxide (CO_2).; Carbonic oxide-Carbon monoxide (CO).; Olefiant Gas- Ethylene (C_2H_2).[6]

[f]Eduard Pfluger (1829–1910) and colleagues helped establish this with a series of publications between 1866 and 1878 including "on the origin and rationale of the oxidative processes in the animal organism." (Garrison, FH. An Introduction to the History of Medicine, W.B. Saunders Company, Philadelphia, 1914 (763 pages)).

chemical absorption[g] using substances such as potassium hydroxide were refined and widely used.[7,8] Additionally, physical methods other than IR approaches for CO_2 measurement were developed including ones based on thermoconductivity.[9]

In 1939, August Herman Pfund (1879–1949) developed a respiratory gas analyzer that was used at Johns Hopkins Hospital in Baltimore to measure carbon monoxide and CO_2.[10,11] Pfund described this thermal method of CO_2 measurement as "mak(ing) possible continuous analysis without disturbing the mixture," in contrast to chemical methods that destroy the material under test.[10] The detector cell was filled with a mixture of 3% CO_2 and 97% dry air. A gas sample was passed into an absorption cell and, if no CO_2 was present in the sample, the radiation would be absorbed in the detector cell and the increase in temperature would be measured by the thermopile. The presence of CO_2 in the absorption cell would cause less radiation to be absorbed in the detector cell and therefore a smaller increase in temperature.

Working at about the same time as Pfund, Karl Friedrich Luft (1909–1999) developed IR technology that used a balanced condenser microphone detector consisting of sealed cells containing pure CO_2 separated by a diaphragm. This kind of detector, now known as the Luft cell, can be traced to the photoacoustic effect first observed by Bell[12] and demonstrated at the Paris Exposition in 1880. This story begins in 1937 when Luft joined BASF, which originally stood for Badische Anilin-und Soda-Fabrik (Baden Aniline and Soda Factory). At BASF, he was confronted with a measurement problem.[13] Plastic fabrication resulted in a highly explosive mixture of butane and air. A method to measure low concentrations of butane was desired to make this process safer. It was observed that butane has strong absorption in the IR band, but that known photometric methods of the time failed since they were too strongly affected by interfering gases in the mixture such as CO_2 and water vapor. Luft postulated that the gas itself could be a "radiation receiver" that would have the necessary selectivity required to differentiate the gases in the mixture. He collaborated with Lehrer who had just successfully developed a recording IR spectrophotometer which led to development of a device using gas-filled detectors (Fig. 2).[h] The superiority of the new device over existing electrochemical devices convinced even the factory chemists who were skeptical about using a device based on physical principles. This device, known as the URAS (Ultrarot Absorptions-Schreiber-IR absorption writer), consisted of a power supply, optics and amplifiers, which were packaged in electrical switching boxes bolted together. Despite

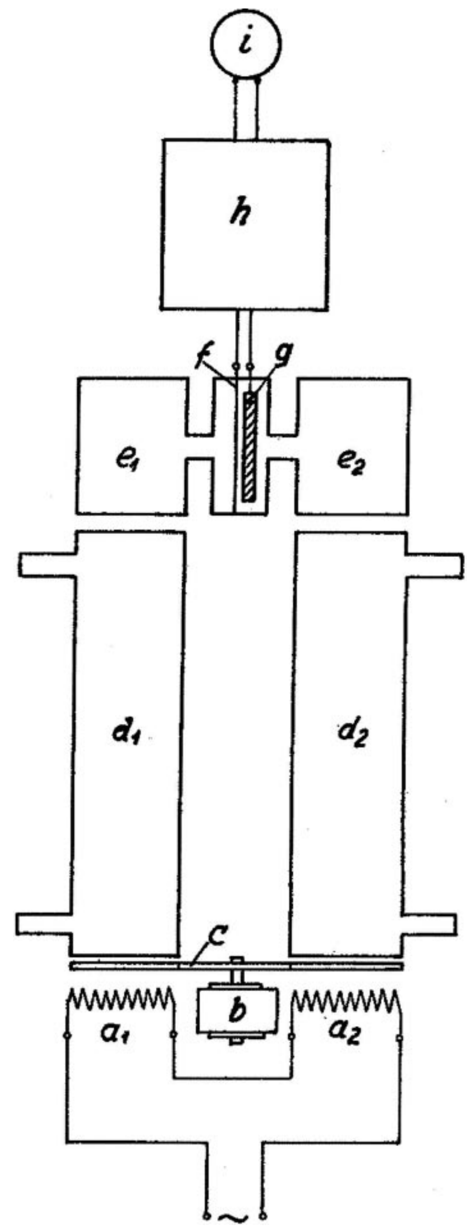

Figure 2. Luft's device–("The radiation coming from the sources a1 and a2 is periodically interrupted through a shutter wheel c that is driven by motor b. The shutter wheel c has slits in such a way the radiation from both sources can pass through at the same time (or is interrupted at the same time). Behind shutter wheel c the radiation runs through the pipes d1 and d2, where d1 contains the gas to be measured and d2 is filled with a reference gas (*at half atmosphere*). The radiation then enters chambers e1 and e2, which contain-as a "reception layer"-the gas that is to be determined. Both chambers are separated (in an almost gas-tight fashion) from each other through a thin [metal] membrane f; this membrane forms with the insulated counter plate g an electrical capacitor. If the gas mixture contains the component that is to be determined, chamber e1 receives a weaker radiation than e2; as a consequence and corresponding to the interruptions by the shutter wheel c there is a periodic pressure difference between the chambers e1 and e2 which can-through membrane f-be transformed in changes of capacitance. The membrane capacitor is followed by an amplifier h, which allows a readout at the measuring instrument i of the capacitance variations and thereby the concentration of the gas that is to be determined." (translated from German) (Reproduced from Lehrer and Luft[15]).

[g]The reduction of the gas volume was measured and indicated the quantity of the gas absorbed.

[h]In 1943 Luft published his often-referenced paper on the device in Zeitschrift fûr Technische Physik[14] and he and Lehrer were awarded a patent (filed in 1938) on the technology.[15]

using common components, the war effort limited the supply of parts. To further complicate matters, the manufacture of these detector cells was considered to be a very tedious and delicate process. Despite all of the problems, BASF was able to manufacture several hundred devices for use in manufacturing in I.G. Farbenindustrie chemical factories, although a number of these devices were destroyed during air bombardments.[13] These devices were deemed sufficiently valuable that many were confiscated by the Allied powers after the war.

At the same time as Luft, Veingerov (1938),[16] at the State Optical Institute of Leningrad under A.A. Lyebyedyev (1893–1969), designed a series of early gas analyzers based on the detection of pressure fluctuations relating to the varying IR absorption in the gas sample. He referred to these analyzers as 'optico-accoustic' gas analyzers.

Commercial Medical IR CO_2 Analyzers

As pulmonary physiology and metabolism became better understood in the 1900s, a convenient method for measuring CO_2 in the breath and avoiding the need for direct arterial measurement was sought. The ability to measure CO_2 by IR absorption was well established, but early devices were too large and impractical for clinical use. Advancements in both mainstream and sidestream clinical devices were enabled by technology developments. The size of these devices was reduced to allow their inclusion in clinical monitors and the known technological and related ease of use weaknesses of the early devices were solved. The story behind the development of these early devices and several of the original equipment manufacturer (OEM) mainstream CO_2 devices is told based primarily upon interviews with key contributors to each of these devices. The story behind some of the CO_2 sensors from Hartmann and Braun, Liston-Becker/Beckman, Cascadia/Novametrix/Respironics, Hewlett-Packard, and Siemens-Elema will be discussed. Other devices will also be mentioned.

