From Novametrix to Philips - A History of Innovation

Technical Staff – Philips-Respironics

Image from 1996 Annual Report.
Summary

Novametrix from its early days as a small medical device startup to a division of a large multi-national corporation has remained patient focused and interested in making a difference in patient outcome. Through all of the changes associated with two acquisitions Novametrix retained its entrepreneurial spirit. Using both in-person and phone interviews with current and ex-employees, and reference materials such as patents, clinical and scientific literature, product literature, regulatory filings, and annual reports, we have attempted to chronicle the innovations in technology, the products and stories behind them over the last 30 years.

Introduction

The following product lines will be the primary focus of this paper while highlighting the innovations, the products and relevant clinical literature.

- Airway Pressure Monitors – devices that measure proximal airway pressure

- Transcutaneous Blood Gas Monitors -- devices which measure oxygen and carbon dioxide levels through the skin.

- Pulse Oximeters – devices which measure arterial blood oxygen saturation levels and pulse rates.

- Capnographs – devices which measure the level of exhaled carbon dioxide.

- Respiratory Mechanics Monitors – devices which measure pressure, flow and volume in a patient’s airway and lungs.

- Volumetric CO2 Monitors - devices which utilize the integration of CO2 and airway flow to provide significant new parameters such as airway deadspace and CO2 elimination and clinical decision support such as VentAssist.

- Reusable and disposable sensors and adapters, related accessories and replacement parts

Figure 1 – Changing corporate identity over the past 30+ years
Novametrix – Brief Corporate History

“The formation of Novametrix was brought about as a result of the extreme need within the medical community for quality instrumentation that could be manufactured and marketed in accordance with the requirements of the users of the equipment. We have responded to this need by creating a flexible environment in which members of the medical community interchange their ideas for improvements with those of our engineers and consultants.” (1979 Annual Report)

The early days - It is with this problem solving spirit that Novametrix Medical Systems, Inc. was incorporated as a development stage enterprise on March 13, 1978, commencing activities April 1978 and shipments to customers during April 1979 (Annual Report 1979). It was founded primarily of ex-employees of another Wallingford medical device company, Corometrics. (Figure 2)

Two of the founders of Novametrix were also founders, in 1968, of Corometrics Medical Systems, which was merged in December 1974 to become a subsidiary of American Home Products Corporation. Lou Pellegrino, and Tom Abbenante (Figure 3) were prevented from competing with Corometrics, either directly or indirectly, "in the field of cardiac monitoring instrumentation for fetal and adult intensive care" during the five year period ending December 31, 1979. Lou who left Corometrics in 1976 commented “Rather than getting ulcers, we decided the marriage wouldn’t work and we got a divorce.” A local paper notes that Lou was explaining why he left a young, promising company (i.e. Corometrics) to start a new business from rock bottom. Wearing an open sport shirt, he said “We need an environment for free thinkers.”

Tom and Lou were interested in starting another company and over a short period of time assembled a team. They knew Dr. Luis Cabal who had expressed the need for a neonatal ventilator monitor and a suction adapter. Dr. Cabal was engaged as a consultant and the primary medical advisor for the company and quickly became the ‘ideas’ man for the company. The C/D (Cabal/Dali) suction adapter became the company’s first product. This was rapidly followed by the Pneumogard Ventilatory monitor. Given that Pneumogard’s market opportunity was viewed as limited, development on the transcutaneous CO₂ blood-gas monitor was initiated.

Its net sales (cumulative- 1st 15 months) from company’s inception (March 1978) was $203,803. To fund the company’s ongoing development efforts an initial IPO of 200,000 shares for 15.7% of the company, in early 1979, raised approximately $1.5M at an offering price of $7.50/share. Of that it was noted that about $240,000 for sales and marketing and about $250,000 would go towards research and development of the ventilatory monitor and transcutaneous blood gas monitors. (Figure 4) With the company’s rapid growth and future potential with portable transcutaneous O₂ monitors (Model 816) in clinical environments

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1 Novametrix was a variant on Corometrics, ‘new’ replaces Coro and ix replaces ics. The name was credited to a Tom Vialante who never joined the company (personal communication-Rich Mentelos)
2 Organized under Delaware law in June 1968, the company acquired by way of merger all of the interests of Corometrics, Inc. (organized in June 1966). The founders of Corometrics and a number of its early employees came from another company, Technical Measurement Corporation, North Haven, Conn., a manufacturer of time-of-flight and pulse height analyzers used in nuclear medicine.
3 The Morning Record and Journal, Meriden, Ct., April 12, 1979.
4 This "team" included Thomas Abbenante, Luis Cabal, Gregory Cox, Carmelo Dali, Eugene Della Vecchia, Ross Dodds, Bill Lacourciere, Donald Lewis, Robert Maggi, Rich Mentelos, Louis Pellegrino.
5 At the time was Assistant Professor of Pediatrics at the University of Southern California School of Medicine and Director, Neonatal Intensive Care Unit of the Los Angeles County-University of Southern California Medical Center.
6 The officers of the company at the time included: Louis P. Pellegrino (President), Thomas J. Abbenante--(Vice President, Engineering and Treasurer), Eugene A. Della Vecchia (Vice President, Marketing), Ross P. Dodds, Jr. (Vice President, Sales), William J. Lacourciere (Vice President, Operations) and Thomas M. Haythe (Secretary).
such as anesthesia, a second IPO was offered in 1980 to raise additional funding.

![Figure 3 – Novametrix founders - (a) Lou Pellegrino (1980), (b) Tom Abbenante (1983) (Photos courtesy of Dirck Spicer)](image)

**Tom and Lou** - Tom left the company in 1984 and Lou remained active with the company until his premature passing in September 1991. The employee newsletter, inNOVAtive News, of November 18, 1991 published the following In Memoriam:

In September, Novametrix suffered a tragic loss. Lou Pellegrino lost his battle with cancer. Lou will be missed profoundly by all who knew and worked for him. He loved this company and all the people in it. He treated us like family trying to keep spirits high when things looked bleak for Novametrix. Always celebrating in Nova’s triumphs (baseball teams, etc.) and commiserating in our defeats; ever ready with a pizza party to show his appreciation for a job well done. A man of few words, who exhibited a zest for life rather than a life of mere existence. A fighter to the end! … Lou may be gone in his physical presence, but his spirit will always live on at Novametrix.

After Lou’s passing, William (Bill) J. Lacourciere, Chief Executive Officer since February 1991 and President since August 1986 also assumed the role of Chairman of the Board of the Company. Bill wrote of both Lou Pellegrino and Dr. Luis Cabal, who had also passed of cancer, an essay titled “Reflections of a Friend” which was published in the employee newsletter (April 1, 1992) of which a portion is excerpted below.

… Both were very positive people, very optimistic about life. They were dream pushers; always giving us all reasons to hope and always forseeing the prospects of bigger and grander things. They saw the good in everything. If something negative were to occur, they would find the positive in it and in some way turn it into an advantage.

For to lose all reason to hope is to die in spirit. Even a difficult life with hope is better than a life without it. Life without hope is untenable for the
dreamers of this world, such as our friends, who saw not “what was,” but “what could be.”

And as time passes, I’m certain of one thing, both men chose to optimistically fight for life. Both were positive that they would prevail. They continued to live full of hope and they wouldn’t have had it any other way.

![Figure 4 – Novametrix family of products (circa 1980) – From left to right, top row: tCO2mette, Pneumogard, TCO2M 816, TCO2M 818. Foreground - Nasal CPAP cannula, Novametrix C/D suction adapter (from 1980 Annual Report)](image)

**Themes** - The company’s original focus was on solving problems in the neonatal space which can account for common themes between these diverse products. The company remained focused on the neonate as it expanded into other technologies and other patient groups and applications over time. It continually sought to innovate as evidenced by its tag line in the 1980s ‘Simply the leading edge.” (Figure 1) Figure 8 summarizes the technology families over the past 30 years and representative products for each family. An additional theme that underlay Novametrix culture was to address clinical needs with innovations in technology by leveraging on developments in sensor, electronics and microprocessor technologies while at the same time maintaining a focus on safety. “Would you put this on your child” was an unofficial metric used internally to help maintain a focus on safety and performance.

**Acquisitions/Licensing** - Internal development combined with company and technology acquisitions helped fuel the growth of the company and formed the basis of much of the current technology portfolio. The company acquisitions included Physiologic Instrumentation Limited of Wales, UK (1983)

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7 Name chosen in a contest – winner Rich Parsons.

8 Incorporated in London by Dawood Parker, David Delpy and David Halsall in January 1980; began operations at Whitland Abbey in February 1982.
which brought in transcutaneous and later pulse oximetry technology, Cascadia Technology Corporation of Redmond, WA (April 1989) which brought in solid-state mainstream CO$_2$ technology, the Ventrik product line assets of Med Science Inc. of St. Louis, MO (1992)$^9$ and Children’s Medical Ventures, Inc.,$^{10}$ (MA) (June 1999) which was acquired to expand the company’s presence in the NICU (and improve cash flow). Additionally, flow technology licensed from Korr Medical (Salt Lake City, Utah) provided the basis for Novametrix’s line of single patient use fixed orifice flow and combined CO$_2$/flow sensors.

Figure 5 – Members of development team meeting at 10 Alexander Drive, Wallingford, CT with PCB light table in foreground (December 1978) (Courtesy of Dirck Spicer)

From Barnes Industrial Park to Research Parkway - In April 1978, the company moved into one of the industrial parks in Wallingford$^{11}$, Barnes Industrial Park, developed by FIP Corp. of Farmington. Starting with a development team of about four$^{12}$, they leased space from the Connecticut Hospital Association on the 2nd floor (1000 sq ft) of 10 Alexander Drive, Wallingford.² (Figure 5) By the end of the year (December 1978) they moved around the corner to roughly ½ of a building (15,000 square feet) at 1 Barnes Industrial Park Road (Figure 6). Given the company’s growth they quickly occupied the whole building (after Union Carbide moved out).

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Figure 6 – View of (a) building, (b) manufacturing floor and (c) engineering lab at 1 Barnes Industrial Park Road (circa mid 1980s)

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$^9$ Medscience product lines sold including to its PFT line to Sensormedics
$^{10}$ a privately owned developer and marketer of neonatal and pediatric products and services now a separate business unit within Philips
$^{11}$ Wallingford has been promoting itself as a town to do business in because it (a) operated its own electric utility (resulting in electricity 15% below the rate charged by the two major competitors in the state) and (b) developing industrial parks. The health-related businesses in the park in 1979 included Corometrics, Galileo Electro-Optics, Seamless Hospital Products, Hewlett-Packard, American Cancer Society, Connecticut Hospital Association and Connecticut General Life Insurance Co.

$^{12}$ Greg Cox, Carmelo Dalì, Rich Mentelos, Gene Della Vecchia (personal communication Carmelo Dalì)
With additional rapid growth and expansion (to 300+ employees) in the 1980's they moved in early 1988 to a larger two story facility, designed and built for Novametrix, less than a mile away at 3 Sterling Drive in Wallingford (Figure 7).

![Building Image](a)

![Team Image](b)

**Figure 7** – View of (a) building and (b) Members of engineering team setting up shop at 3 Sterling Drive (November 1990) Left to right – Tony Esposito, Andy Kersey, Rich Daniels, Ivan Bustamante (Photo in 7(b) courtesy of Dirck Spicer)

However, due to various circumstances (including a “softening hospital marketplace” and temporary injunction in a patent lawsuit (Annual Report 1990))\(^\text{13}\) they were forced to scale back. This included the closing of the UK facility, sale of the Magnetic Stimulator business, reduction in employee headcount and return of the corporate headquarters to their previous address at 1 Barnes Industrial Park Road. With growth returned, Novametrix moved to a new building off Research Parkway at 56 Carpenter Lane in Wallingford in August 1996 (Figure 8). The official address was later changed to 5 Technology Drive which was the access street at the rear of the building.

Novametrix as an independent corporate entity ended when Respironics, headquartered near Pittsburgh, PA, acquired Novametrix in early 2002 for a stock-for-stock transaction of approximately $90 million. Philips looking to enter the Homecare business acquired all of Respironics in 2008 for a cash purchase totaling $5.1 billion\(^\text{14}\).

![Carpenter Lane Image](a)

**Figure 8** – Artist’s rendering of 56 Carpenter Lane (circa 1996)- a 52,700 square foot facility on 14.4 acres designed and built for Novametrix.

**Novametrix and the OEM Business**

Although Novametrix started as a box manufacturer, its business model has slowly migrated towards being a primary OEM model. Although the company did private label arrangements with companies such as Spacelabs (Model 500) it did not start focusing its efforts to become an OEM component supplier until after the financial problems in the 1989-90 timeframe. It signed Siemens (Danvers, MA) as the company’s 1st OEM partner for capnography providing a desperately needed infusion of cash. Since then the company has grown into an OEM business with over 100 OEM partners. Over the years the company has sold pulse oximeter OEM boards and sensors, capnography sensors and disposables, flow OEM boards and sensors as well as combination CO₂/flow sensors to an ever increasing business customer base.

\(^{13}\) In April 1989, an adverse decision with respect to patent infringement was entered by District Court. In early 1990 on appeal CAFC reversed the District Court judgment of literal infringement and remanded it back to the District Court for consideration of infringement under the doctrine of equivalents who found non-infringment in September 1990. (Annual report 1990)

Figure 9– Product and technology timelines from 1978 to present (approximate dates and representative products shown)
Product lines

C/D suction adapter

Figure 10 – Side hole C/D suction adapter (US Patent #4,291,691) 15 Access port on each side may be opened by moving a serrated slider control downward.

