Respiratory control

Small companies are developing hospital equipment for lung problems

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On the screen, the Timpel tomograph allows medical professionals to know the precise volume of air in the patient's lungs

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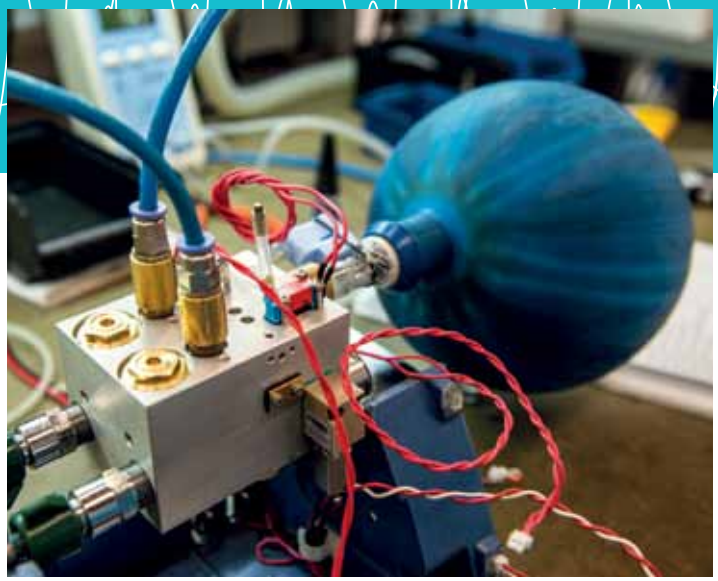
Two São Paulo companies have developed intensive care medicine equipment that is being sold to hospitals in Brazil and abroad. One of the companies is Timpel, whose name represents the Portuguese acronym for the product it created, an electric impedance tomograph (EIT) used to enable precision ventilation for patients who breathe with the help of mechanical ventilators. The other company is Magnamed, which makes two types of ventilators: one for intensive care units (ICUs) and the other for the emergency transport of patients with breathing problems.

Timpel's tomograph functions by using the difference in resistance to an electrical current at a particular voltage (impedance) found among the various parts of the body. To make a diagnosis, a belt containing 32 electrodes is placed around the patient's thorax and linked to a monitor. Low-intensity electrical pulses travel through the body and find varying resistances along the way. This allows the physician to determine the quantity of air that is entering the thorax and where it is going. "Blood conducts electricity well," explains physician Carlos Carvalho, director of the Pulmonology Division of the Heart Institute (InCor), at the School of Medicine of the University of São Paulo (FM-USP), who participated in the clinical studies for creation of the tomograph.

Medical professionals can check the monitor to determine whether air is being directed to both lungs, which is good, or to just one, a situation that can cause complications. It is now possible to control the volume, pressure and flow of injected oxygen, improving the prognosis and reducing the risk of pulmonary injury while enabling individualized treat-



Test of ventilation equipment at Magnamed

ment for each patient. "Nearly 40% of patients admitted to the ICU require artificial respiration, and of these, 40% die as a result of complications caused by the procedure," says pulmonologist Marcelo Britto Passos Amato of the FM-USP, who also took part in the clinical studies that led to the creation of the EIT. "Our goal is to reduce those rates."

Of the two devices developed by Magnamed, the first was OxyMag, a portable ventilator (artificial respirator) for patients being transported in any type of mobile ICU. "The device helps physicians and paramedics respond more quickly in emergencies," says electrical engineer Wataru Ueda, company president. "OxyMag is light, weighing only 3.25 kilograms, is easy to handle and has a touch screen color display and a battery life of over six hours. With this apparatus, it's possible to ventilate extreme low-weight neonatal and pediatric patients as well as adults."

RESEARCH PRODUCT

FlexiMag, on the other hand, is a mechanical ventilator to be used in ICUs. The device identifies when there is an absence of a respiratory stimulus: when it senses that the patient has not inhaled, it does the work for him, forcing the breathing. "The device quickly responds to any breathing difficulty the patient may have and offers better control of ventilation because the physician is able to see the volume, pressure and distribution of air in the lungs right on the screen," Ueda reports.

New strategies in artificial ventilation began to be developed through a FAPESP-funded research project headed up by Amato from 2002 to 2008 (see *Pesquisa FAPESP* Issue No.151). Those strategies demonstrated the need for a device that allows real-time visualization and individualized treatment. "In the beginning, we weren't thinking that the study would result in a product," he recalls. "When we realized that that was possible, we created Timpel in 2004." The company, incubated at the Center for Innovation, Entrepreneurship and Technology (Cietec), on the main campus of USP in São Paulo, included researchers from the School of Medicine, the Polytechnic School (Poli) and the Institute of Mathematics and Statistics (IME), all from USP.

Timpel soon signed a partnership agreement with Dixtal Biomédica, a company specializing in medical equipment for hospitals, to jointly develop the tomograph, which took nearly four years. "In 2008, that company was purchased by Philips, which did not want to purchase the EIT project because it was still under development," Carvalho says. "We managed to attract some investors so that Timpel could produce the device."