Hartmann and Braun/Godart

At the end of 1952, Hartmann and Braun acquired the trademark and license to manufacture and distribute the URAS device from BASF.[13] The Luft detector is shown in Figure 2 and is described as in the original German patent. Representative systems using the Luft detector included the Hartmann and Braun URAS series of instruments and Godart capnographs[i,17] (Fig. 3), a modification of the URAS4.[18] These systems were widely used for CO_2 measurement in clinical settings in the 1960s and 1970s.

Figure 3. The first CO_2 analyzer (Godart Capnograph medical CO_2 analyzer) in the Central Military Hospital, Utrecht, The Netherlands (1962). On top is the one channel Omniascriptor,. Photo: Lt. Klunder (Photo used with permission from Prof. Bob Smalhout).

Liston-Becker/Beckman Instruments

The story of the development and commercialization of breathe-through IR CO_2 devices would not be complete without a discussion of the contributions of Max Liston, who had worked with Prof. Pfund at Johns Hopkins during the Second World War. Prof. Pfund had conceived of and had patents on both the Luft type detector-pneumatic type using thermocouples and negative type[j] using gas filters.[11] Although Liston was aware of the concept of the Luft type detector, it was not until after the war that he became aware of Luft's work.

> I was at the army chemical research center in Bethesda-we were working on some IR applications for target detection-they took me around and showed me—these instruments—they did not know what they were—I immediately recognized them as positive type infrared analyzers—that is how I became aware of Luft devices. What I saw was quite primitive-two boxes source with mechanical chopper-windows were rock salt and were attached with Apiezon[k] wax.—quite a few built during the war in the synthetic rubber industry—chopper rate very slow—like 4 Hz.[19,l]

Max describes how he got into the gas analyzer business.

> "Dr. [James] Elam[m] and Dr. George Saxton [working out of Drinker Laboratory, Harvard Medical School], two of the doctors that I worked with on the Oximeter

[i]Previously termed IR CO_2 meters or analyzers from the 1950s and into the early 1970s, it appears that the term "capnograph" was derived from the Godart Capnograph.

[j]Negative filtering typically uses the difference in absorption between 100 percent of gas A in one chamber and the "unknown" sample gas mixture containing gas A in another chamber.

[k]Low melting point wax.

[l]At a data sampling rate of 4 Hz it is difficult to resolve breath-to-breath changes.

[m]This story from Dr. Elam's perspective (1918–1995) has been told as well[20] and discusses how these devices helped Dr. Elam and colleagues discover a problem with canisters of the day, identify three characteristics of CO_2 absorption with respect to these canisters, report on the property of channeling[21] in soda lime and how they modified the canisters to minimize this effect.

during the war, and some of the other doctors (e.g., Dr. Whittenberger[n]) had been down in Atlantic City at a convention, [and during a dinner] got into an argument. All of them had experienced [shock and] some cardiac arrests on the operating table. These were anesthesiologists. They thought it was due to CO_2 [carbon dioxide] accumulation. So they [drove up to Connecticut to my home] and got me out of bed at two o'clock in the morning and in my weakened condition at that time, talked me into building a CO_2 analyzer for them so they could resolve this concern. That's how I happened to get into the gas analyzer business. I had just left Perkin-Elmer at the time so I was looking for something to do . . . . The first CO_2 analyzer was sent to Dr. Drinker's lab under Dr. Whittenberger at Harvard University.[19]

In 1950, Morris Folb and Max Liston formed the Liston-Folb company in Stamford (Springdale), Connecticut. The company later became the Liston-Becker company with the financial backing of Dick Becker and Albert Austin. The first prototype device (precursor to the Model 16) was a breath-through arrangement. Max recounts:

We took 3/4" copper tubing and smashed it down the middle to give us (a) flat (area for the) windows [about 1/10" between windows] and that plugged directly into the face mask of the subject. Originally we used thin quartz windows but later I got in contact with Union Carbide which were making sapphire for phonograph needles, and they occasionally they would get a boule[o] which was large enough for a window-and I had arrangement with them so I got their full production-I had a monopoly of their sapphire for quite a few years and Union Carbide were the only ones making it in the early 1950s (Max Liston, 2004).

The light source was incandescent, micro type wire, potted in ceramic which ran at a fairly low temperature, and mechanically chopped at 60 Hz with a Luft detector. This prototype introduced in about 1951 was "received with quite little interest" and was sold primarily to universities for research such as Harvard. Max describes one setback:

Dr Stow[p] published on an infrared unit that he had developed[22] and said it was no good because of what he called the Stow effect[23] if you put the sensor in a Nitrous oxide background you got a different reading than you got if you put it in a nitrogen/air background. Pressure broadening–Thought he discovered a new phenomena-that hurt our sales because at that time nitrous oxide was used for induction at very high levels-80%. However, it did not affect the Luft detector-particularly the way we were charging them because our resolution was so high the so called Stow effect was negligible Dr Elam finally published a paper refuting Stow and that brought the business back. Elams [classic] four papers were with our instruments.[24–27]

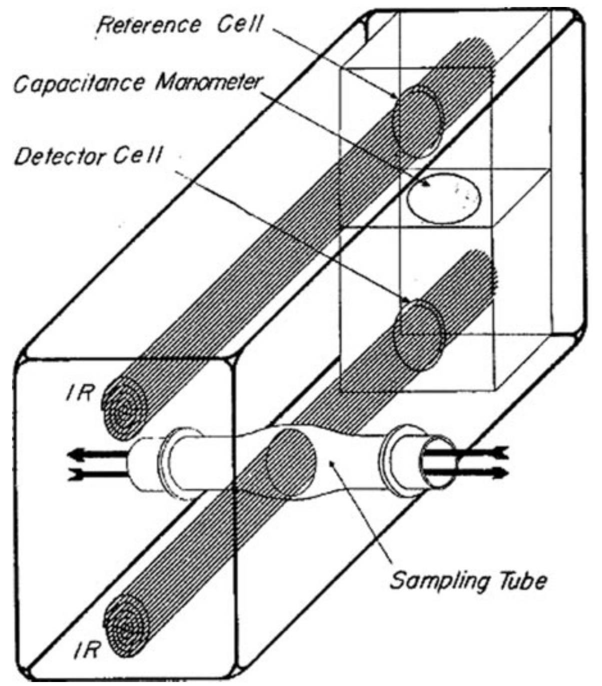

Figure 4. Schema of pick-up box of rapid infrared carbon dioxide analyzer. Gas flowing through sampling tube transverse one infrared path, causing pressure difference between carbon dioxide filled detector and reference cells (Reproduced from Elam et al.[24], with permission).