Prior to the advent of closed suctioning methods, endotracheal suctioning of children required breaking into the breathing circuit, suspending ventilation for up to a minute and suctioning. Due to the inevitable accumulation of fluids suctioning of mechanically ventilated children’s lungs is considered necessary but potentially dangerous. For effective suctioning, high flow rates and catheters with large lumens were used. The disconnection from the ventilation in conjunction with suctioning has a negative impact on functional residual capacity (FRC) and often resulted in significant drops in oxygen saturation. To counter this drop, the child was often pre-oxygenated with the inherent risks of retinopathy of prematurity. The C/D adapter, named after the inventors, Luis Cabal 16 and Carmelo Dali, was the first device of its type that allow suctioning to be undertaken without disconnecting the patient from the ventilator. Suctioning was achieved using two access ports in the suction adaptor (Figure 10) to insert a suction catheter. After suctioning has been completed, the catheter is removed and the access port is closed by moving the slide control upward. This approach helps to minimize the risk of contamination of the patient’s airway without “breaking” the circuit.

This suction adaptor was shown to minimize bradycardia and hypoxia from airway suctioning (Cabal et al. 1979). Gregory (1980) also demonstrated that the use of C/D suction adapter in infants resulted in a 3%±3% drop in saturation vs. a 26%±4% (±1SD) drop with standard suctioning procedures described earlier.

These advantages of the C/D suction adapter resulted in safer care of the ventilated infant and proposed changes in clinical practice. Zmora and Merritt (1980) using both the Novametrix Pneumogard and transcutaneous device to evaluate the C/D suction adapter concluded “by retaining a portion of presuctioning airway pressure during tracheal aspiration (see Figure 11), TcPO2 remained in acceptable ranges making preoxygenation unnecessary” Spiss (1981) as well found that the side-hole C/D adapter resulted in a significantly smaller drop of arterial pO2 during suctioning than conventional end-hole suctioning methods. Cassini (1984) suggested an alternative protocol which incorporated use of the C/D adapter, manual ventilation with an FiO2 10% greater than baseline before, during and after suctioning and hyperventilation with an FiO2 10% greater than baseline after the final suctioning. They indicated that this should diminish the incidence of hypoxemia while preventing hyperoxemia in these infants.

The simple innovation of the C/D suction adapter helped change clinical practice, remaining popular with clinicians for two decades. It was sold by Novametrix to Westmed, Inc. (Tuscon, Az) in the late 1990’s.

Figure 11 – IMV waveforms with endotracheal tube suctioning. End-hole adapter suctioning reduces pressure to 0 cm H2O during suctioning procedure while fraction of mean airway pressure remains during side hole aspiration (adapted from Zmora and Merritt, 1980)

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15 (510(k) #K781713 cleared 12/12/1978)
16 At the time was Assistant Professor of Pediatrics at the University of Southern California School of Medicine and Director, Neonatal Intensive Care Unit of the Los Angeles County-University of Southern California Medical Center.
Airway Pressure Monitoring

The company’s initial focus on the neonatal market led them to innovate with respect to improvement in monitoring during mechanical ventilation. NICU’s of the 1970s often used adult ventilators, such as the Puritan-Bennett (PB) PR2, PB MA-1 and Bird Mark-8 adapted for use on neonatal patients with built-in monitoring that consisted of little more than basic pressure monitoring. Clinicians often inserted needles into the breathing circuit in order to measure pressure. Novametrix in conjunction with Dr. Luis Cabal recognized the clinical need to better leverage the information available in the shape of the ventilation (e.g. flow/pressure) and oxygen waveforms. Also the need for improvements in monitoring and surveillance of mechanically ventilated patients was highlighted by Rattenborg and Mikula (1977) which illustrated the range of clinical issues that can be diagnosed with airway pressure monitoring including disconnections, faulty valves, and obstruction.

Existing devices for ventilation monitoring were considered inadequate. For example, the Bournes Ventilator Monitor, Model LS-160 calculated only Ventilator Rate, Inspiratory Time, Expiratory Time and I/E Ratio. The Novametrix Pneumogard 1230A Ventilatory monitor\(^\text{17}\), introduced in 1979, leveraged on recent technology developments in piezoresistive pressure sensors and microprocessors to provided a flexible monitoring platform that included all of the LS-160 parameters as well as a host of other parameters (see Table 2, Figure 13) whose value would be soon recognized. Pneumogard Model 1230A monitor, the first microprocessor based product (8085 based) from Novametrix, was a multi-purpose ventilation and oxygenation monitor and included measurements for various pressures (peak, distending, mean, transpulmonary), timing (I/E positive pressure ratio), airway temperature and inspired oxygen concentration (FIO\(_2\)). Table 1 lists the respective sensors used for these measurements.

### Table 1 – Model 1230A Sensors

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Sensor</th>
</tr>
</thead>
<tbody>
<tr>
<td>Airway pressure</td>
<td>Data Instrument 6 psi gauge Model AB</td>
</tr>
<tr>
<td>Esophageal pressure or central venous pressure</td>
<td>Bentley Model 800</td>
</tr>
<tr>
<td>Oxygen concentration</td>
<td>Ventronics Model 5510 fuel cell</td>
</tr>
<tr>
<td>Airway temperature</td>
<td>YSI thermistor</td>
</tr>
</tbody>
</table>

Of these parameters airway temperature, mean airway pressure and FIO\(_2\) are considered particularly important when monitoring neonatal patients. For example, Ciszek et al. (1981) studied mechanically ventilated infants with respiratory distress syndrome (RDS) to determine if mean airway pressure (MAP) could be an effective means of controlling adequate oxygenation and ventilation while PEEP and duration of positive pressure was altered. They found little change in oxygenation when MAP was held constant as ventilator changes were made supporting the work of Boros, et al., which determined that MAP is an effective means of monitoring the pressures transmitted to the airway while maintaining optimal oxygenation. To specifically address the need for ventilation monitoring, the Model 1200 monitor\(^\text{18}\) with a single pressure transducer for airway pressure measurement was introduced within a couple of years. Glenski et al. (1984) describes a study in which mean airway pressure calculated using 4 different equations all using PIP, PEEP, T\(_i\) and T\(_{total}\) was compared to mean airway pressure as

\(^{17}\) (510(k) #K781714 11/27/1978)

\(^{18}\) (510(k) #K802955 12/19/1980)
measured by the Pneumogard Model 1200 ventilatory monitor. The authors found that calculated Paw using any of the four methods described was inaccurate and impractical for clinical use as variations in ventilator flow, respiratory rate, patient compliance, and individual characteristics such as disease state altered the calculated values. The Paw is an important consideration in the ventilation of the neonate. However, since calculated Paw is of limited value and in the clinical setting, the Paw as measured by the Pneumogard monitor should be used. Banner et al (1981) noting the clinical importance of mean airway pressure as a “major determinant of both respiratory and cardiovascular function” welcomed the introduction of the Pneumogard 1230A monitor which replaced the manual methods of planimetry for estimating mean airway pressure with automated and continuous methods during all variations of positive airway pressure therapy.

The Pneumogard monitor helped make measurements such as esophageal pressure more clinically available predating monitors such as the Bicore monitor by about a decade. Korvenranta (1982) measured esophageal pressure with a saline filled feeding tube interfaced to a pressure transducer connector to a Pneumogard. Using estimates of esophageal pressure over the 1st 96 hours of life and measurements of heart rate, arterial blood pressure and severity of respiratory distress syndrome (RDS), they found that esophageal pressure correlated well with the severity of RDS and provided an objective measure for determining severity as well as the need for assisted ventilation. Pokora et al (1982) describes a technique using air filled balloons for measurement of esophageal pressure in ventilated neonates with pressure transducers connected to a Pneumogard Model 1230. Korvenranta and Kero (1983) used external pressure transducers interfaced to a Pneumogard to measure both intrapleural and intraesophageal pressure in sick infants. They demonstrated the strong linear relationship between pressure variations in the pleural cavity and in the esophagus during spontaneous respiration. They suggested that continuous monitoring of esophageal pressure could be useful in the early detection of pulmonary air leaks in neonates with respiratory disorders.

The introduction of the Pneumogard family of monitors helped shape the future of ventilation as the capabilities of the Pneumogard monitor were over the next several years adopted by most ventilator manufacturers. This cycle of introduction of pioneering and innovative technology followed by its introduction into the ventilator as a standard feature has been repeated several times in the history of Novametrix.

19 Using 100 Hz sampling rate mean airway pressure is calculated using the arithmetic average of the samples in a window ranging from 5 to 60 seconds.
### Table 2– Pneumogard Parameters and Ranges

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Range</th>
<th>Alert</th>
</tr>
</thead>
<tbody>
<tr>
<td>Airway temperature</td>
<td>20-50 deg C</td>
<td>High/low</td>
</tr>
<tr>
<td>Peak airway pressure</td>
<td>-20 to 99 cm H2O (2 digit LED)</td>
<td>High/low</td>
</tr>
<tr>
<td>Distending airway pressure</td>
<td>-20 to 99 cm H2O (2 digit LED)</td>
<td>High/low</td>
</tr>
<tr>
<td>Mean airway pressure</td>
<td>-20 to 99 cm H2O (2 digit LED)</td>
<td>High/low</td>
</tr>
<tr>
<td>High resolution mean airway pressure</td>
<td>20 to 99 cm H2O (4 digit LED)</td>
<td></td>
</tr>
<tr>
<td>Duration of intermittent positive pressure</td>
<td>300 ms to 5 seconds (4 digit LED)</td>
<td></td>
</tr>
<tr>
<td>Inspiratory/Expiratory relationship of intermittent airway pressure (I/E ratio)</td>
<td>1:10, 10:1 (4 digit LED)</td>
<td></td>
</tr>
<tr>
<td>Transpulmonary pressure</td>
<td>+,-25 cm H2O (3 digit LED)</td>
<td></td>
</tr>
<tr>
<td>Ventilator Rate</td>
<td>3 br/min to 120 br/min (3 digit LED)</td>
<td>Absence of pressure for 20 and 60 secs for neonatal and adult, respectively</td>
</tr>
<tr>
<td>Pressures of the patient (esophageal, central venous or intrathoracic pressures)</td>
<td>+,-25 cm H2O (calibrated strip chart recording)</td>
<td></td>
</tr>
<tr>
<td>FiO2 (%)</td>
<td>0-99% (2 digit LED)</td>
<td>High/Low</td>
</tr>
<tr>
<td>Duration of ventilator treatment</td>
<td>0-99 days, 23 hrs, 59 mins (6 digit LED)</td>
<td></td>
</tr>
<tr>
<td>Duration of O2 treatment related to 4 ranges of FiO2</td>
<td>Room air, 22-40, 41-60, 61-100% Four individual times each with 99 day 23 hr 59 minute capacity (6 digit LED)</td>
<td></td>
</tr>
</tbody>
</table>

(adapted from Pneumogard literature)
Figure 13 – Pneumogard calculations (from Pneumogard ventilatory monitor, a technical guide) (a- ventilator rate, b-peak airway pressure, c- distending pressure, d-mean airway pressure, e-duration of positive pressure (DPP), f-I/E g-transpulmonary pressure (TPP), h-CPAP mode in which rate, DPP, I/E ratio and peak pressure are not calculated.
Transcutaneous (through the skin) blood gas monitors provide continuous and non-invasive measurements of oxygen and CO2 levels in the skin tissue of patients. The transcutaneous values are not equal to the arterial values; rather, they are a measurement of the skin tissue gas values. Even though the skin tissue gas values are different parameters than arterial blood gas values, they can reliably follow the trend of arterial blood gas values when patients are hemodynamically stable. Because they are different parameters, they have different "normal" values.

Transcutaneous monitors use single or combination parameter sensors attached to the patient's skin surface to measure the amount of oxygen and CO2 diffusing through the skin. Vasodilation by heating the skin improves gas diffusion but heating also raises the PO2 by shifting the HbO2 dissociation curve. Fortunately for O2 measurement, this increase is equally offset by the gradient induced by the consuming electrode. However, for CO2 the heating increases local metabolism, raising the CO2 pressure, but where the CO2 sensor is "non-consuming" there is no offsetting correction and the PCO2 is overstated. Severinghaus introduced a metabolic correction factor to bring the values closer to ABG levels. Based upon the magnitude of the diffusion of the blood gas molecules, the monitor converts the sensor readings into a value corresponding to the oxygen or CO2 at the patient’s skin surface and displays the information on the monitor. Premature and other critically ill newborn infants were and remain to this day the primary patient group who benefit from the use of transcutaneous monitoring. In view of their limited blood supply, frequent invasive blood sampling has been recognized as traumatic and unsatisfactory for these patients. Novametrix was an early innovator in transcutaneous monitoring being the first to develop heated tcPCO2 and dual sensors. The very first CO2 sensors marketed by Novametrix were not heated and although the measurements were much closer to arterial levels, the slow response time hampered market acceptance.
Transcutaneous devices of the late 1970s were cumbersome to use and often required laboratory skills to use. For example, replacing the membrane and zeroing the monitors was a labor intensive and cumbersome process. For example, devices from Radiometer (the major player in transcutaneous measurement at the time) required manual replacement of the membrane which consisted of taking loose die cut O₂ and CO₂ membranes from a vial using a tweezer and stretching the membranes over the face of the sensor held by an O-ring. Novametrix with a sharp focus on ease of use introduced a series of sensor innovations including the Novadisk fixation apparatus (US Patent # 4280505). Novametrix addressed the ease of use in a number of areas: all the items to change the membrane were included in a "prep kit" (membrane, electrolyte and cleaning pad); first with a single use zero solution in a crushable glass ampule; and auto calibration with disposable gas cylinders.