Although it had been used on an experimental basis with patients in the respiratory ICU at the Hospital das Clínicas of FM-USP and at InCor in 2006, sales of the EIT only began in 2015. "Up to now in Brazil, we have sold more than 60 of the devices to private, public and university hospitals," says electrical engineer Rafael Holzhacker, Timpel director. "We have an established distribution network in Brazil. We opened Timpel Medical abroad, headquartered in the Netherlands, to facilitate logistics and provide local customer service. We have already obtained the CE brand for marketing it in the European market, and we have buyers in Spain, Germany, France and Sweden in addition to Peru, Chile, the United States and Canada, these last two for now limited to research, given the regulatory restrictions." Company sales in 2016 were R$972,000, and in the first six months of this year they have reached R$1.1 million.

The history of Magnamed began in the garage of Ueda's mother's house, where he lived for six months in 2005. Then, in association with mechanical engineer Tatsuo Suzuki and electrical engineer Toru Kinjo, Ueda developed the business plan. "In the following year, the project was selected to be a part of Cietec," he recalls. "There, we conducted product R&D, putting the business concept into practice. It took two years of incubation, with research studies funded by agencies like FAPESP, CNPq [National Council for Scientific and Technological Development] and FINEP [Brazilian Innovation Agency]."

OxyMag is a portable respirator for use in ambulances with ICU equipment

The Criatec seed capital investment fund, maintained with funds from the Brazilian Development Bank (BNDES) also contributed to the venture. In all, R$5 million were invested in Magnamed during those years. "That funding breathed new life into the business, which found itself needing funds to continue product development," says Ueda. "In late 2008, OxyMag was completed and the first Magnamed factory was set up in the city of Cotia (São Paulo)." The device began to be sold in 2010. Sales of FlexiMag began in 2013.

By August 2017, nearly 5,000 devices had been sold. "In 2011, 70% of Magnamed's sales volume came from exports," Ueda reports. "Today, the situation is reversed: 70% of the sales, out of a total sales volume of R$34 million for 2016, were in the Brazilian market." The company was the official supplier of emergency ventilation equipment at the 2016 Summer Olympics in Rio de Janeiro, and it exports to more than 50 countries, especially in Latin America and Southeast Asia.

With a focus on foreign markets, Timpel has filed over 50 patents in several countries

EQUIPMENT MARKET

Neither of the two companies is alone in the respective markets for the devices they developed. "We have major competitors in Brazil and abroad," Ueda says. "But FlexiMag offers faster response. And Oxymag is very versatile and one of the lightest on the market. Besides that, it uses a Magnamed-patented system, which ensures better performance, prevents failures and reduces maintenance costs."

In the case of Timpel, Holzhacker says that the company is a pioneer in developing the electric impedance tomograph and holds more than 50 patents filed in major countries all over the world, protecting essential aspects of the technology. "There are two other companies in the world that are making similar devices: one in Germany and the other in Switzerland," he says. Now the company is preparing to take a giant leap forward to increase its market. It is seeking approval from the Food and Drug Administration (FDA), the federal agency in the United States that controls the consumption of foods, medications and medical devices. "Given the EIT's level of innovation and clinical potential, from the very beginning we've focused on internationalization, fostering scientific collaboration projects with research centers in several countries, including the United States," Holzhacker explains. "FDA approval is crucial for Timpel's ability to access the U.S. market, which represents more than 40% of the global market.

The problem is that, since no company has as yet sold similar equipment in the United States, the FDA is treating the electric impedance tomograph as an innovation. "That is why the path to approval is more complicated than it would be for the process of medical equipment traditionally used," says Holzhacker. "The technical documents for the EIT have been drafted and submitted, and there is still some back-and-forth with FDA specialists on issues such as usability, among other things that are being resolved so that the equipment can be approved." ■

PHOTOS EDUARDO CESAR

Projects

1. High frequency neonatal electronic pulmonary ventilation (No. 09/52357-4); **Grant Mechanism** Innovative Research in Small Businesses Program (PIPE); **Principal Investigator** Toru Miyagi Kinjo (Magnamed); **Investment** R$71,643.27.

2. High resolution signal acquisition and parallel processing of image reconstruction for Electrical Impedance Tomography (FAPESP – PIPE/PAPPE 2013 Disbursement) (No.13/50775-9); **Grant Mechanism** Innovative Research in Small Businesses Program (PIPE); **Principal Investigator** Rafael Holzhacker (Timpel); **Investment** R$245,475.00.

3. New strategies in artificial ventilation: diagnosis and prevention of barotrauma/biotrauma through electrical impedance tomography (EIT) (No. 01/05303-4); **Grant Mechanism** Thematic Project; **Principal Investigator** Marcelo Britto Passos Amato (USP); **Investment** R$5,102,802.63.