The only improvement of the Model 16 over the first design was that it was smaller. The Liston-Becker Gas Analyzer and it successor designs (Model 28, 30) consisted of a "pickup" unit (the portion containing the IR bench) and "control" unit. The pick-up unit, located near the patient's head, was sealed and could be pressurized with air to prevent ambient gases from entering the pick-up unit, therefore making it safe for use with "explosive" anesthetic gas mixtures.[29]

While the early devices included breath-through systems (Figs. 4 and 5), catheter sampling (i.e., side-stream) (Fig. 6) became more prevalent.[q] Liston described how the use of his CO_2 analyzer helped to improve the management of patients' ventilation on iron lungs and thereby reduced mortality:

The objection to the breath-through system that we had was the instrument was so large that it obscured the anesthesists view of the face that they relied on-color, facial reactions during the surgery-so they objected to that-as far as the surgical application goes. Catheter sampling came as the result of the work of Affeldt[r] and Farr at Rancho Los Amigos in Downey, California. They were working on the polio situation-the mask not suitable-so we developed the catheter approach for them which became the preferred method of sampling (Fig. 7).[30] In the-mid 1950, they

[n]James Whittenberger chaired of the Department of Physiology at Harvard School of Public Health from 1948 to 1980.

[o]A single-crystal ingot produced by synthetic means.

[p]Richard W. Stow, Ph.D. Associate Professor of Physical Medicine, OH State University, Columbus, OH; 1916–1995.

[q]Different sampling methods pictured in Figure 7.

[r]John E. Affeldt, medical director 1957–1964, Rancho Los Amigos Respiratory Center for Poliomyelitis, Hondo, CA.

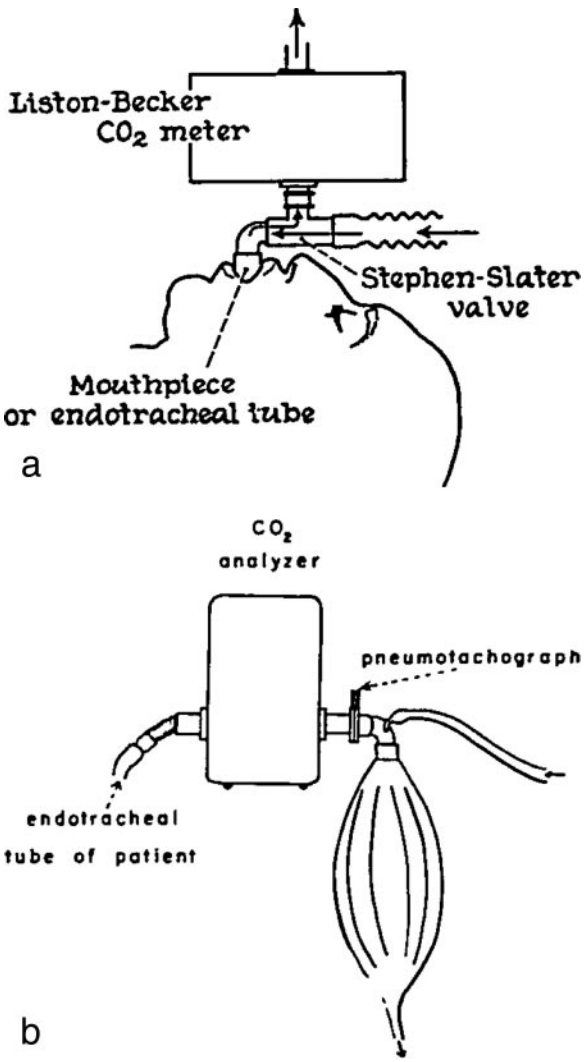

Figure 5. Different early breathe-through connections on CO_2 analyzer to patient. (a) Liston-Becker CO_2 meter in expiratory gas stream and Stephen-Slater nonrebreathing valve (Reproduced from Ref. 28, with permission from Philadelphia, Lippincott). They note the carbon dioxide meter must be as close to the patient and respiratory valve as possible, to minimize dead space (Reproduced from Eckenhoff et al.,[32] with permission). (b) Partial rebreathing system (Reproduced from Elam and Brown,[27] with permission).

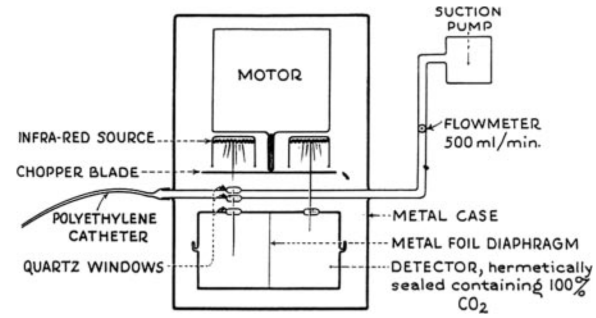

Figure 6. Fractional sampling with the rapid infrared CO_2 analyzer. The sample is pumped from the airway through the catheter and analyzer. The CO_2 in each chamber of the detector absorbs specific portions of the infrared spectrum, heating each chamber equally if no CO_2 is present in the sample. When CO_2 is present in the sample, the chambers are heated unequally, causing displacement of the diaphragm. The degree of displacement is detected electrically and recorded (Reproduced from Collier et al.,[34] with permission).

published a very favorable report which noted that the time on Drinker respirators[31] dropped in half after using that [device] to adjust their respirators-the fatality rate dropped by 30% on polio subjects-equipped all 7 of the polio foundation bulbar polio centers with the Model 16 (Fig. 8) (Max Liston, 2004).

The next big break we got was that the polio foundation decided to equip all their polio centers with our analyzer, and that was quite successful. In fact, their cure rate doubled after they started. What they had been doing with these Drinker-type, what the press called, "Iron Lungs" is adjusting them for normal tidal volumes for their weight. When they're paralyzed, their metabolism is way down, so they were blowing all of these patients into alkalosis. When they got the analyzer, they could control the carbon dioxide and keep it to normal levels.[s] Their success rate with patients and time in the Iron Lungs dropped in half and the death rate dropped in half. So that was a very successful program.[19]

In 1955, the financial backers of the company, Albert Austin and Dick Becker agreed to sell Liston-Becker Company to Beckman Instruments. The Liston-Becker Model 16 was renamed the LB-1 (Fig. 9).

It is interesting to note that the LB-1 was originally intended for use in operating rooms where ether and cyclopropane were commonly used anesthetics. As a safety precaution, it also included a pressure actuated switch that disabled power to the pick-up unit if the pressure decreased precipitously. The LB-1 was also sold with a separate sample pump, which was intended to permit its use outside the operating room.[t] Its successor, the LB-2 (and LB-3[u]), included technological improvements that replaced the vacuum tubes with solid-state circuitry.

Liston and his friend Miles Lowell of Edwards, having recently sold his company to American Hospital Supply [in 1966], were interested in pursuing other ventures and formed Liston-Edwards Corporation with the purpose of providing an IR analyzer to the pollution monitoring field. In the mid 1970s, Liston-Edwards decided to make a medical gas analyzer, marketing OEM versions of a CO_2 analyzer and anesthetic agent analyzer. In 1980, Liston-Edwards had one flagship customer, Electronics for Medicine,[v]

[s]Affeldt et al notes "Because of the relationship between alveolar ventilation and alveolar carbon dioxide . . ., the alveolar carbon concentration is the best means of determining the ventilatory status of the patient. It eliminates the need of estimating the required minute volume and thus allows accurate adjustment of the respiratory pressures and rates.[33]

[t]Allen Norton, 2003, personal communication.

[u]LB-3 510(k) #K782138, cleared 01/31/1979.

[v]Marquette later acquired Electronics for Medicine in 1995; Marquette itself was later acquired by General Electric.