Novametrix first introduced a combined O₂ and CO₂ transcutaneous device in 1980. The Model 818 monitor, of analog design (Figure 15 and 19) originally provided only a heated O₂ sensor. A separate unheated CO₂ sensor, as well as a heated CO₂ sensor, followed in short order as the Model 818A but required the filing of the first and only Premarket Approval (PMA) in Novametrix’s history because no predicate existed for the tcCO₂ sensor. The tcO₂ sensor would have also required a PMA filing, as noted by Bradbury (1983) if a single unit of a tcO₂ monitor was not sold about three weeks before the enactment of the 1976 Medical Device Amendment which established three regulatory classes for medical devices. This fortuitous timing exempted tcO₂ sensors from the more stringent filing requirements for a PMA.

The O₂ and CO₂ sensors were originally designed and manufactured by a 3rd party, Normand Hebert, with Rich Mentelos serving as the project engineer for the instrument. Working with them was Richard S. Burwen of Analog Devices fame. This collaboration resulted in the second of Novametrix’s patents which was filed June 21, 1979 (US patent# 4,290,431) with the first having been filed the day before.

After the 818/818A monitors, both the monitor and sensor evolved. At the urging of clinicians such as Dr. Kevin Tremper, the company developed small portable battery powered oxygen only transcutaneous monitors for use in clinical environments such as the emergency room. The first of these portable monitors, the model 809, was a big success and was responsible for much of the company’s early growth. Several smaller single gas monitors, known as tcomettes were introduced. Several oxygen only (model 816/816A, model 809A, 811, 910 and model 807) and carbon dioxide only (model 810) transcutaneous monitors were introduced as well as battery operated versions of these monitors (model 809, model 811) intended for transport applications. The portable tcO₂mettes 809A and 810 with the model 312 NovaGraph recorder were marketed as three independent building blocks which broke apart the all-in-one instrument to provide flexibility to the user. The model 809A was powered 8-10 hours on its own batteries or via 12 volt ambulance power or 115 volt wall power.

The model 850B, developed in Wales by the UK division of Novametrix, replaced the models 809 and 810. It was the first portable monitor from Novametrix to include both oxygen and carbon dioxide.

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20 Named 818 by the project engineer Rich Mentelos after the date which he began working on the design, 8/1/78.
21 (510(k) #K791152 08/03/1979)
22 PMA (#P810022) as a transcutaneous CO₂ monitor (heated) Original decision date 11/19/1981
23 At the time was the President of Microelectrodes, Inc. and previously a research scientist at Corning Glass Research Center.
24 In 1965, Ray Stata founded Analog Devices, Inc. with his former MIT roommate, Matthew Lorber ’56 E.E. and Richard Burwen (a Harvard alumnus).
25 Since 1990 Chairman of the Dept. of Anesthesiology, Univ. of Michigan Medical School
Two models offered transcutaneous oxygen with other clinically useful parameters. The Model 816A combined transcutaneous oxygen with the measurement of FIO2 and the Model 910 Physiological Monitor (Figure 17) offered transcutaneous oxygen but also provided heart rate with a standard 3 lead ECG, respiration using impedance pneumography derived from the chest leads, and blood pressure using a transducer connected to either an arterial or central venous catheter.

In an effort to expand the opportunity into adult and vascular applications, the model 800 monitor was introduced with a three slot rack into which any combination of O2, CO2 or combined O2/CO2 modules (Models 801, 802, 803, respectively) could be inserted.

The Model 840, both battery and AC powered, was designed as a replacement for the Model 850B and was intended for transport applications. It is compared with other competitive devices of the same timeframe in Table 4. To simplify and automate the calibration, the Model 898 Portable Gas Calibrator with low and high point calibration gases (5 and 10%), was interfaced to the Models 840 and 860. The TCO2M Model 860, the successor to the Model 840, was also a portable unit with a menu which guided the user through set-up and operation. The Model 860 was the first transcutaneous monitor to provide on-screen graphical trending information (Figure 18) allowing patient data to be reviewed directly at the bedside.

After a number of years of no investment in transcutaneous measurements, the product line was discontinued in 2009.

---

26 (510(k) K840993 4/24/1984)
Figure 19 – Model 818 – (a) block diagram and (b) photograph (circa 1980)
Sensors - The sensor technology evolved from separate heated sensors for O₂ and CO₂ to a combination O₂/CO₂ sensor (CO₂/MMO₂N sensor) which allowed both PtcO₂ and PtcCO₂ levels to be monitored from a single sensor site. The separate heated sensors originally introduced (Series A) were larger than needed and with advancements in technology were reduced in size (Series C). (Figure 20) The original sensor design employed a single thermistor design but soon evolved into a dual thermistor design for improved reliability, safety and redundancy.

![Figure 20](image)

Figure 20 – Separate Sensors – (a) Oxygen and (b) Carbon Dioxide and (c) calibrator.

The O₂ sensor comprises two basic parts (1) A Clark-type polarographic electrode consisting of: low oxygen consuming platinum cathode, silver anode, electrolyte and oxygen-permeable membrane (2) a heating section and precision thermistor for measuring and controlling of O₂ sensor temperature. The carbon dioxide sensor utilizes a pH electrode based on the Stow-Severinghaus principle. The CO₂ sensor is comprised of two parts (1) A CO₂ electrode consisting of a pH electrode, reference electrode, electrolyte and carbon dioxide-permeable membrane and (2) a heat section and a precision thermistor for measuring and controlling electrode temperature.

Introduction of the miniaturized combined O₂/CO₂ sensor presented unique challenges in the design of the NOVADISK. With the individual sensors, the characteristics of the membranes and electrolyte could be tailored to their differing requirements. Combining both electrochemical systems under a shared membrane (e.g. Teflon) with a common electrolyte lead to development and patenting of a unique NOVADISK (patent #4280505), incorporating what has since then been referred to as a “split membrane”. When Teflon membranes were utilized on the PtcO₂ electrode sensor, there was no noticeable interference of the PtcO₂ values with any anesthetic gases in clinically used concentrations, including halothane, ethrane, forane and ether.

The Novadisk (Figure 21) ring provided the gas sensor with a removable fixation ring to which the membrane can be attached prior to application of the fixation ring to the sensor. The fixation ring has mounted within it a membrane for maintaining the solution in contact with the cathode and anode thereby permitting the gas to be measured to permeate into the ion solution. A cover ring on the fixation ring helps compress the periphery of the membrane to tension it and provides an engaging surface which has an adhesive coating for adherence to the skin. A cap member that can be removed was attached to the fixation ring for protecting the membrane prior to use, and resiliently urging the membrane toward the electrodes to bleed any entrapped air from the system and displace excess electrolyte between the membrane and the electrodes, and to cause the membrane to conform to the profile of the electrode surfaces thereby further enhancing gas measurements.

![Figure 21](image)

Figure 21 – Exploded view of Removable Fixation Ring Apparatus (Adapted from US Patent #4280505)

![Figure 22](image)

Figure 22 – Transcutaneous sensors
Figure 23 - CO₂MMO₂N sensor – cross-sectional, bottom and exploded views and sensor with adhesive rings and contact gel
Clinical applications  – The transcutaneous sensors were cleared and marketed for use with both neonates and adults in a number of environments of use. With figures from the 1980 annual report, several applications using Novametrix monitors are highlighted.

Newborn and pediatric

Figure 24 – Transcutaneous monitor in use on a neonate in an incubator in the NICU (circa 1984)

Figure 25 – Novametrix transcutaneous sensor on a “model” baby

The use of transcutaneous monitoring of O₂ and CO₂ in the NICU (Figure 22) remains to this day the primary market for this technology.

A number of studies support its use in this setting including an early study with Novametrix equipment by Monaco and McQuitty (1981) with neonates in the NICU. They found a good correlation (0.91) between PaCO₂ and PtcCO₂ values and conclude that the trend of PtcCO₂ values is a valuable tool in the care of sick neonates. The preferred sites for monitoring both O₂ and CO₂ in a neonatal patient are shown in Figure 26. Figure 27 illustrates the range of tcPO₂ values which may be seen in healthy and sick newborns.

Figure 26 – Transcutaneous electrode placement for neonates

Figure 27 – Changes in tcPO₂ early in the hyperoxia test in healthy and sick newborns (Adapted from Schachinger H, Schneider H, Huch R, Huch A: Birth Defects 15: 495, 1979)

Anesthesia and Surgery

Rafferty et al (1981) at Yale compared PtcCO₂ (with an 818) and PaCO₂ in 30 adult neurosurgery patients undergoing nitrous oxide-enflurane and nitrous oxide-fentanyl anesthesia
and concluded that it was an accurate trend indicator of PaCO₂ in these patients "and may be particularly useful in situations in which the control of PaCO₂ is essential to patient management." A study (Nolan and Shoemaker, 1982) in 48 patients during anesthesia concludes that transcutaneous gas monitoring provides a useful non-invasive technique for following hemodynamic stability.

**Adult Intensive Care Monitoring**

Transcutaneous applications in the ICU have been reported by several studies including one by Tahvanainen (1983) who monitored 47 adult patients with transcutaneous oxygen (TCOM. 818) prior to extubation to determine whether or not transcutaneous oxygen values could predict successful extubation. They felt that PtcO₂ monitoring and determining the PtcO₂/PaO₂ index may be a valuable tool in assessing the patient’s condition during weaning. The preferred sites for monitoring both O₂ and CO₂ in an adult patient are shown in Figure 28.

![Figure 28 - Transcutaneous electrode placement for adults](image)

In over 100 critically ill adults, Tremper and Shoemaker (1981) assessed normal values for PtcO₂ in hemodynamically stable adults and defined the relationship of PtcO₂ and PaO₂ during progression of shock. They found that during circulatory problems when PtcO₂ values were compared to PaO₂ values, the changes reflected trends in the severity of low flow shock. In a separate study, Tremper and Shoemaker (1981, p752-5) they found that PtcCO₂ was a valuable trend monitor of arterial CO₂ tensions of adult during adequate cardiac function in the ICU and operating room.

Tremper and Shoemaker (1981) concluded that transcutaneous sensors provide invaluable continuous information with respect to perfusion and oxygen delivery during CPR and, for the first time, allow real time assessment of the effectiveness of CPR in terms of peripheral perfusion as determined by tissue oxygenation.

**Patient Transport**

Okikawa et al. (1983) describes their effective use of Novametric models 809 (tcO₂) and 810 (tcCO₂) monitors mounted on their transport ventilator for transporting the neonates between medical centers.

**Other**

Other applications of transcutaneous technology include the diagnosis and management of patients with peripheral vascular disease, use of PtcO₂ tension to determine the appropriate level of amputation, wound healing potential, and effectiveness of bypass procedures (White et al, 1982).
### Table 3 – Comparison of Selected Novametrix Transcutaneous Monitors (adapted from ECRI report, 1988)

<table>
<thead>
<tr>
<th>Model</th>
<th>818</th>
<th>809A</th>
<th>System 800</th>
<th>850 B</th>
<th>811</th>
<th>840</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>PDA “Clearance”</strong></td>
<td>Adult and neonate</td>
<td>Adult and neonate</td>
<td>Adult and neonate</td>
<td>Adult and neonate</td>
<td>Adult and neonate</td>
<td>Adult and neonate</td>
</tr>
<tr>
<td>510(k)# Date</td>
<td>K791152 08/03/1979*</td>
<td>K800988 05/28/1980</td>
<td>K840993 04/24/1984</td>
<td>K842374 09/17/1984</td>
<td>K844253 01/10/1985</td>
<td>K870805 05/27/1987</td>
</tr>
<tr>
<td><strong>Quantities measured</strong></td>
<td>TcpO2, TcpCO2</td>
<td>TcpO2</td>
<td>TcpO2, TcpCO2</td>
<td>TcpO2, TcpCO2</td>
<td>TcpO2</td>
<td>TcpO2, TcpCO2</td>
</tr>
<tr>
<td><strong>Display</strong></td>
<td>LED, Backlit LCD</td>
<td>LED</td>
<td>LCD, continuous</td>
<td>LED</td>
<td>Backlit LCD</td>
<td>Vacuum fluorescent</td>
</tr>
<tr>
<td><strong>Range pO2 mmHg</strong></td>
<td>0 to 800</td>
<td>0 to 999</td>
<td>0 to 999</td>
<td>0 to 999</td>
<td>0 to 999</td>
<td>0 to 999</td>
</tr>
<tr>
<td><strong>pCO2 mmHg</strong></td>
<td>0-199.9</td>
<td>NA</td>
<td>Not specified?</td>
<td>0-200</td>
<td>NA</td>
<td>0-199</td>
</tr>
<tr>
<td><strong>Temperature range</strong></td>
<td>37-45</td>
<td>42-45</td>
<td>37, 42-45</td>
<td>42, 5-45</td>
<td>37, 42-45</td>
<td>37, 42-45</td>
</tr>
<tr>
<td><strong>Increments, °C</strong></td>
<td>0.5 (from 42-45)</td>
<td>0.5 (from 42-45)</td>
<td>0.5 (from 42-45)</td>
<td>0.5</td>
<td>0.5 (from 42-45)</td>
<td>0.5 (from 42-45)</td>
</tr>
<tr>
<td><strong>Site change, hr</strong></td>
<td>2-4</td>
<td>2-4</td>
<td>2-4</td>
<td>2-4</td>
<td>2-4</td>
<td>2-4</td>
</tr>
<tr>
<td><strong>Site timer, hr</strong></td>
<td>Not specified</td>
<td>Not specified</td>
<td>Not specified</td>
<td>2-5</td>
<td>Not specified</td>
<td>0-5</td>
</tr>
<tr>
<td><strong>Alarms</strong></td>
<td>TcpO2, high/low</td>
<td>0-999/0-99</td>
<td>0-999/0-99</td>
<td>Not specified</td>
<td>0-999/0-999</td>
<td>0-999/0-999</td>
</tr>
<tr>
<td><strong>Other</strong></td>
<td>Heater power, site timer, electrode power shutoff</td>
<td>Site timer, low battery, thermistor</td>
<td>Heater power, electrode disconnect, site timer, low voltage, temperature</td>
<td>Temperature site timer, overtemp fail-safe</td>
<td>Low battery, overheat</td>
<td>Temperature, site timer, overtemp fail-safe, low battery</td>
</tr>
<tr>
<td><strong>Reset</strong></td>
<td>Yes, not over 8 sec</td>
<td>Automatic audible</td>
<td>Yes, not over 8 sec</td>
<td>Not specified</td>
<td>Automatic audible</td>
<td>Yes</td>
</tr>
<tr>
<td><strong>Sensor</strong></td>
<td>Separate</td>
<td>Single</td>
<td>Separate</td>
<td>Combination</td>
<td>Single</td>
<td>Single/combo</td>
</tr>
<tr>
<td><strong>Probe Type</strong></td>
<td>2 point, 2 gas</td>
<td>Zero solution and room air, 2 point</td>
<td>Auto 2 point, 2-gas</td>
<td>Auto 2-point, 2-gas</td>
<td>Room air, optional zero solution</td>
<td>1-point O2, 2 point CO2</td>
</tr>
<tr>
<td><strong>Calibration method</strong></td>
<td>2-4</td>
<td>Not specified</td>
<td>Not specified</td>
<td>4</td>
<td>Not specified</td>
<td>4-6</td>
</tr>
<tr>
<td><strong>Microprocessor</strong></td>
<td>No</td>
<td>No</td>
<td>Yes</td>
<td>Yes, built-in diagnostics</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td><strong>Battery-operating time hrs</strong></td>
<td>NA</td>
<td>10</td>
<td>NA</td>
<td>4-8</td>
<td>8</td>
<td>2</td>
</tr>
<tr>
<td><strong>Weight (lbs)</strong></td>
<td>28</td>
<td>19</td>
<td>22</td>
<td>12</td>
<td>4</td>
<td>8</td>
</tr>
<tr>
<td><strong>Price</strong></td>
<td>$11,500</td>
<td>$6,000</td>
<td>$12,500</td>
<td>$8,200</td>
<td>Not specified</td>
<td>$6,300</td>
</tr>
<tr>
<td><strong>Special features</strong></td>
<td>Event marker, buildin recorder, calibration unit optional</td>
<td>Automatic heater shutoff, portable</td>
<td>3 module system, information alert center</td>
<td>Audible &amp; visual alerts. Optional recorder &amp; calibrator. Aux output and silencer</td>
<td>Portable, automatic calibration, pole mount</td>
<td>Optional recorder, calibrator, RS-232 output</td>
</tr>
</tbody>
</table>