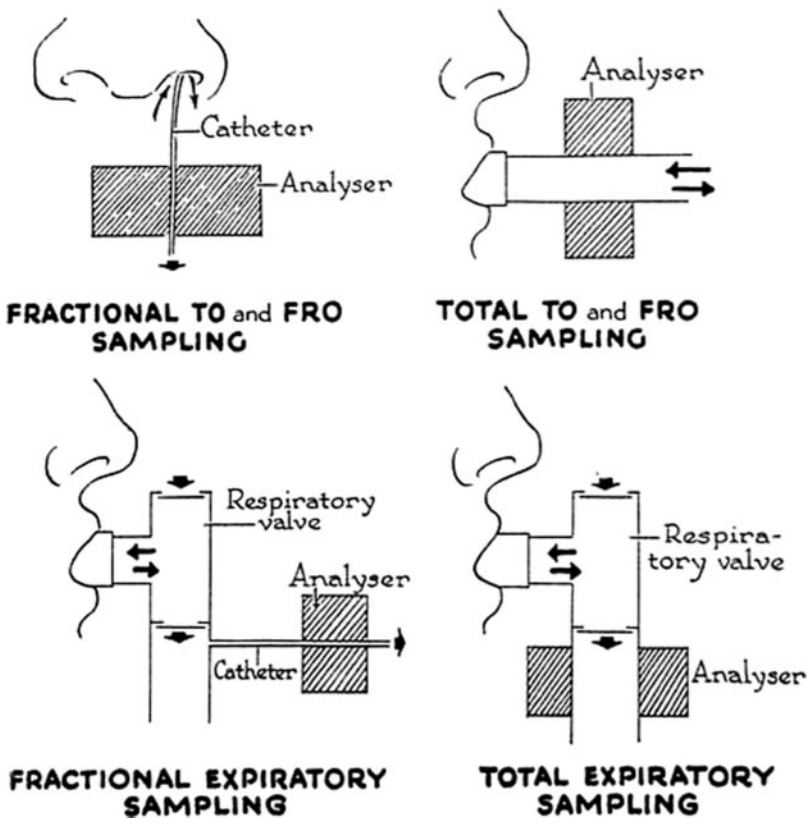

Figure 7. Sampling methods of infrared alveolar CO_2 analysis (Reproduced from Collier et al.,[34] with permission).

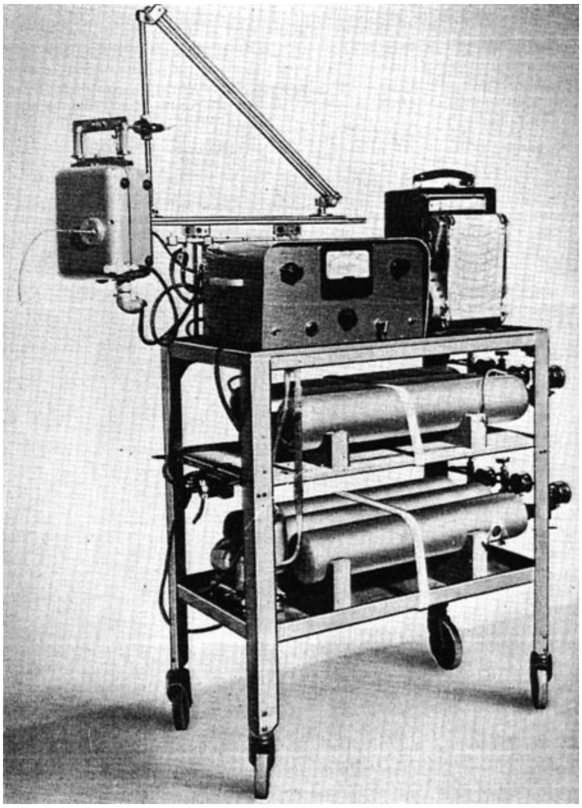

Figure 8. Rapid infrared CO_2 analyzer arranged as a portable unit. Upper left, catheter and pick-up unit; table top, amplifier and recorder; lower left, pump and flowmeter; lower, high pressure tanks for calibration mixtures (Reproduced from Collier et al.,[34] with permission).

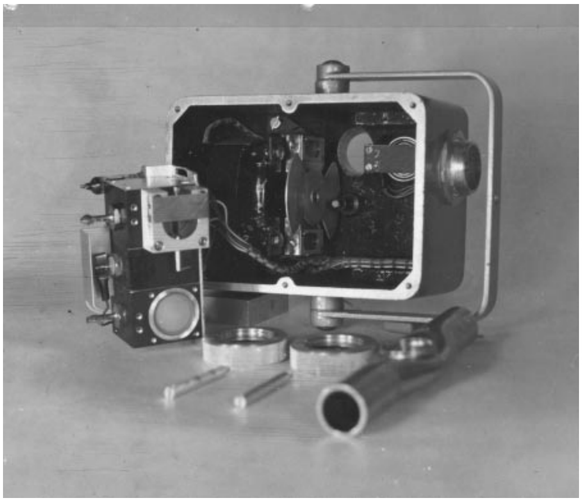

Figure 9. Beckman LB-1 Sensor Head with detector assembly removed. Chopper visible in center of photo (Photo courtesy of Max Liston).

and provided an early sidestream CO_2 module for a cardiac monitor. Liston Scientific continued until recently with Max at the helm to make gas monitoring devices for environmental applications.[w]

Hewlett-Packard Corporation

The story of the development of the Hewlett-Packard's (HP) mainstream CO_2 gas sensor is part of the overall story of HP's entrance into medical devices. It is also a story of adapting technology developed for

[w]Liston Scientific, Irvine, CA was acquired by CA Analytical Instruments (CAI), Orange, CA.

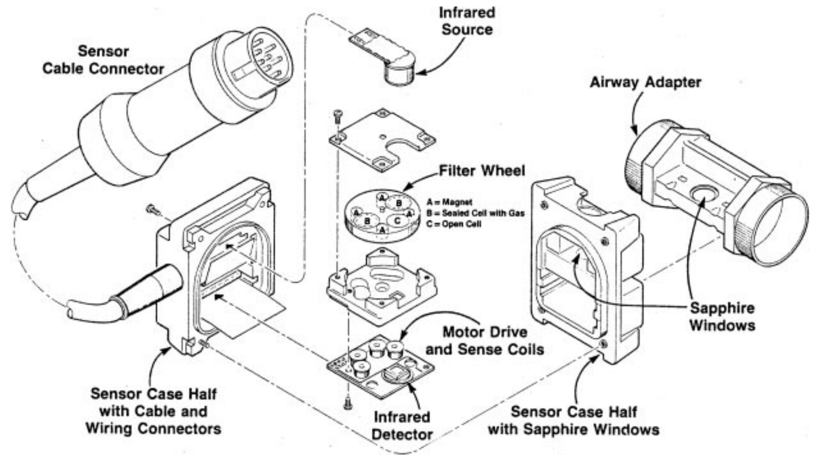

Figure 10. Exploded view of the assembly for the 14360A sensor (Reproduced from Solomon,[37] with Permission Copyright (1981) Hewlett-Packard Development Company, L.P.).

automotive applications to medical applications. This story is presented as told by both of its project managers (Jacob Wong), who led its development at HP Laboratories (Palo Alto, CA) and brought it to the newly established medical division in Waltham, and (Rodney Solomon) who took the product from prototype to a manufacturable product.

Jacob Wong started working in about 1967 at HP Labs, which was established in 1966 as the company's central research facility. At HP Labs' inception, its primary areas of research included solid-state physics, physical electronics, electronics, and medical and chemical electronics instruments. In the early 1970s, there was a greater recognition of the problem of air pollution from automobiles and HP Labs received a large contract from General Motors to design an exhaust gas analyzer to measure carbon monoxide, CO_2, methane, hydrocarbons, and nitric oxide. When the device was demonstrated, the sensor worked well but only if it was cooled with liquid nitrogen which turned out to be a big problem.

> We were saved by one of the lawyers at HP-he looked through the contract and observed that the contract never said it had to operate at ambient temperature-somebody forgot to specify that—so if it operated at liquid nitrogen temperatures we would still be OK—so obviously General Motors was not very happy—nobody was very happy—but the fact of the matter is that we went away and spent their money and learned a lot. It was right after that we were asked by Mr. Hewlett since we spent all this money is there anything we can use from that technology (Jacob Wong, 2005).

From the remnants of an automotive program, the idea of a medical CO_2 sensor was born. The group at HP Labs had the theoretical understanding of IR absorption of all the gases and Jacob Wong was asked to spearhead a program to develop a medical CO_2 sensor. When the development of the medical CO_2 sensor started, HP had already developed its well-known eight wavelength ear oximeter.[35]

HP had recently entered the medical field with the purchase in 1961 of Sanborn Company, Waltham, Massachusetts. Bill Hewlett's vision for Sanborn was to be the foundation of the HP medical division. Sanborn had an electrocardiograph and HP was going to refine the technology. The medical division idea was solidified with Lew Platt[x] as the engineering manager and Dean Morton[y] as the divisional manager. It was the late 1960s and 70s and HP took risks thus paving the way for monitoring devices that are now considered commonplace.

The technology was transferred to HP Medical Products Division in 1972. HP reduced the size of the sensor significantly using interference filters and IR detectors which were not available when the first capnometers for clinical use were developed. Because the device was to be placed near the patient's airway, HP had to devise a special adapter to interface with the airway. This airway adapter, which contains the sample chamber (Fig. 10), consisted of a hollow aluminum casting with sapphire windows. The sensor, which mated with the airway adapter, comprised an IR source (heated broadband black body radiator) and a detector assembly consisting of a rotating filter wheel which included hermetically sealed gas cells serving as bandpass filters and a lead-selenide detector. The IR source,[36] the only portion of the device that was patented, is basically a thin film heater.[37]

The concentration of CO_2 within the sample chamber is determined by measuring the intensity of the transmitted radiation reaching the IR detector when each of the filters on the wheel is in alignment with the source and detector. This measurement technique, known as optical chopping,[z] is a mechanical method

[x] 1941–2005; Rose from an entry-level engineer in the company's medical products group, succeeded HP co-founder David Packard in 1993 as chairman as well as chairman of the Boeing Company (HP website).

[y] 1932–; Became Executive Vice President, Chief Operating Officer and a director of Hewlett-Packard Company until his retirement in October 1992 (Forbes.com).

[z] Three types of optical choppers are available including rotating disc choppers (e.g. filter wheel), tuning fork choppers, and optical shutters.

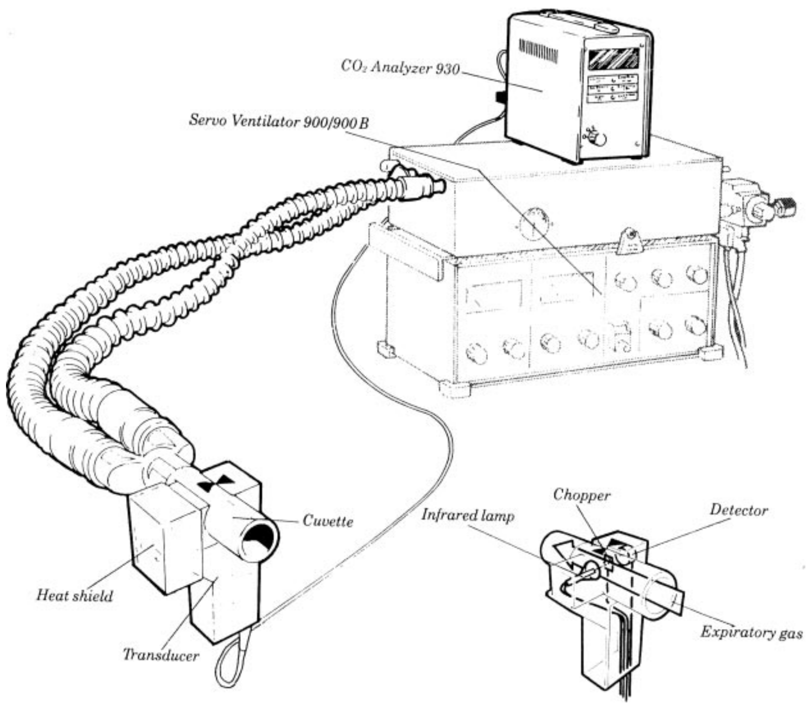

Figure 11. CO_2 Analyzer 930 with Servo Ventilator 900 (Reproduced from Ref. 41, with Permission Copyright (1981) MAQUET Critical Care AB.).

of periodically interrupting a light beam which is effective for eliminating electronic "drift" in the detector and the system electronics. The filter wheel driven by a motor drive rotates at sufficiently high angular velocity permitting 40 measurements per second through each filter wheel element. The filter wheel includes three separate elements through which IR radiation passes of which one is an opening in the filter wheel and the other two are sealed gas cells, a reference gas sample containing a known concentration of CO_2 and a cell with only nitrogen (Fig. 10).

The device was connected *via* a cable to one of the earliest microprocessor-based instruments. Motorola had just introduced the 6800 microprocessor (1975) and HP was given the opportunity to use this microprocessor. Jacob notes

> We were all fighting for it-Waltham medical division fought for it and we won that right because of Lew Platt. We got the 2nd prototype system from Motorola and it was used to develop the capnometer (Jacob Wong, 2005).

They designed the 6800 microprocessor into the 47210A Capnometer. The first microprocessor system as a development system was quite clumsy at the time and used five separate boards: I/O board, RAM/ROM boards, central processing unit and power supply boards.

Jacob left HP in 1978 and returned to the West Coast to work at Hughes Aircraft's Santa Barbara Research Center. Rod Solomon then served as project manager for the capnometer. Rod notes that they spent a few years tuning the basic concept, but that the foundation laid by HP labs during Jacob's tenure was substantial. The primary focus of the last two years of the development cycle was to reduce sources of error and variability in the design so it could be more easily manufactured. The problems worked on included cell filling, which was required so they could get an exact filter for CO_2 rather than using a narrow band optical filter. Most current NDIR CO_2 sensor designs use bandpass, lowpass and/or high pass optical filters of the type known as interference filters.[aa]

Other problems included getting the wheel to rotate evenly in order to remove output signal jitter, temperature control and overall robustness of the sensor, particularly the filter wheel, in the clinical environment. The filter wheel being dropped was considered primarily a manufacturing cost issue. Figure 6 from the HP Journal paper[37] showed two of the four rubber bumpers placed in corners of transducer housing to act as shock absorbers. It was noted that this alludes to what Dr. Smalhout[39,40] stated "gravity is twice as strong in the hospital than anywhere else and implored us to do the best we could to make it rugged."