- Edited sensor details removed
- *PMA filed
Table 4 – Comparison of Model 840 with competitive devices (circa 1987-89)

<table>
<thead>
<tr>
<th>FEATURE</th>
<th>NOVAMETRIX MODEL 840</th>
<th>RADIOMETER TINA</th>
<th>SENSORMEDICS SHUTTLE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Display</td>
<td>VFD</td>
<td>LED</td>
<td>LCD</td>
</tr>
<tr>
<td>Display Range (mmHg)</td>
<td>02-0-999</td>
<td>02-0-800</td>
<td>02-0-999</td>
</tr>
<tr>
<td>CO2-0-199</td>
<td></td>
<td>CO2-5-200</td>
<td>CO2-0-199</td>
</tr>
<tr>
<td>Alert Limits</td>
<td>Always Visible</td>
<td>On Command</td>
<td>Always Visible</td>
</tr>
<tr>
<td>Sensor Temp Range (°C)</td>
<td>37.42-5-45°C</td>
<td>37.41-45°C</td>
<td>40-45°C</td>
</tr>
<tr>
<td>(0.5° inc.)</td>
<td>(0.5° inc.)</td>
<td>(0.5° inc.)</td>
<td></td>
</tr>
<tr>
<td>Sensor Temp. Display</td>
<td>Set &amp; Actual</td>
<td>Set</td>
<td>Set</td>
</tr>
<tr>
<td>Temperature Accuracy</td>
<td>±0.2°C</td>
<td>±0.3°C</td>
<td>±0.2°C</td>
</tr>
<tr>
<td>Sensor (T90) Response</td>
<td>02 - 7 sec.</td>
<td>02 - 20</td>
<td>02 - 15 sec.</td>
</tr>
<tr>
<td>Membrane Assembly</td>
<td>Pre-mounted Twist-On</td>
<td>Mounting Tool</td>
<td>Forceps</td>
</tr>
<tr>
<td>Site Timer</td>
<td>OFF, 0-5 hrs.</td>
<td>0-8 hrs.</td>
<td>0-9.9 hrs.</td>
</tr>
<tr>
<td>Battery Operation</td>
<td>2 hrs./AC</td>
<td>3 hrs./AC</td>
<td>8 hrs./DC Only</td>
</tr>
<tr>
<td>Recorder</td>
<td>Optional for Real Time Trend and/or Histogram</td>
<td>Optional for Real Time Trend or Trend Memory</td>
<td>Base Station for Real Time Trend Histogram or Trend Memory</td>
</tr>
<tr>
<td>Weight</td>
<td>10 lbs.</td>
<td>6 lbs.</td>
<td>7.5 lbs. (Shuttle)</td>
</tr>
<tr>
<td>List Price with sensor and calibrator</td>
<td>$7,000.00</td>
<td>$7,100.00</td>
<td>$8,500.00</td>
</tr>
<tr>
<td>Probes</td>
<td>Combination 02/CO2 Sensor or single parameter sensor</td>
<td>Combination 02/CO2 Sensor or single parameter sensor</td>
<td>Combination Sensor only</td>
</tr>
<tr>
<td>Calibration</td>
<td>Automatic two-point</td>
<td>Automatic one-point</td>
<td>Automatic two-point</td>
</tr>
<tr>
<td>CO2 Display</td>
<td>Choice of Corrected CO2 or Actual PtcCO2</td>
<td>Choice of Corrected CO2 or Actual PtcCO2</td>
<td>Corrected CO2 Only</td>
</tr>
</tbody>
</table>

(from Novametrix marketing data sheet)
Pulse Oximetry

The story of pulse oximetry and Novametrix (Figure 29) begins with the acquisition of Physiological Instrumentation Ltd. (PI) Whitland, Wales, an R&D house. Physiological Instrumentation (PI) founded by David Delpy and Dawood Parker (associated with University College, London (UCL)) had been developing transcutaneous products for various companies including Critikon and Johnson and Johnson. With Dr. Dawood Parker’s reputation for expertise in electrochemical sensors and Novametrix seeking to expand its offerings in transcutaneous technology, they acquired PI in 1983.

Pulse oximetry, an alternate method of assessing oxygenation than transcutaneous PO$_2$, first commercialized by Biox$^{27}$ in 1981 was provided a significant boost by the introduction by Nellcor of the N-100 pulse oximeter in 1983. In 1984, Novametrix decided to initiate preliminary work on pulse oximetry technology at UCL. Given the apparent rapid growth of pulse oximetry in the market it was decided to act on the opportunity in early 1985. In less than one year’s time, a prototype was readied by PI for showing at the 1985 American Society of Anesthesiologists meeting. This became the model 500$^{28}$ (Figure 30), the 3rd entrant after the Biox and Nellcor N-100 pulse oximeters. It was based on an 8 bit microprocessor (National Semiconductor NSC800) and used a novel algorithm$^{29}$ for calculation of saturation. With it a line of sensors including a finger sensor and a family of wrap sensors was introduced. The Model 505$^{30}$ soon followed with an improved display (Vacuum Fluorescent) and the Model 515 (Figure 31) for cost reduction. The front end electronics from the Model 505 was combined with CO$_2$, acquired from another acquisition (Cascadia Technology Corp.), to produce the 1st combined CO$_2$/SpO$_2$ monitor, the model 7000$^{31}$.

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27 Biox Technology founded in 1979 introduced the first pulse oximeter for commercial distribution in 1980 was purchased by the BOC Group in 1984.

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28 K853124, 11/6/1985
29 Taylor, AC. US4759369: Pulse oximeter, 7-26-1988
30 K873078 09/23/1987
31 K874036 11/06/1987
In 1989, an impending loss and possible injunction in a patent infringement lawsuit (later reversed on appeal\textsuperscript{32}) at the District Court level necessitated the need to innovate in a hurry. With advance notice of the release of a 20 bit A/D from Crystal Semiconductor Corporation\textsuperscript{33} the engineers at Novametrix realized that they could obtain sufficient dynamic range without the need for additional circuitry for gain and sensor brightness adjustments commonly used at the time. Additionally, given that "motion" would often cause designs with automatic gain adjustment to shift the signal off-scale resulting in clipping, the use of a sufficiently wide dynamic range (e.g. 20 bit) would avoid clipping. Also, through the use of a wide dynamic range input employing two 20 bit A/D convertors, the need for constant scaling of the measured signal due to the inherent instability of the DC components of the red and infrared signals was avoided. This paradigm shift in pulse oximetry termed ‘digital technology’, patented\textsuperscript{34} by Novametrix, appeared first in the model 515A with advanced software (known as the VENUS technology). It was soon followed in the other devices utilizing pulse oximetry. Also defeatured versions of the 515A appeared several years later as the Model 515B, and 515C.

Recognizing that exploration of methods to reduce or work through motion artifacts was desirable, research by Dr. Peter Hall was funded in the mid/late 1980s at UCL. Unfortunately, the premature death of the investigator and lawsuit noted above prevented this technology\textsuperscript{35} from being pursued beyond the prototype stage.

The Company's next full-featured oximeter, the 2\textsuperscript{nd} generation Oxypleth model 520A\textsuperscript{36} introduced in 1992 became the company's standalone workhorse for the next two decades. This monitor provided high visibility of the plethysmographic waveform (a graphic display of arterial pulse, also known as a plethysmogram) and embodied the 20 bit 'digital technology' and VENUS software. The VENUS algorithm effectively determines the presence of unacceptably high levels of artifacts such as motion and prevents erroneous data from being

\begin{figure}
\centering
\includegraphics[width=\textwidth]{Figure30.png}
\caption{Figure 30 – Model 500 pulse oximeter with early finger sensor}
\end{figure}

\begin{figure}
\centering
\includegraphics[width=\textwidth]{Figure31.png}
\caption{Figure 31 – (a) Model 515 pulse oximeter, (b) Model 515A pulse oximeter with TB500A sensor simulator and (c) Model 515 (left) and Model 515A (right) with units disassembled.}
\end{figure}

\begin{thebibliography}{10}
\bibitem{33} Acquired in 1991 by Cirrus Logic
\bibitem{35} Hall, Peter R. 4,955,379. Motion artefact rejection system for pulse oximeters.
\bibitem{36} K913516 11/04/1991
\end{thebibliography}
reported on the display. If high levels of artifact are detected, VENUS based pulse oximeters continue to display the last “good” value for a time period determined by the user.

Novametrix was the first and for a long time the only company to provide the raw 20 bit infrared and red signal via an external serial interface. This was a boon to a number of researchers who adopted this platform which allowed them to improve their understanding of the pleth signal and explore new applications of the technology with a cleared and easy to use device.

Novametrix’s family of pulse oximeters also included a battery operated hand-held pulse oximeter, the $\text{SpO}_2 \sqrt{}$ (Model 510 and 511 with DC input)(Figure 32) and later models 512/513 (Figure 33). Weighing less than 1 pound, this portable monitor found application in emergency transport situations, doctors' offices, clinics during outpatient procedures, performance of spot checks on patients in all areas of the hospital and data logging on ambulatory patients. Also of interest, the electronics of the Model 510 served as the basis of $\text{SpO}_2$ boards later sold to OEM partner companies.

To address the trend of multi-parameter patient measurement systems, a pulse oximeter front end was developed, the Model 509 (Figure 34), which allowed the leading multi-parameter platform of the time, the HP Merlin system to receive the waveform and its calculated parameters via its VueLink interface module.

The VENUS advanced signal processing front end and software was implemented in later combination devices to follow including the CO$_2$SMO Model 7100 monitor, CO$_2$SMO Plus! monitor and handhelds such as the Tidalwave Sp model 710/715 monitor.

Also of interest is Novametrix’s brief and early entry in the late 1980’s into the central station market with an 8 channel oximeter display, the Tele-sat Model 1010 monitor (Figure 35) developed in conjunction with a wireless consulting firm. It received waveform and parameter data from compatible Novametrix pulse oximeters wirelessly (using biotelemetry frequencies from 174 to 216 MHz) via an add-on box on back of the pulse oximeter connected to a “RS-232C” connector.
Given the perceived need for a pulse oximeter to work over a wider range of adverse conditions (e.g. low pulse and high levels of motion artifact) Novametrix began work on a more robust platform in the late 1990s. Initial algorithm development at an external research institute resulted in the development of the MARS algorithm (Edgar, 2002) that was introduced into the Model 2001 pulse oximeter (Figure 36) and soon afterwards into the Model 509M module. The MARS based pulse oximeters utilize the same robust front end as VENUS-based systems. In addition, the approaches to pulse detection, AC and DC component extraction, and saturation computation are similar for both the VENUS and MARS algorithms. Both algorithms attempt to distinguish arterial pulsations from other artifact by utilizing rhythm as the differentiating characteristic. The difference lies in the way MARS exploits the computational power of the digital signal processing to replace the pulse interval and rate-based decision tree algorithm with a more robust frequency-based algorithm. The MARS algorithm consisted of five basic steps – frequency domain transformation, spectral peak analysis, time domain filtering, pulse window analysis and arbitration. Figure 37 illustrates a frequency transformed IR signal with (a) low level and (b) high level of artifact. The spectral peak analysis coupled with the other steps permits the peaks corresponding to the pulse to be determined. Bench testing (Jaffe, 2000) using functional testers and independent clinical comparison testing in critically ill patients (Emberger and Fulda, 2001) has demonstrated the excellent performance of this algorithm. Emberger and Fulda studied the performance of three 3rd generation pulse oximeters in 15 adult ICU patients with low perfusion or hypothermia. They enrolled patients when the N-200 pulse oximeter was unable to obtain a reading or when the pulse rate and/or pleth waveform did not correlate with other monitored parameters (ECG). They found that the MARS algorithm performed the best of the oximeters under test, achieving excellent results for accuracy of readings relative to the co-oximeter (-0.07±-1.67), percentage of time the monitor failed to obtain a reading (0%) and percentage of time the pulse oximeter heart rate correlated with the ECG (93.3%).