The HP Journal article[37] on this device provides an extraordinary amount of disclosure on processes and design of a medical device. Rodney notes that "we were encouraged to write articles for the journal-it's hard to believe in today's environment this would never happen. This article is basically a treatise on how to build a competitive device."

This device[38] remains one of the most successful of its type with perhaps 50,000 of these transducers manufactured and sold. It served as the "gold standard" for medical CO_2 sensors for more than a decade since its introduction in the early 1980s.

[aa]Interference filters consist of multiple thin layers of dielectric materials with different refractive indices.

Siemens-Elema AB

The story of the development of the Siemens-Elema AB mainstream CO_2 sensor[41–43] (Fig. 11) and its associated Model 930 CO_2 analyzer, the first commercial volumetric capnograph, is presented as told by Rolf Castor, a scientist who was closely tied to the project (Castor Rolf, 2004/5). In the early 1970s, Rolf Castor started working in the medical industry, after receiving an MSc in applied Physics (Lund University) and a short stint at Ericsson, he joined the Elema-Schönander company, famous for the Mingograph electrocardiogram inkjet recorder and the implantable pacemaker. He worked in a group of four headed by Sven-Gunnar Olsson, the father of the Servoventilator.[44] Olsson asked Rolf if he believed they could make a small, fast CO_2 analyzer since, to Mr. Olsson, nothing was impossible. With no company library at his disposal, he consulted available IR textbooks of the day[45–48] at the local university. At this early stage in the product development, Rolf notes there was an "old" guy, Gabriel Tchang, in the company sitting nearby him who was developing a colorimeter for blood hemoglobin.[49] Although this product was considered outside of the Elema business area, he had a contract with the company and Rolf was asked if Gabriel could be of some help. So, Mr. Gabriel Tchang entered the scene with valuable knowledge in analyzing instruments and a long experience in analog electronics.

Rolf notes that no acceptable off-the-shelf motors were available at that time and, as small size was very important, they developed a kind of "tuning fork" chopper[bb] which resulted in an inconvenient long chopper design which determined the length of the housing (Fig. 11). The first transducer prototype and an electronic box with an analog meter was developed and powered from the Servoventilator. This hand built prototype was used clinically for some time and is now in the museum at Lund University.

The device, intended for use with the 900 Servoventilator (SV) series of ventilators, assumed that inhaled air had a low and stable CO_2 level that could be used for reference and that timing and respiratory phase information was known from the "mother" SV900 device. The reference signal (i.e., considered a fixed voltage) and the continuous signal were used to create a linear signal and the output was available both as a "continuous signal as well as the peak and end expiratory values."[50cc] The result was that CO_2 concentration could be displayed as a function of time as well as the instantaneous peak and end expiratory values. The device was marketed as the "CA 130"[dd] but was never a commercial success.

Sven-Gunnar, working with Prof. Bjorn Jonsson and Dr. Lars Nordstrom at the Lund University hospital, continued further system development which resulted in the Model 930 module. This module was integrated with the SV series of ventilators and reported CO_2 minute elimination, the effective and ineffective tidal volumes, and effective ventilation and tidal elimination. Rolf notes that this project was an interesting task for the analog engineer given that "everything had to be solved with the now mature opamp technology," because microprocessors were not yet available.

In about 1976, Siemens-Elema began shipping CA 930 units for sale. With the analog recorder outputs provided from the rear of the unit and the values on the panel display, Rolf notes it was considered an ideal tool for researchers. Together with the SV, the CA 930 created a methodological platform for research and an everyday tool for the clinician that was widely used in Europe. Although few reached the United States' "everyday clinic," researchers throughout the world found a versatile tool.

Cascadia Technology Corporation/ Respironics-Novametrix, LLC

The story of the development of the Respironics-Novametrix mainstream CO_2 sensor is presented as told by Les Mace and Dan Knodle who (along with two others) co-founded Cascadia Technology Corporation which developed the original Capnostat mainstream CO_2 sensor. This author (and many others) have continued the development at Novametrix, Inc (and now Respironics-Novametrix, LLC) since joining the company in 1994.

In the late 1970s Les was at Physio-Control (Redmond, WA) and was invited to join a startup in the Seattle area by Ralph Astengo formerly the founder of ATL. Les notes that

> We stumbled across a technology for respiratory monitoring for sleep apnea based on acoustic style technology that did not work well but we were very interested in the market and began looking for the most direct method to measure breathing and what we came up with was an inexpensive way to measure exhaled CO_2 (Les Mace, 2005).

That was the beginning of Trimed, which was organized in 1981 for the "development, manufacture, and marketing of monitoring instruments for the medical field." At Trimed they developed a qualitative CO_2 detector based on non-dispersive IR (NDIR) technology consisting of a simple incandescent light bulb as a source, a lead selinide (PbSe) detector, and CO_2 bandpass filter. The sensor was non-ratiometric, not chopped and had a tendency to drift. Because the

[bb] The tuning fork choppers are fixed frequency electromechanically driven light choppers. Vanes attached to moving tines of a fork modulate a light beam.

[cc] Rolf notes for those that have closely studied the schematic may notice that there is possibility to disconnect the device and use it external power supply without ventilator for spontaneously breathing patients.

[dd] CO_2 Monitor 130 510(k) K802459 cleared 10/23/1980.

primary interest was in the measurement of respiration rate, quantitative measurements were not important and it was introduced in an infant respiration monitor.[ee] A quantitative sidestream analyzer with a rotating chopper wheel and the associated disposables were also developed and cleared for marketing. This included the Model 126 sample line,[ff] with extended life, using for the first time NAFION® in a braided shield so it could be easily manipulated.[gg] After 3 years of funding their new start up, Trimed's parent company, Integrated Circuits Inc., a hybrid circuit manufacturer (including thermal print heads), pulled the plug and gave the division 4 months to find a buyer.[51,52] Trimed's assets were finally sold to a Midwest-based company, Biochem International (now known as BCI). The founders of TriMed found themselves unemployed, but they still believed in the technology and subsequently put together a team at a new company called Cascadia Technology Corporation in order to build a quantitative system that was a true ratiometric, chopped and stable NDIR system. Further research led to the development of the pulsed thermal broadband IR source still being used today in Respironics-Novametrix capnometers.

In 1985, Cascadia Technology Corp was founded by Larry Labuda as VP of Production, Dan Knodle as VP of Research, Bob Lamson as Chief Executive Officer and Les Mace as Chief Operations Officer. Les notes he was the first and only full-time employee for about a year. Once Cascadia Technology was started, the founders realized that they needed to build an IR source with sufficient IR energy and very low thermal mass that could also be pulsed on/off at rates of up to 100 Hz. This quickly led them to the use of low thermal mass, thick film technology similar to that found in thermal print heads.

The pulsed thermal IR source technology was a result of some early work the founders did using thick film technology while at ICI. Trimed engineers had originally attempted to develop a stable and robust IR emitter (to replace the incandescent light bulb), but quickly realized this was not an easy task. Les notes:

> There was a lot of chemistry going on-we had to pulse this thing in a bipolar fashion so that we did not get migration of the ionic components of the chemistry-we worked heavily with the thick film manufacturer to optimize the ink chemistry for this particular application. It was not optimal for a normal thick film application where you wanted long term thermal stability. We were overstressing this thing-heating it up to 600°C–700°C-which was much beyond what most people said we could do (Les Mace, 2005).

A number of sources and ideas have appeared since this device was developed, all with their pros and cons, but the pulsed thermal source turned out to be one of the optimum devices. It could be made very inexpensively, is very robust and could be pulsed in a bi-or unipolar fashion at relatively low power levels with sufficient IR output.[53] As did other manufacturers of mainstream devices, Cascadia's founders spent the early days of Cascadia (and later as employees of Novametrix) refining the IR source to make it easier to manufacture, more shock insensitive and with higher optical output. Les notes:

> We initially thought to develop a sidestream CO_2 sensor and someone said if you could develop a low power source without any mechanical moving parts-why aren't you doing mainstream-the more I looked at mainstream the more I found this was a niche that needed a better solution and which had considerable application advantages over sidestream (Les Mace, 2005).

Other mainstream CO_2 sensor solutions at the time included Siemens-Elema (Solna, Sweden), which used a mechanical tuning fork chopper, and HP (Waltham, MA), which used a rotating wheel. Each of these devices had their own respective problems, including accuracy and durability. While at Trimed, the founders looked very closely at the HP Journal article (describing their mainstream sensor) and subsequently met Jacob Wong (see HP section); this led them to thinking there was an opportunity for improving the mainstream application. Les notes:

> The HP sensor, although very good, did have an Achilles heel-it was subject to damage and breakage if you dropped it. Our goal was to develop a solid state sensor that was "bullet proof," and we were eventually successful at accomplishing this task. This gave us a huge market advantage over other fragile sensors like HP (Les Mace, 2005).

When Les was at Trimed he met clinicians from St. Joseph's Hospital in Bellingham WA, Phil Nuzzo and Ivan Bustamante. Phil, a licensed respiratory care practitioner, had previous experience as a user of Liston-Becker, Beckman and other devices and had previously written papers on capnography.[54,55] Phil notes that his interest in capnography started in the early 1970s during his tenure at University of Southern California County hospital with the development of a neonatal sidestream capnometer. Working with Cavitron (Santa Ana, CA), a sidestream bench with an adjustable sampling rate between 0 cc/min to 300 cc/min was developed. Humidity proved to be a problem since the sampling system was prone to water accumulation, so a method of dehumidication was sought. They bought unsheathed tubes of a fragile water permeable membrane (NAFION) from Dupont which they wrapped in a three foot coil and this proved to be effective. Given the uniqueness and

[ee]Model 511, 510(k) # K833397, cleared 11/28/83.

[ff]One of the first to build oral and nasal sampling cannulas with NAFION.

[gg]Tri-Med Model 126 Sample Line w/extended life NAFION 510(k) # K850746 – later assembled by PermaPure.

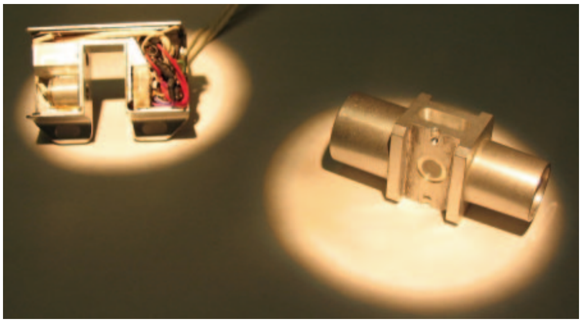

Figure 12. Original prototype Capnostat CO_2 sensor and airway adapter (Image courtesy of Respironics, Inc., Murrysville, PA.).

scarcity of the device, the capnograph was used primarily in a spot-checking manner and for applications such as ventilator management and asthma screening. Great care had to be taken with using the devices available. For example, due to the long warm-up time and vibration sensitivity of the Beckman LB-1 head, the head was placed on a piece of foam for increased stability, and on a large and portable cart, with calibration gases and large batteries to keep power always applied. Phil moved north to Washington state in 1979. A few years later after the founders started Cascadia, Phil, then a product manager at Novametrix, called Les to see what progress was being made on their CO_2 sensor (Fig. 12). As Les recounts:

> Mike Polson, Novametrix's director of engineering at the time, paid us a visit and peaked under our skirts. Two weeks later Bill Lacourciere, president of Novametrix, came out and the rest is history. It only took 15 years . . . a lot of Edisonian experimentation, it still has a lot of promise . . . and remains very well suited for medical capnography (Les Mace, 2005).

In 1987, Cascadia licensed their technology to Novametrix Medical Systems and in 1989 they were purchased by Novametrix (now Respironics-Novametrix, LLC). A number of the staff remained on in Redmond, WA as a sensor development group for Novametrix until the facility was eventually closed in 2001.

Additional innovations to the sensor included increased performance and accuracy under conditions of optical window contamination by the use of a coaxial optical design[56] (Fig. 13). The next generation Capnostat mainstream CO_2 sensor continues today with the introduction of the Capnostat 5 mainstream CO_2 sensor, a sensor that leverages on the latest developments in micro-electronics to create a full functional capnometer within the sensor housing.

Others Companies

The stories of two additional companies are of interest both from the technological perspective as well the inter-relationships between them and the companies previously highlighted.

Square One,[hh] a design firm founded in late 1987 by Jim Braig and Dan Goldberger, developed a mainstream device smaller than the HP device as they were not happy with the capabilities of existing solid state devices and also wanted to develop sources with longer IR wavelengths to be able identify and quantify anesthetics. Jim Braig, a veteran in the gas analysis business, also spent some time before this venture working with Max Liston[57] and also for Nellcor. Jim went to work at Nellcor for the sole purpose of building their second generation technology, the N-1000 multi-gas monitor.[58] Jim notes "It gave Nellcor the second technology to let it go public-they were told at the time that oximetry wasn't enough-it got them public and their second technology." Square One developed a mainstream solid state non-modulated technology for Critikon[59] that was not manufactured.

Pryon's development of a mainstream device was described by Dan Knodle. Pryon[ii] had developed a mainstream device based upon the HP capnometer that used a chopper wheel on the detector with sealed cells. They reduced the size of the chopper wheel in an effort to make it less sensitive to shock. However, they were still using an incandescent lamp as a source. If the device was dropped, the filament would move and the device would be out of calibration. In the meantime, Dan was pursuing an electrochemical sensor with his firm Evergreen Sensor Technology Corporation. Unfortunately, this project ran out of funds so they started looking for consulting work. About the same time, a company that they had previously visited, Pryon, called and asked if Evergreen Sensor Technology Corporation would be interested in working with them. Pryon sought to develop a solid state source to replace the incandescent lamp. Dan notes that to make a thick film resistor work under the conditions they had was an extreme challenge given that the power supply had a "wide power distribution." Dan Knodle and Tom Clary developed the source with sufficient IR light output at the lowest current input level, yet still able to plug into the highest power opportunity and still work. They also built the manufacturing facility that could make the source[60] for Pryon (later sold to Pryon). In 1994, Pryon began manufacturing the SC-300 CO_2 Monitor, a stand-alone instrument that incorporates both mainstream and sidestream CO_2 monitoring modalities. Pryon designed and manufactured a stand-alone instrument, the N-6000 UltraCap, for Nellcor Puritan Bennett incorporating Nellcor Puritan Bennett's oximetry and Pryon's mainstream CO_2 monitoring capability.[61]

[hh]Square One which was sold to OSI Systems later became part of Dolphin Medical.