Given the need to perform high level signal processing, this algorithm was executed on a separate DSP processor and was available on the 509M (an updated 509) module, Model 2001 and NICO and NICO2 monitors.

Although no MARS based platforms remain on market as a consequence of the sale of the product line in 2007, it showed that a small focused team with limited resources could effectively innovate.

Sensors – As noted earlier, the Model 500 was introduced with a reusable adult finger sensor (Figure 38) and a family of multi-position wrap sensors for adult, pediatric and neonatal applications (Reflex sensor), using 660 nm (red) and 940 nm (IR) LEDs with accuracy of ±2% 1SD >=80% and unspecified less than 80% saturation. Within a short time improvements in LED technology were leveraged allowing the introduction of the Superbright™ line of sensors – that is sensors with brighter and narrower spectral characteristics for the 660 nm (red) LED permitting improved signal to noise characteristics and as such accuracy and performance, particularly on poorly perfused patients.
Figure 37 – Power spectrum of two IR signals (a) with primary frequency peak at 70 bpm and a secondary frequency peak at 128 bpm and (b) with several interfering frequency components.

Figure 38 - Finger sensor

The reusable finger and reusable multi-site sensors became the business model for Novametrix in stark contrast with the disposable driven model of competitors such as Nellcor in which the whole sensor was discarded. Novametrix helped lead the effort to offer the clinician the option to only discard the means of attaching the sensor thereby significantly reducing the cost to the hospital and waste. The Y-Sensor which replaced the Reflex sensor allowed for a very flexible set of attachment options with the two LEDs in one head and the detector in a separate head. These attachment options include applicators such as the adhesive/non-adhesive foam wrap, butterfly wrap, and Y-Strip (Figures 39, and 40) which allowed application to a number of sites in all patient populations. (Figure 41) For added convenience the butterfly wraps were offered on a roll.

Figure 39 – Y sensor and use with film applicator and foam wrap.

Figure 40 – Wraps – (a) foam wraps; (b) butterfly wraps – pediatric and adult (available on a dispenser roll)
This focus on reusable sensors allowed Novametrix to offer Hospitals a Sensor Management Program which was designed to reduce hospital operating costs. For a fraction of existing operating costs and with no capital expenditure by the customer, hospitals could upgrade to Novametrix pulse oximeters with reusable sensors under the Novametrix Capitated Oximetry Conversion Program. This program capitated (or limited) contract expenditures while providing the hospital with new pulse oximetry monitors, sensors, and accessories, each of which is warranted over the life of the contract. The program provided an unconditional guarantee for the sensors and monitors over the life of the contract, for a fixed, predictable cost which was often just one-half of the hospital's prior spending levels for disposable sensors alone.

The Novametrix’s direct involvement in the pulse oximetry market ended with the sale by Respironics of the pulse oximetry technology and associated assets in October 2007 to an OEM partner of the company, Dixtal Biomedica of São Paulo, Brazil which was later acquired by Philips.

Figure 41 – Different site placement of Y sensor (a) neonatal toe and foot, (b) finger and hand, (c) ear.
**Debate – Transcutaneous vs. Pulse Oximetry**

In the early 1980s as the transcutaneous market began to develop and expand into the adult population, pulse oximetry monitors began appearing on the market. This fueled a clinical, technical and market debate about which technology is better for measurement of oxygenation (see Table 5). For various reasons particularly including ease of use, pulse oximetry won that debate and is now considered a ‘standard of care’ while transcutaneous remains important in the NICU, its use in adult patients remains limited.

Transcutaneous monitoring’s advantages relative to arterial blood sampling are relatively straightforward.

- noninvasive and no associated morbidity.
- continuous value, unlike direct sampling, which is a periodically obtained value and might not be checked until something is already seriously wrong with the patient.
- earlier warning of a sudden drop in arterial oxygen tension than do blood pressure and heart rate monitors.

With respect to oximetry, several arguments were made including (from BioChem) -

- \( \text{tcPO}_2 \) is linearly related to \( \text{PaO}_2 \). The relatively flat upper portion of the Hgb dissociation curve poses a major drawback in the capability of oximetry to provide an early warning of hypoxemia.
- The affinity of hemoglobin for oxygen is increased due to the rise in pH and less oxygen is liberated to the tissues resulting in tissue hypoxia. In this case, neither \( \text{PaO}_2 \) or \( \text{O}_2 \text{ Saturation} \) may show a significant change, but \( \text{tcPO}_2 \) will immediately indicate any change in the level of skin oxygenation, alerting the clinician to possible impairment of oxygenation of vital organ tissues.
- A normal \( \text{tcPO}_2 \) provides assurance that the skin is properly oxygenated, which, in all likelihood, means that the vital organs are properly oxygenated. The advantage, then, of transcutaneous monitoring is that it gives the clinician the ability to diagnose the drift toward pathophysiological states sooner, and begin corrective action sooner.

Drs. Tremper and Shoemaker wrote a Letter-to-the-Editor responding to a paper published in the The New England Journal of Medicine in which they stressed that transcutaneous oxygen tracks oxygen delivery during conditions of low cardiac output which makes it a very valuable monitoring tool. They also emphasized that transcutaneous oxygen is a new variable and has its own range of normal and abnormal values. In conclusion, Tremper, et al. stressed that transcutaneous oxygen monitoring provides early warning of circulatory failure and that they find it extremely useful in daily practice.

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**Table 5 – Comparison of Transcutaneous Oxygen Tension Monitor and Pulse Oximeter**

<table>
<thead>
<tr>
<th>Advantages/Disadvantages</th>
<th>PtcO2</th>
<th>Pulse Oximeter</th>
</tr>
</thead>
<tbody>
<tr>
<td>Advantages</td>
<td>Measures oxygen tension noninvasively and continuously</td>
<td>Measures arterial oxygen saturation noninvasively and continuously</td>
</tr>
<tr>
<td></td>
<td>Provides trend of PaO2 over entire range</td>
<td>No calibration needed</td>
</tr>
<tr>
<td></td>
<td>Detects low cardiac output</td>
<td>No warmup time needed</td>
</tr>
<tr>
<td></td>
<td></td>
<td>No site changes necessary</td>
</tr>
<tr>
<td>Disadvantages</td>
<td>Requires calibration</td>
<td>Provides no trend of PaO2 until low, 70 mmHg</td>
</tr>
<tr>
<td></td>
<td>Requires 10 minute warmup time</td>
<td>Provides no information about peripheral blood flow</td>
</tr>
<tr>
<td></td>
<td>Requires weekly membrane changes</td>
<td>Calibration is purely empirical and cannot be checked</td>
</tr>
<tr>
<td></td>
<td>Requires site changes every 4-6 hrs</td>
<td></td>
</tr>
</tbody>
</table>

(Adapted from Barker and Tremper, 1985)
Novametrix first entered the capnography market in 1985 with a sidestream CO₂ monitor, the microprocessor based Model 1250 capnograph \(^{38}\) which used an infrared CO₂ bench from Andros Inc.\(^ {39}\) (model 412, Andros, Inc., Berkeley, CA). The Model 1250 (Figure 43) employed a dual function 2 digit LED segment display. It allowed toggling between ETCO₂ and minCO₂ as well as respiratory rate and % mean N₂O. Several LEDs on the front panel provided functionality such as SYSTEM READY, and sample line occlusion. There were alert LEDs above each numerical display for ETCO₂ and respiratory rate. Upper and lower limits for ETCO₂ and respiratory rate were set using thumbwheels with ETCO₂ set between 0 and 99 mmHg and RR between 0 and 999, although 150 b/min was the maximum RR specified for measurement. An oxygen compensation button was provided to indicate if level was less than or greater than 60% O₂. Flow rate was selectable as either 50 or 150 ml/min. Analog output (via BNC connectors) was available for direct interfacing to the NovaTracer Model 350 recorder, the CAPNOGARD CO₂ Meter Model 1255 or an input channel of a monitor. The sample cell (see Figure 43) was located in sample chamber on the front panel where it could be easily removed and inspected for contamination.

In an effort to provide an innovative single sensor solution for both mainstream and sidestream monitoring, later designs adapted Novametrix’s mainstream technology with special adapter (Figure 44a) to provide cost effectively both mainstream and sidestream capabilities in the same monitor.\(^ {40}\) (Mace et al., 1990) This approach was used in the CO₂SMO and CO₂SMO Plus! monitors and TidalWave Model 710/715 handheld monitors (Figure 44b).

Mainstream - The story of the development of the Novametrix mainstream Capnostat CO₂ sensor has its roots in another company, Cascadia Technology Corporation. Cascadia was founded from the aftermath of a previous company Trimed, which was organized in 1981 and developed a qualitative CO₂ detector followed by a quantitative sidestream analyzer with a rotating chopper wheel and associated disposables. This included the Model 126 sample line\(^ {41}\) with extended life using Nafion for the first time in a braided shield so it could be

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\(^{38}\) K844010 02/21/1985, used Motorola 6809 microprocessor

\(^{39}\) Now owned by Lumasense Technologies.


\(^{41}\) One of the first to build oral and nasal sampling cannulas with Nafion
easily manipulated. After three years of funding their new start up, TriMed’s parent company, “pulled” the plug and sold its assets.

Figure 44 – Sidestream airway adapter (a) line drawing (b) in use with a Tidalwave monitor

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 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.

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 and that could also be pulsed on/off at rates of up to 100 Hz. This quickly led them to the use of thick film technology similar to that found in thermal print heads. 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. 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 (Figure 45) to make it easier to manufacture, more shock insensitive and with higher optical output.

Figure 45 - IR emitter (ref US patent #5,369,277)

Other mainstream CO₂ sensor solutions at the time used a mechanical tuning fork chopper; or a rotating wheel with their own respective problems, including accuracy and durability. While at Trimed the founders began thinking there was an opportunity for improving the mainstream application. The original prototype sensor head and airway adapter (Figure 46) led to the Capnostat “1” sensor (Figures 47-49,55), a single beam dual detector design which used a ball detent to align the sensor with the airway adapter. Along with mainstream designs from HP and Siemens, it helped to expand the use of capnography (Figure 48). It greatly simplified its use and application.

Figure 46 – Original prototype Capnostat CO₂ sensor and airway adapter

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42 Tri-Med Model 126 Sample Line w/extended life NAFION® 510(k) # K850746 – later assembled by PermaPure.
In 1987 Cascadia licensed their technology to Novametrix Medical Systems and in 1989 they were purchased by Novametrix. 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. Concerns with accumulations on the window affecting the measurement led to the coaxial beam innovation which first appeared in the Capnostat II sensor (Figure 50). The coaxial beam approach assured that both the measurement (data) and reference (no CO₂) channels would ‘see’ the same signal to be able to effectively correct for interference (Figure 51). Given that these devices were used on airway, the devices had to be particularly robust. This led to internal design improvements which allowed the device to survive multiple 6 foot drops onto a hard surface. This design also continued to provide a gasless optically based means to check the zero and reference settings of the device (Figure 49).
The CAPNOSTAT 3 CO₂ sensor (Figure 52) introduced in 1995 has been known for its reliability and ruggedness. The introduction of the fully integrated CAPNOSTAT 5 CO₂ sensor (Figure 53) with its greatly increased density of electronics and component count necessitated even more careful attention to the robustness of the device in the clinical setting. This sensor leveraged on the latest developments in micro-electronics to create a full functional capnometer within the sensor housing. Given the increased complexity from the previous generation, it was essential for such devices to be sufficiently robust to withstand the occasional severe impact. Given that the CAPNOSTAT 5 CO₂ sensor is used in clinical environments ranging from the less abusive environments such as the operating room and intensive care unit to more abusive environments such as in emergency or pre-hospital medicine and in the field, the need to withstand drops of the sensor from a greater height and significant number of times is apparent. Pre-hospital use includes both intubated patients and spontaneously breathing patients who can be monitored using CAPNO2mask face mask (Figure 54) which includes the Capnostat sensor in combination with supplemental oxygen delivery. Robustness in this environment required innovations in both optical and electrical assembly. Internally developed drop testing procedures in excess of published medical device standard requirements has demonstrated this robustness.

**Figure 51** – Capnostat III mainstream sensor - (a) Exploded view of the case with the integrated source/detector assemblies; (b) cross-section showing source 134, mirror 140, beam splitter 286, detectors 270/272 and filters 302/304. (US patent #5,793,044)

**Figure 52** – Capnostat III sensor – (a) line drawing illustrating on-cable verifier cells, (b) photograph of sensor with verifier cell, (c) closeup of sensor.

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43 CAPNOSTAT 5 CO2 Sensor – A Robust and Reliable Sensor, Respironics white paper.
Figure 53 – Capnostat 5 – (a) view with airway adapter; (b) cover removed; (c) rigid-flex electronics unfolded and (d) computer model of a Capnostat 5 sensor coupled to an airway adapter illustrating coaxial optical design (Jaffe, 2010)

Figure 54 – CapnoMask™ facemask (US Patent 7,004,168) with supplemental oxygen delivery inlet located distal to the airway adapter so that the delivered oxygen does not mix with the expiratory gases prior to their measurement but is still available to enrich the gas stream during inhalation.
Figure 55– Capnostat advertisements - (a) Early advertisement for Capnostat I sensor (Note- the “guts” of a Model 1250 is shown on the left); (b) Capnostat III advertisement
Sidestream - Novametrix recognized that although the mainstream sensor offered a number of advantages over a sidestream solution, they needed to provide a sidestream solution as well. The novel approach taken was to use the mainstream head with a sidestream airway adapter which was connected via a sampling tube of several feet to a pump that was integrated into the monitor. Figure 56a show a Capnostat I sensor engaging an airway adapter intended for use in a breathing circuit whereas Figure 56b shows the same sensor engaging a sidestream airway adapter. In order to address the needs of different markets, both neonatal and pediatric/adult reusable and disposable mainstream airway adapters were developed in addition to the sidestream airway adapter. (Figure 57)

Plug and Play is born- The use of a sidestream airway adapter with a mainstream sensor remained the only approach offered by the company until it became apparent from market conditions that Novametrix needed to offer a separate OEM sidestream solution. Given the large installed base of legacy monitors with mainstream only connectors and the company’s OEM focus, the concept of a single connection for plugging in either a mainstream sensor or sidestream module known then as “plug and play” was born. (Pierry and Rich, 2005) and now known as “co2nnect & go.” (Figure 58) This novel approach coupled with a new sidestream bench, LoFlo, was quickly adopted by several major monitoring companies. Whether gas monitoring is performed by a diverting (sidestream) or non-diverting (mainstream) gas monitor is often determined by what is available to the clinician and not what is optimal for the application. The LoFlo and Capnmostat sensors provide the clinician with the ability to choose between a compact mainstream and/or sidestream solution.

![Figure 56 - Capnostat I sensor (a) with mainstream airway adapter and (b) with sidestream airway adapter.](image1)

![Figure 57 – Airway adapters for use with Capnostat III and later (note larger windows than previous airway adapter in Figure 52).](image2)

![Figure 58 – co2nnect & go – LoFlo and Capnostat 5 (a) sensors; (b) marketing logo](image3)
address the "clogging" problems associated with conventional sidestream sampling systems. This novel solution (Figure 59) consisted on making the sample cell part of the disposable. Thus contrary to conventional sample sets, the LoFlo sidestream sample set provided the complete sampling path from the patient's airway to the sample cell. The sample set includes a removable and disposable sample cell which effectively obviates the need for preventive maintenance of the sample cell associated with other sidestream systems. The sample cell is inserted into a receptacle to which the measurement optics is mounted. The measurement optics consists of detector and source assemblies. The sample cell windows are configured and oriented to be properly aligned with the measurement optics when inserted into the sample cell receptacle.

Figure 59 - Exploded view of the sample cell receptacle assembly from the detector assembly side

The sample set consists of a sample cell, filter, sampling tubing, dehumidification tubing in some kits and an interface to the patient or the breathing circuit. The sample cell portion of the sample set is designed to permit easy connection and disconnection. A latching arm of the sample cell mates with the sample cell receptacle to permit proper alignment of the measurement optics with the optical apertures in the sample cell and proper seating of the sample cell output port with the pneumatic input. This device is simple to use and provides both familiar and intuitive operations for insertion and removal of the sample cell. The receptacle further contains a photo detector that detects when a sample cell is present and serves as a signal to turn on the sampling pump.

After exiting the sample cell through the output port, the gas enters the pneumatic system and into a pump of the sidestream module prior to exiting via the exhaust or scavenging port. The system is optimized for low flow using an integrated sample pump under active flow control. With the introduction of the external sample cell, a new line of novel disposables was created including a low deadspace neonatal airway adapter, and an adult airway adapter both with sampling ports that help minimize the introduction of contaminants (Figure 62).

LoFlo “C3” - The CAPNOSTAT® 3- based LoFlo platform permitted system integration with existing mainstream only monitors. This patented innovation allowed LoFlo technology to be incorporated into legacy monitoring systems as an external sidestream module (Figure 60). This novel approach permitted interfacing the existing installed base of multi-parameter monitors with external sidestream gas sensor modules that have been designed only to interface with the Capnostat mainstream CO₂ sensors. To accomplish this, the sidestream module needed to emulate the mainstream sensor’s physical, signal/control and power interfaces.

Figure 60 - LoFlo OEM modules (a) module for GE Dash monitor, (b) module compatible with ZOLL M series defibrillators
Respironics LoFlo “C5” sidestream monitoring platform adapted the technology in the mainstream Capnostat 5 sensor platform to a sidestream platform. This platform contains in a single package all of the front-end electronics, signal processing and optical components needed for a capnometer. By integrating all of the signal processing and control functions into the sidestream module and assembling it in a compact way using a novel manifold structure, a simple to use, compact sidestream solution has been achieved (about the size of a computer mouse (Figure 61)) . This enables a complete sidestream module to be provided that requires only a power source and serial connection.

LoFlo - The LoFlo “C3” sidestream monitoring platform interfaced to host monitors via existing mainstream connector and emulated the signals required to interface to those connectors. The

Figure 61- LoFlo module (a) engine (b) with sample cell . in a package only measuring only 4.5 cm (W) by 7.5 cm (L) by < 3 cm (H) and (c) with pole attachment

Figure 62 - LoFlo accessories – (a) airway adapters (adult and neonatal) and representative nasal cannula with sampling tube and sample cell, (b) current neonatal airway adapter, and (c) neonatal nasal cannula with sampling tube and sample cell.
Algorithms - Respiratory rate measurement in both the Capnostat 5 and LoFlo families of CO₂ sensors employ a robust breath detection algorithm with an adaptive threshold criteria followed by a selectable screening/validation algorithm. This screening algorithm termed the ReNÉ™ algorithm uses waveform morphology including the area under portions of the waveform to exclude breaths which are unlikely to be "real" breaths. These two algorithms have been developed over a twenty year period and are in use in hundreds of thousands of systems worldwide.

Table 6. Comparison of Mainstream Capnostat and Sidestream LoFlo CO₂ Measurement Solutions**

<table>
<thead>
<tr>
<th>Features</th>
<th>Mainstream</th>
<th>Sidestream</th>
</tr>
</thead>
<tbody>
<tr>
<td>Location of analysis unit</td>
<td>At the airway connector</td>
<td>In the “monitor”</td>
</tr>
<tr>
<td>Required components to sample gas</td>
<td>Airway adapter and sensor</td>
<td>Airway adapter, sample tube, water trap or filter</td>
</tr>
<tr>
<td>Use on extubated patients</td>
<td>Yes with a facemask or mouthpiece</td>
<td>Yes with a nasal adapter or O₂ prongs</td>
</tr>
<tr>
<td>Connecting tube or cable</td>
<td>Thin medium weight flexible cable – no sample tube</td>
<td>Small bore (1 mm ID) sample tube</td>
</tr>
<tr>
<td>Airway connector disposable?</td>
<td>Both reusable and disposable</td>
<td>Only disposable</td>
</tr>
<tr>
<td>Cost of replacing airway connector</td>
<td>Low</td>
<td>Inexpensive but dependent on how wet circuit is</td>
</tr>
<tr>
<td>Can be used in collaboration with O₂ administration</td>
<td>Yes with facemask, captures oral and nasal gases</td>
<td>Yes with nasal prongs- concerns about sample dilution</td>
</tr>
<tr>
<td>Zeroing</td>
<td>If requested – manual &lt; 20seconds</td>
<td>If requested? (infrequently)</td>
</tr>
<tr>
<td>Response</td>
<td>Negligible</td>
<td>&lt; 3 seconds</td>
</tr>
<tr>
<td>Delay between sampling and waveform</td>
<td>&lt; 60 msecs</td>
<td>Approx 200 msecs</td>
</tr>
<tr>
<td>Sensor 10-90% rise time</td>
<td>Not affected – measures actual partial pressure</td>
<td>May be affected by condensation and drying of sample</td>
</tr>
<tr>
<td>Changes due to water vapor pressure</td>
<td>Window heater or treatment to prevent or reduce droplet condensation on window</td>
<td>Water trap or blocking filter (may use Nafion tubing as well)</td>
</tr>
<tr>
<td>Moisture handing</td>
<td>None with disposable adapters</td>
<td>Varies-none if sample set disposed and no return of gas to circuit; otherwise proper protective means required</td>
</tr>
<tr>
<td>Potential of cross-contamination between patients</td>
<td>Not required</td>
<td>Scavenging/return to circuit issues and anesthetic “pollution” risk must be assessed</td>
</tr>
<tr>
<td>Gas scavenging</td>
<td>Not required</td>
<td>Pressure fluctuations due to sampling system may be compensated</td>
</tr>
<tr>
<td>Airway pressure compensation</td>
<td>Not required</td>
<td></td>
</tr>
</tbody>
</table>

**Weight of airway adapter similar and location at end of ETT., calibration not routinely required

Adapted from Mainstream or Sidestream Capnography? Respironics White paper.
As noted earlier, Novametrix’s 1st capnograph, the Model 1250 (Figure 64), to enter the market was a sidestream device based on an IR bench from Andros Inc. The introduction of the Model 1260 (Figure 65) marked Novametrix’s entry in mainstream capnography.

The Model 1260 capnograph and Model 7000 combined capnograph/pulse oximeters (Figure 67) became the first monitors from Novametrix to use the Capnostat 1 sensor. It used built-in zero and span cells in front panel of monitor (see #12 and 14 in Figure 64) which was replaced with on-cable cells with the Capnostat 2 Sensor. It displayed the capnogram, both in real-time and as a trend (Figure 65).

The Model 1260 (and 7000) introduced Teach Mode (Figure 66), a permanent library of illustrative capnogram displays and descriptions.
This mode provided the ability to freeze a waveform and load a stored library waveform with explanatory text in order to compare. This ‘teach’ mode (Figure 66) helped the clinician more quickly learn the characteristic CO₂ shapes and uses. Teach mode derived from digitized versions of capnographic tracings based on ideas from Smalhout text (Figure 71a/b).

The Tidal Wave family of handheld capnographs introduced in 1996 were eventually offered in models with mainstream CO₂ only (model 610), CO₂ and pulse oximetry (model 710) as well as each of the above models with and without sidestream gas sampling (models 615 and 715). It used 3 “soft” keys for menus and has been used in hospital setting (e.g. crash carts) and in emergency medicine systems throughout the world. The Tidalwave model 610 capnograph (Figure 68) has been shown to perform well during emergency intubations outside the OR as well in the OR both in adult and neonatal patients (Nochimson et al., 1997). It also has been used to evaluate respiratory depression in laboring women who have received intrathecal sufentanil (Atkinson et al., 1998).

![Figure 67](image1.png)

**Figure 67** – (a) Models 1260 and 7000 and (b) system block diagram

The Capnogard Model 1265 and CO₂SMO Model 7100 (Figure 69) were the first to use the Capnostat II or III sensor technology and combine it with the VENUS digital pulse oximetry technology.

Besides the usual environments of use, Novametrix CO₂ technology has served both the space program and military. For example, the CO₂SMO CO₂/SpO₂ monitor has “served” on two Space Shuttle missions (STS-69, launched September 7, 1995, and STS-72 launched January 11, 1996) (Figure 70) in order to study the effects of microgravity on pulmonary oxygen exchange. Also a ruggedized version of the Capnostat III sensor is in use with a military version of a commercial defibrillator.

![Figure 68](image2.png)

**Figure 68** – Tidal wave handheld monitor (K963327 11/20/1996)
Figure 69 – Capnographs with Capnostat III technology – (a) CO₂SMO (and NASA mission patches) and (b) Capnogard

Figure 70 – Photo of astronaut testing a CO₂SMO CO₂/SpO₂ monitor with Capnostat CO₂ sensor and finger pulse oximeter sensor, and mission patches for STS-69 and STS-72 shown (Photo courtesy of NASA)
Figure 71 – Use of “Teach Mode.” - (a) “Frozen” Capnograms with Normal; (b) “Frozen” Capnograms with Partial Obstruction
Flow-Sensors and Modules

Figure 72 – Innovations in proximal flow sensing

Sensors - The measurement of proximal flow in the critical care environment can often be challenging particularly given the high humidity and secretions present and that the length of mechanical ventilation can last from days to weeks. Due to their robustness, differential pressure based flow sensors are often used in clinical environments. Respironics flow sensors, particularly suited to these harsh environments, are fixed orifice, target type flowmeters, and as such the pressure drop is proportional to the square of the flow. The Respironics family of fixed orifice flow and CO₂/flow sensors grew from an alliance with a research group in the Department of Anesthesiology at the University of Utah (Korr).

Due to the need to avoid individual sensor calibration and robustness in the harsh environment of a breathing circuit, a fixed orifice design was chosen. Early prototypes consisted of adding pressure sensing ports on both the proximal and distal sides of the optical window in a mainstream CO₂ cuvette. (Orr, 1993) An adult flow only sensor was designed first (Kofoed, 1996). It featured a target geometry composed of a center strut and side-mounted flow restrictions (having a notch in the strut) that are designed to minimize localized streamline effects about the pressure sensor aperture. The use of a fixed orifice design in the mid-1990s challenged available state-of-the-art low pressure sensors because to achieve a 200:1 range in flow required greater than a 10,000:1 range in differential pressure. Improvements in pressure sensor performance coupled with high dynamic range (20 bit) analog to digital convertors made this approach both technically and commercially viable. Airway pressure is measured from the proximal pressure sensing tube with a gauge pressure transducer. Barometric pressure is measured with an absolute pressure transducer with built-in temperature compensation.