[ii]incorporated in April 1988, co-founded by Daniel F. Carsten and Robert H. Ricciardelli who was also a principal in the startup of Biochem International; On July 10, 1996, the Protocol completed the acquisition of Pryon Corporation.[61]

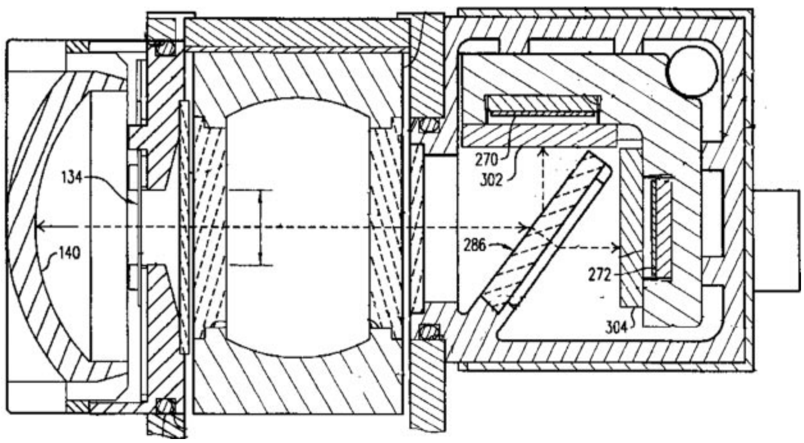

Figure 13. Cross-section of solid-state mainstream device employed in Capnostat II from patent (Reproduced Mace et al.[56]) showing source 134, mirror 140, beam splitter 286, detectors 270/272 and filters 302/304.

Table 1. Representative Commercial Mainstream Infrared CO_2 Analyzers Used Clinically (from 1950s Through Present)*

Manufacturer (location)	Model	Features of interest
1950s, 1960s, and 1970s		
Liston-Becker (Springdale, CT)	16	Total sampling (i.e. mainstream) using 7/8 inch tubing with 90% response time of 50 msec
1980s		
Hewlett-Packard (Waltham, MA)	M14360A†	Mainstream, solid state source, chopper wheel on detector
Siemens-Elema (Solna, Sweden)	Model 930‡	Mainstream integrated with 900 series ventilators
Cascadia Technology Corp.§ (Redmond, WA)	Capnostat®	Mainstream, all solid-state design with thick film source
1990s		
Andros Analyzers (Berkeley, CA)	Breathwatch™ Model 4210	Mainstream design with IR lamp source
Novametrix Medical Systems (Wallingford, CT)	Capnostat® II, III	Mainstream, smaller versions of previous generations
Pryon Corp‖ (MenomoneeFalls, WI)	SC-300	Mainstream, all solid state design
2000s		
Respironics-Novametrix (Wallingford, CT)	Capnostat® 5	Mainstream, all signal processing in on-airway sensor head

* Table adapted from Gravenstein et al.[67]

† Several other models marketed as well including the 47210A and 78345A.

‡ Also marketed the PCO_2 cartridge and Model 130.

§ Acquired by Novametrix Medical Systems, Inc.

‖ Acquired by Protocol Systems and Protocol acquired by Welch-Allyn.

Model name may list either the monitor name or sensor name (if mainstream), also ordering within decades approximate to year of product introduction, sources include Medical Electronics, various years, medical literature and company product literature. Trademarks are property of their respective owners.

The reader should also be aware of the contributions of other companies with a long history in gas measurement including Andros which introduced in 1994 the Model 4210 On-Airway Carbon Dioxide sensor,[62] Draeger (Germany) with the on-airway Capnolog D sensor,[63] Nihon Kohden (Japan) which has offered both qualitative and quantitative mainstream devices,[64] Instrumentarium (Finland),[65] and others which have not published widely or in the English language. Companies in the former Soviet Union manufactured a number of analyzers for continuous CO_2 monitoring in humans including the GUF-2 photoelectric gas analyzer, GUKh-2 chemical gas analyzer and GUM series of IR analyzers.[66] The GUM-2 and GUM-3 CO_2 analyzers were manufactured by the Smolensk Measuring Instrument Plant and designed by "Medfizpribor" Special Technical Design Office (SKTB). In addition, the G-1 gasograph was provided so that CO_2 and volume data could be combined.

Modern IR Devices

Both mainstream (nondiverting) and sidestream (diverting) gas measurement technologies have found clinical applications for monitoring both intubated and nonintubated subjects. The vast majority of instruments (both mainstream and sidestream) in clinical use rely on IR-based technologies. However, in the past, other sidestream technologies have been used and include mass spectrometry, photoacoustic and Raman spectroscopy. Of these, only mass spectrometers found relatively wide clinical use. The magnetic sector with fixed detectors and the quadrupole mass spectrometers have been the predominant types. These instruments have been used either as a dedicated instrument providing continuous monitoring of single patients or as a shared instrument (multiplexed) providing discontinuous monitoring of several patients in sequence. In particular, the most well-known manufacturer of such devices for clinical use was Perkin-Elmer.

Today, IR-based capnometers are finding their way into a wide range of platforms including multiparameter monitors used throughout the hospital, critical care and transport ventilators, anesthesia machines and defibrillators with monitoring capabilities. They may be found integrated into bedside units, and hand-held units often in conjunction with pulse oximetry as well as stand-alone units. A greater number of clinical organizations, including those in anesthesia, critical care, respiratory care and emergency medicine, are either mandating or strongly recommending the use of capnography. Volumetric capnography (the combination of capnography and volume) is also finding greater application both in ventilated and nonventilated patients.

Currently marketed mainstream capnometers are based upon either solid-state electronically pulsed sources and solid-state detectors (e.g., Respironics, Draeger, Nihon Kohden) or filter-wheels with solid-state detectors (Phase-In). Most sidestream devices use solid-state sources which are either electronic pulsed or mechanically chopped and solid-state detectors, with the exception of a hermetically sealed gas source excited by a high voltage radio frequency electromagnetic field (Oridion) and dispersive IR (multi-gas) spectrometer (LumaSense Technologies, formerly Andros). Many of the anesthesia machines use multi-gas benches (either of their own design or from an OEM).

CONCLUSIONS

The history of IR CO_2 gas measurement technology has been presented from the viewpoint of a number of the original developers (Table 1). It has more than a century of development, but measuring CO_2 in the respiratory gas can now be accomplished using cost-effective, reliable devices. This technology has become an integral part of patient care worldwide and is fundamental to patient safety. Future technological improvements in gas measurements promise greater sensor robustness, and the ability to monitor multiple gases and extract information from these measurements to support both diagnosis and therapy.

ACKNOWLEDGMENTS

The contributions to this article of following people who have served in various key roles in the development of this technology are acknowledged: Jim Braig of Optiscan (formerly of Square One); Rolf Castor (retired) formerly of Siemens-Elema; Dan Knodle (formerly of Cascadia Technology Corporation and Evergreen Sensor Technology Corporation); Max Liston (retired) of Liston Scientific (formerly of Liston-Becker and Beckman Instruments); Les Mace (retired) formerly of Novametrix Medical Systems; Phil Nuzzo of Respironics, Inc., Rodney Solomon of Philips Medical; and Jacob Y. Wong, PhD, of Airware, Inc. (formerly of Hewlett-Packard).

This article is dedicated to the memory of Allen Norton, PhD, who passed away in the Fall of 2004. I have been proud to know Allen, a former colleague of mine at Beckman Instruments, Inc. and Sensormedics, Inc. for nearly the past 25 yr and to call him my friend.

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