In an effort to simplify the calculation of volumetric capnography variables, reduce deadspace and improve ease of use, a family of combined CO₂/flow airway adapters (Kofoed et al, 1998) was developed. This included sensors optimized for neonatal, pediatric and adult patients (Table 7). The combination adult sensor design included the sample cell and fixed orifice portion side-by-side with the sample cell proximal to the patient (Figure 73) whereas the combination neonatal sensor combined the sample cell and fixed orifice portion by use of a split orifice design. These designs allow for relative immunity to unpredictable flow velocity profiles, without the need to add excessive length to the flow sensor adapter (i.e. minimizing dead space). (Figure 73).

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45 Novametrix acquired an exclusive license of the patents and related technology from Korr Medical Technologies Inc., the stockholders of which are Joseph Orr, Dwayne Westenskow and Scott Kofoed, pursuant to a License, Technical Assistance, Cooperation and Noncompetition Agreement (the "License Agreement") dated as of December 10, 1993 and amended as of June 21, 1994. (10-Q filing)

46 With fixed orifice designs flow is proportional to the square root of the pressure difference.
With several valves required for the zeroing and purging functions in bedside flow monitoring systems, the number of connections between different components (e.g. valves, sensors) results in a greater potential in leaks at these connections thus affecting the reliability of the measurement. Also this complexity results in increased variability in the pneumatic pathway thereby increasing the variability in the measurements particularly under loaded conditions (e.g. low compliance, higher pressures).

The replacement for the FloTrak, the FloTrak Elite module (Figure 75b,c) provides a cost-effective respiratory measurement solution that (a) eliminates the pneumatic connections that must be made manually by using a manifold that incorporates all of functionality of a existing flow/pressure measurement systems that use either multi-piece manifolds or individual pieces of tubing with fittings, (b) improves long term reliability and (c) improves performance and (d) improves inter-unit repeatability by reducing the variability between pressure transmission tubing pathways. The FloTrak Elite module consists of an electronic circuit board with valves and pressure sensors assembled with a manifold and pump. The manifold has two connectors to which the tubing from the flow sensor receptacle is connected. It is formed to include channels for transmitting pressure, a cavity to serve as a pressure reservoir, and openings and channels to pneumatically interface the sensors and valves with each other and the measurement ports. The size and complexity of a flow measurement system has been significantly reduced by integrating all of the pneumatic tubing and the reservoirs into a single low-cost manifold and at the same time eliminating the need for individual unit balancing creating a more reliable and manufacturable product.

**Figure 73** – CO₂/flow sensors (a) Cross section of adult combination CO₂/flow sensor; (b) (left to right) neonatal, adult and pediatric combination CO₂/flow sensors.

**OEM modules** – In order to maintain performance and function in the clinical environment over time, differential pressure based respiratory measurement systems generally include measurement as well as zeroing and purging functions. The original FloTrak module (Figure 75a) included this functionality and this technology was directly or indirectly integrated into OEM monitoring systems and ventilators from companies such as Marquette (GE), Siemens (Draeger), Biomed Devices and Philips.

**Figure 74** - Capnostat CO₂ sensor “mating” with (a) combined neonatal CO₂/flow sensor and (b) combined combined adult CO₂/flow sensor.
**Table 7 – Nominal Ranges and Values of Selection Criteria for Combined CO₂/flow Sensors**

<table>
<thead>
<tr>
<th>Combined Sensor</th>
<th>ETT Range (mm)</th>
<th>Min. Volume (ml)</th>
<th>Max Volume (ml)</th>
<th>Min. Flow* (LPM/ml/sec)</th>
<th>Max Flow** (LPM/ml/sec)</th>
<th>Dead Space (ml)</th>
<th>ID*** (mm)</th>
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</thead>
<tbody>
<tr>
<td>Neonatal</td>
<td>2.5-4.0</td>
<td>1</td>
<td>100</td>
<td>0.2</td>
<td>25</td>
<td>&lt;1</td>
<td>5</td>
</tr>
<tr>
<td>Pediatric</td>
<td>3.5-6.0</td>
<td>30</td>
<td>400</td>
<td>0.5</td>
<td>120</td>
<td>&lt;4</td>
<td>10</td>
</tr>
<tr>
<td>Adult</td>
<td>&gt;=5.5</td>
<td>200</td>
<td>3000</td>
<td>2.0</td>
<td>180</td>
<td>8</td>
<td>15</td>
</tr>
</tbody>
</table>

*Min Flow – nominal minimum flow of sensor;**Max. Flow-nominal maximum flow of sensor;***ID-nominal inner bore diameter of sensor. Note: Min. volume and Max. volume represent the recommended operating range in volume for each flow sensor and not necessarily the absolute minimum and maximum volume values. (from Selecting the Right Flow Sensor with Respironics Combined CO₂/Flow Sensors. Respironics White paper.

Other than the flow modules, the company’s only platform that offered proximal flow monitoring with their fixed orifice flow sensors was the Vent\textsuperscript{48} (Figure 76), a hand-held respiratory mechanics monitor. It measures flow, pressure and volume at the airway and graphically displays flow and pressure waveforms and loops, breath by breath. This monitor was intended for spot checking mechanically ventilated patients and, when used during transport, provides an additional level of safety for the patient. Respiratory therapy and critical care departments with patients requiring mechanical ventilation represent the primary users of the Vent\textsuperscript{48}.

**Figure 75 – Original FloTrak OEM module (a) top view and Flotrak Elite Module\textsuperscript{47} - Two views (b)**

\textsuperscript{47} (K080652 06/20/2008)

**Figure 76 - Vent\textsuperscript{48} hand-held monitor, measuring 8" high, 3" wide and 1-1/2" deep and battery operated.**

\textsuperscript{48} K964360 04/04/1997
The evolution of Novametrix's cardiorespiratory monitors and its continued innovations in volumetric capnography and related measurements goes back to the early 1990's with the introduction of the Ventrak monitors. The Ventrak series of respiratory mechanics monitors provided continuous and non-invasive graphical monitoring of airway flow, airway pressure and lung volume. They also had the ability to perform waveform (graphical) analysis and calculate a variety of physiologic parameters relating to lung function which was not previously available on a continuous, non-invasive basis for infant through adult patients.

**Model 1500** - The interest in this type of monitoring can be traced back to the influential Pneumogard series of monitors. Novametrix expanded its product offerings in on-line respiratory mechanics monitoring with the acquisition from Med Science of its product named Ventrak (for ventilation tracking) to create the Respiratory Mechanics Monitor (RMM). The Ventrak RMM Model 1500 system consisted of a 'box' with the front end electronics (Figure 78) that was integrated with an all-in-one personal computer. It was popular with respiratory therapists for research. It allowed for a number of different flow and pressure sensors to be interfaced to it (see Figure 79) and used a disposable variable orifice flow sensor for adult monitoring and either a Fleisch type or heated wire flow sensor for neonates (Bear NVM monitor) (Figure 80). A syringe was usually provided for calibration of the Fleisch type and variable orifice flow sensors as well as for verification purposes.

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49 Med Science was exploring with clinicians at the University of Texas Medical Branch at Galveston (UTMB) applications using post-processing of signals of bedside volumetric capnography using the Ventrak monitor and Novametrix Model 1265 capnograph. This work interested Novametrix and was eventually embodied in the Ventrak 1550/Model 1265 monitor.
Figure 80 – Ventrak Model 1500 (a) variable orifice adult flow sensor (Carlsbad Varflex flow sensor) and (b) neonatal low deadspace flow sensor (Hans Rudolph flow sensor) (also compatible with NVM flow sensor).

Figure 81 – Ventrak model 1500 “in-use” in the ICU (image from 1995 annual report)

Model 1550 - The Model 1550\(^50\) was based upon the Model 1500 but (a) replaced the 3\(^{rd}\) party flow sensors with Novametrix fixed orifice flow and combination CO\(_2\)/flow sensors optimized for the pediatric/ neonate and pediatric /adult flow rates which eliminated the need for user calibration and (b) allowed a capnometer (CO\(_2\)SMO or Capnogard) to be interfaced via a serial port to the 1550 module (Figures 83, 84) so that volumetric capnographic variables such as VCO\(_2\) and dead space could be computed. The flow connector which plugged into the receptacle on the front panel of the monitor consisted of 3 ports – two for the differential pressure measurement and a third for an optional auxiliary measurement which could be used for carinal and esophageal pressures. It also provided for a Bear NVM connection as well. The monitor interfaced to an all-in-one PC which provided for waveform and data display. Figure 82a/b illustrates one such display in which the patient and mechanical breath data are displayed in separate columns and the averaged data noted, and a flow-volume and pressure-volume loop screen with an esophageal pressure measurement available. In addition to the “normal” respiratory mechanics parameters, the addition of esophageal pressure permitted the calculation and display of work of breathing (mechanical, patient and imposed), P\(_{0.1}\) and pressure-time-product.

\(^{50}\) K960831, 05/29/1996
CO₂SMO Plus! - The CO₂SMO Plus! monitor (Figure 85) was the first monitor to integrate on-airway flow measurements with capnography (and pulse oximetry) in a single small package to enable continuous bedside monitoring of mechanically ventilated patients. The CO₂SMO Plus! monitor followed the Venttrak monitors to provide continuous, non-invasive measurements of flow, pressure and volume in a patient's airway, as well as measurements of other pulmonary mechanics, CO₂ elimination and arterial oxygenation. It included screens for waveform, trend and data monitoring (Figure 87) as well as screens to help implement weaning protocols. Applications for this monitor include the clinical management of proper pressure and flow of airway gases being delivered to a mechanically ventilated patient's lungs, allowing therapists to wean a patient from costly mechanical ventilation to spontaneous breathing at the clinically appropriate time. The use of these parameters, and the impact of each parameter on patient ventilation, provides the clinician with important feedback to optimize the patient's care. Thus the use of the CO₂SMO Plus! enhances patient care by minimizing the trauma, length of stay and costs associated with mechanical ventilation.

Clinical literature - Castle et al (2002) validated the performance of the CO₂SMO Plus! monitor and compared it to a ventilator commonly used in vivo (adult rabbits). Average differences between results calculated automatically and by the Bohr-Enghoff equation were -0.79 ml for \( V_{D}_{alv} \) (95% confidence interval -2.02 to 0.44 ml) and -0.23 ml for \( V_{D}_{phys} \) (-0.6 to 0.14 ml). They concluded that the V&C can be used in newborn infants undergoing mechanical ventilation, if changes in VD are < 5 ml, interactive analysis or the Bohr equation should be used. Roske et al (1998) assessed the accuracy of volume measurements by different instruments using standardized laboratory conditions included both the Venttrak 1500, Venttrak 1550 with an adjustable calibration syringes (volume range 2-60 ml, breathing rates 30/min-60/min) and humidified (>95%), heated (35 °C) breathing gas with adjustable FIO₂ (0.21-1.0). They concluded as long as the increased FIO₂ value is taken into account, neonatal spirometry devices such as the Venttrak 1500 and 1550 allow sufficiently accurate volume measurements in the range of 10-60 ml and at frequencies between 30-60/min.

Clinical literature - Published validation studies for the Venttrak 1550 system appeared in the mid- late 1990s, including Wenzel et al. (1999, Br J Anesth) who validated the Venttrak 1550/Capnogard 1265 (V&C) for deadspace (\( V_D \)) measurement in vitro (lung model) and in vitro and compared it to a ventilator commonly used.
for pediatric and neonatal population. They concluded that

the accuracy of tidal volume values is crucially dependent on the site of measurement. Unless measured at the airway opening, displayed values are an inconsistent and misleading indicator of the true volumes delivered.

Riou et al (2004) provided additional validation for the monitor finding the measurement of airway dead space by the CO₂SMO Plus! reproducible over a 1-h period in children requiring mechanical ventilation with the ventilatory parameters remaining constant during the study. The CO₂SMO Plus! monitor remains a research tool to this day as evidenced by Roehr et al (2010) evaluation of PIP and VT during simulated manual ventilation on an intubated neonatal mannequin.

Figure 85 – CO₂SMO Plus! (a) monitor (Note: connector for flow sensor on front and on rear panel for Capnostat CO₂ sensor) (b) screen displays available.

Figure 86 - CO₂SMO Plus! monitor “in use” at the bedside (Image from 1998 annual report)

Figure 87 - CO₂SMO Plus! (a) waveform and (b) trend screens.
Non-invasive partial rebreathing cardiac output has been of interest to Novametrix since the publication by Capek and Roy of their work in the late 1980s. (Capek and Roy, 1988) The NICO monitor introduced to the market in 1998 (Figure 88a), was the first widely available clinical device to non-invasively measure pulmonary capillary blood flow (and as such cardiac output) using the indirect Fick partial rebreathing technique. With the use of a NICO sensor (i.e. combined CO₂/flow sensor with valve and adjustable loop of tubing (Figure 91)) and the use of a rebreathing maneuver controlled by an in-line valve (Figure 92), cardiac output and pulmonary capillary blood flow (PCBF) can be estimated every 3 minutes. The NICO monitor(s) (Figure 88) offer several advances including "hands off" automatic continuous operation, completely non-invasive techniques and easy to use functionality. Although cardiac output is considered by many to be the best indicator of heart function, it has not been routinely monitored in patients undergoing general surgery because available techniques were too invasive (risky), costly or technically difficult. The NICO monitor remains to this day the only commercially available monitor that measures PCBF which unlike cardiac output directly reflects the amount of blood involved in gas exchange. As such PCBF can serve as a useful clinical parameter suitable for measurement and optimization.

The original Fick method, which requires invasive measurements and labor-intensive manual tasks, is a well-accepted standard reference technique used to evaluate all other means of determining cardiac output. Until the NICO monitor came to market, the Fick method has been too difficult to use in most clinical practice circumstances such as surgical operating rooms and intensive care units. All of the NICO family of monitors, ranging from the original NICO, NICO₂ and NM3 monitors (Figure 88), use a differential form of the Fick principle applied to CO₂ produced by the body and eliminated through gas exchange in the lungs (Jaffe, 1999). However, these monitors have used innovative algorithms which incorporate all of the VCO₂ and end-tidal CO₂ data points during the rebreathing cycle to estimate PCBF. That approach known as the cluster algorithm applied with a simple model of the CO₂ stores of the lung and blood finds the slope of the VCO₂ vs PetCO₂ curve which is directly related to the PCBF (Figure 89) (Orr JA and Kuck K, 2003)

53 K091459 07/28/2009
Another innovation of the NICO monitor is the use of an adjustable deadspace (Figure 91) controlled by dual diaphragm valve (Figure 92) and settable with a volume guide provided with each NICO sensor, to better optimize rebreathing to the patients tidal volume (Figure 90) (Orr, 1996).

The NICO monitor provides a continuous display of cardiovascular monitoring variables (Figure 93) including PCBF, cardiac output, stroke volume, cardiac index and heart rate. In addition, NICO provides real-time displays of other physiologic variables including CO₂ elimination, end tidal CO₂, respiration, oxygen saturation, heart rate and respiratory mechanics parameters based on measurements of capnography, airway flow and pulse oximetry. These monitors are the only stand monitors which monitor physiologic gas exchange and reveal dead space, CO₂ elimination and effective tidal volumes at the alveolar level.

Clinical literature - In 68 patients Botero et al. (2004) validated the NICO monitor and thermodilution against a more direct standard, transit-time flowmetry of the ascending aorta using an ultrasonic flow probe (UFP) and found clinically equivalent accuracy of these methods relative to the invasive UFP standard. Since the NICO monitor’s introduction over 150 peer reviewed papers and abstracts have been published either validating the measurement or applying it clinically in anesthesia, critical care medicine (Figure 96) and emergency medicine. A recent study, Young and Low (2010) summarized the clinical literature to date for the device.
Clinical applications of this versatile device include monitoring patients during surgery (in the operating room), in the emergency room and in the intensive care unit. It provides a needed alternative to the conventional invasive procedure for monitoring cardiac output, (thermodilution), which requires insertion of a catheter through the heart and into the pulmonary artery (PA). Patient safety can be enhanced by eliminating the documented hazards of PA catheters which include infection, embolism and heart or lung tissue damage. By eliminating the costs, risks and complications associated with the use of PA catheters, the NICO monitor is dramatically simpler and less costly to utilize. Further, since the NICO monitor is non-invasive and easy to operate, the use of this technology may be expanded to other applications where it was previously deemed too risky or costly.

Figure 93 – Screens – (a) Cardiac output screen from NICO monitor; (b) waveform screen from NM3 monitor

Figure 94 – NICO monitor sitting on top of an anesthesia machine during a surgical procedure (Image from 1999 annual report)

Figure 95 – Trend plot comparing NICO measurements (NICO) with bolus thermodilution (DualTherm) in an animal study in which cardiac output was varied between 1-8 LPM with dobutamine and halothane. (n=41, r=0.98 bias±precision of 0.14±0.43 LPM).
Beyond NICO - Leveraging on the NICO technology and working with clinicians and researchers at the University of Florida and others since the late 1990s, the NM3 monitor has served as the platform for the introduction of the VentAssist™ software. This innovative software adds a new screen page for displaying selected measurement parameters in a bar chart format with their “normal” ranges (Figure 97). What differentiates this software over existing software packages is the addition of a parameter for patient effort, non-invasive work of breathing per min (Banner et al., 2006) and a user-selectable soft key to provide on-demand advice for the level of pressure support and ventilation (open loop) for mechanically ventilated adult patients (Banner et al, 2008).

The next step for the NICO family (yet to be released) may be to integrate flow, infrared and luminescence quenching technologies in a single airway adapter (Mace et al, 2008). These technologies were shown to work well as an in-line measurement of metabolic measurements (VO₂ and VCO₂, REE and RQ) in both laboratory bench and clinical environments. Studies in a bench model, normal volunteers and intensive care unit patients found excellent agreement with the standard or comparison device. (Table 8)

Additionally, this technology was applied for the automatic measurement of functional residual capacity (FRC), the volume of gas left in the lungs at the end of a breath, using a wash-in method. Excellent agreement was reported for the comparison methods for bench, animal and patient studies (Brewer et al, 2007; Brewer et al. 2008)

The NICO, NICO₂ and NM3 monitors, often referred to as a physiologist in a box, remain at the forefront of innovation and continue to be used to explore new opportunities of physiologic monitoring.

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54 This included the engineering firms Neurodimension and Convergent Engineering who were instrumental in the research and development of the original software.
Other Products

**MAGSTIM.** - An interesting product line that was quite unrelated to the core business was the MAGSTIM line of magnetic stimulators. The technology based on the doctoral work of Mike Polson and Reza Jalinous at the University of Sheffield was first introduced as the MAGSTIM 200 (Figure 98). The MAGSTIM, an instrument used in the magnetic stimulation of neuromuscular tissue, is capable of stimulating neuromuscular tissue by inducing small currents in the tissue using a brief pulse of electromagnetic energy. The MAGSTIM delivers pulses (100 µsec rise time of 2 ms duration) at rates once per 2 to 4 seconds at power levels from 50 to 100% using a coil generating a strong magnetic field (1.5 tesla max at center of coil dropping to 0.2 tesla max 1 meter from coil). Its main advantage over the conventional nerve stimulator is its ability to stimulate deep and otherwise inaccessible nerves easily and painlessly. In addition, no skin preparation is required and the device can stimulate through clothing. In the US the device was cleared for peripheral nerve stimulation but although it remains classified investigational in the US it is also used for cortical magnetic stimulation. Its use includes diagnostic applications such lesion localization as well as therapeutic uses (Hovey and Jalinous, 2006). This business was sold in 1990, and exists today as separate company ([www.magstim.com](http://www.magstim.com)).

**Other.** - In addition to the product lines described, Novametrix ventured into other monitoring technologies and variants of the existing technologies with products such as the NOVO2X Model 400 oxygen analyzer (Figure 99) with a disposable polarographic sensor developed at PI, and Model 902/903 neonatal physiological monitor (Figure 100) with heart rate using a three lead ECG and respiration with impedance pneumography using the chest ECG leads.

Also of interest was Novametrix’s innovation in patient interfaces for neonatal CPAP. This early neonatal nasal cannula (Figure 101) (US patent #4367735) was designed to be resistant to compression and damage cause by pinching of the cannula and included a cap with straps to help hold it in place.

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55 K871338 08/04/1987
56 K840392 02/27/1984 (400)
57 K831578 08/12/1983 (902)
58 K840560 04/17/1984 (903)
59 K792722 01/24/1980 (CPAP)
60 Heavily cited patent, 71 forward references.
**Software tools** - In support of Novametrix's monitoring products and associated research, software data collection and analysis tools with names such as Novacard, and Analysis+ were developed (Figures 102 and 103). Analysis+ provided tools for data review (differences, trends, values of data samples on curves), data reports and data exporting (parameters and selected time intervals of waveforms).

**Figure 102** – Novacard screens

**Figure 103** – Analysis Plus! screen (a) Main menu options, (b) waveform display

**Clinical Utility and Advances**

External relationships with research universities and hospitals throughout the United States and Europe have been key to Novametrix’s continued innovation. These have been integral in the development of nearly all of the core technologies of Novametrix.

Researchers and clinicians who have worked with Novametrix over the years either in a clinical application or product evaluation role include current and past thought leaders from the anesthesia, pulmonary medicine and emergency medicine domains. This included Drs. Luis Cabal and Edward J. Quilligan who were involved with the company in the early days. This has also included some of the most well known names in clinical medicine of which a small sampling is shown in Tables 9 and 10.

Novametrix through the use of medical advisory board meetings sought the guidance of clinicians. These clinicians helped lead the way and often were willing to pioneer in areas including transcutaneous, capnographic and volumetric capnographic monitoring.

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60 At the time Professor of Obstetrics and Gynecology and Vice President for Health Affairs of the University of Southern California School of Medicine, also one of the principal founders of the subspecialty of maternal fetal medicine. (http://www.obgyn.uci.edu/QuilliganBio.html)
Table 9 - Model1260/7000 capnograph research sites (early 1990s)

<table>
<thead>
<tr>
<th>Institution</th>
<th>Clinician(s)</th>
</tr>
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<tbody>
<tr>
<td>Vanderbilt University - Knoxville, TN</td>
<td>Drs. John Marini, John Truwit</td>
</tr>
<tr>
<td>Charity Hospital of New Orleans</td>
<td>Dr. Kevin Ward</td>
</tr>
<tr>
<td>Hospital for Sick Children-Toronto</td>
<td>Dr. Jerrold Lerman</td>
</tr>
<tr>
<td>University of Maryland - Division of Pediatrics, Baltimore</td>
<td>Drs. R. Viscardi, Alice Ackerman</td>
</tr>
<tr>
<td>Mass General -Boston</td>
<td>Drs. Todres and Castillo</td>
</tr>
<tr>
<td>Institute of Anesthesiology, University Hospital, Utrecht, Netherlands</td>
<td>Prof. Bob Smallhout</td>
</tr>
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<td>University of Iowa</td>
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<tr>
<td>LAC/USC Women's Hospital - Los Angeles CA</td>
<td>Dr. Luis Cabal</td>
</tr>
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</table>

Table 10 - NICO research sites (late 1990s)

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<td>University of Utah</td>
<td>Dr. Peter Bailey</td>
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<tr>
<td>University of Washington, Seattle</td>
<td>Dr. Jenny Souders</td>
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<tr>
<td>Ohio State University</td>
<td>Dr. Mike Jopling</td>
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<tr>
<td>University of Florida, Gainesville</td>
<td>Drs. Nik Gravenstein, Emilio Lobato, Monica Botero</td>
</tr>
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<td>Florida Hospital</td>
<td>Dr. Lou Guzzi</td>
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<tr>
<td>Duke University</td>
<td>Drs. Ira Cheifetz, TJ Gan</td>
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<td>Dr. Joel Slade</td>
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<td>University of Arizona, Tucson</td>
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<tr>
<td>University of California, San Diego</td>
<td>Dr. Ronald Dueck</td>
</tr>
</tbody>
</table>

Most recently the CO₂SMO+ and NICO product lines have almost single handedly driven the development of the volumetric capnography market by making this technology available. Nearly all of the leading ventilator manufacturers now recognize the value of volumetric capnography. The parameters which are being leveraged include VCO₂ for ventilator patient management and deadspace ratio as an outcome predictor.

Acknowledgements

Thank you to the following current and former employees who provided anecdotes and material for this paper - Ivan Bustamante, Carmelo Dali, Dave Ellis, Patrick Freeman, Ed Harvie, Gary Hochstetler, Andy Kersey, Mike Lineback, Les Mace, Bob Narciso, Phil Nuzzo, Herb Pittman, Rich Mentelos, Tony Pierry, Mike Polson, Dave Rich, and Dirck Spicer.

Trademarks

Capnostat, LoFlo, NICO, NICO₂, NM3, Novametrix, CO2SMO Plus!, Analysis!, Novacard, Venttrak, Ventcheck, Tidal Wave, and FloTrak are trademarks belonging to Koninklijke Philips Electronics N.V. Magstim is a trademark of the The Magstim Company Ltd.

Dedication

This paper is dedicated to the memory of those employees and their family members who passed away prematurely during their service to Novametrix or are featured in this whitepaper.

Lou Pellegrino (president)
Tom Abbenante (VP Engineering)
Carol Marchand (administration)*
Kevin Beardsworth (engineering)*
Joey Condon (son of employee)*
Kim Weems (purchasing)* and
Linda Chilemi (manufacturing)*
Kay Infante (stockroom)*

*A Memory Garden at 5 Technology Drive planted in their memories.

v2.6 May 25 2011 – Prepared by M Jaffe
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inNOVAtive News, issues 1-16.

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Novametrix Prospectus, 1979

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Pneumogard - Airway and Esophageal Pressure


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**Pulse Oximetry**


Cardiothorac Anesth. 1990 Feb;4(1):30-4. (Model 500)


Capnography


Nuzzo PF. Capnography in infants and children. Pediatric Nursing 1978;May-June:30-8


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From RP, Scamman FL. Ventilatory frequency influences accuracy of end-tidal CO2

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Mace, LE. et al.US7335164: Multiple function airway adapter, 2/26/2008. (flow+CO2+O2)

Orr, JA. and Kuck, Kai. US6540689: Methods for accurately, substantially noninvasively determining pulmonary capillary blood flow, cardiac output, and mixed venous carbon dioxide content. 4/1/2003. (NICO)


Other


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(From [www.fda.gov](http://www.fda.gov) 510(k) database)
A PROMISE

We the people who are Novametrix promise to provide the best possible products, to market them honestly, to price them fairly, and to support them completely.

We promise to provide a team of sales, service, and support professionals that is second to none.

We promise to afford to both our customers and competitors the high level of respect they deserve.

We promise to deliver the highest degree of integrity and professionalism in our daily business practices.

And we promise to nurture and maintain the trust of the healthcare industry—based on the Novametrix commitment to quality products from quality people.

Louis P. Pellegrino