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ITAMAR MEDICAL LTD.

pat signals

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SECOND ISSUE • MARCH 2001

FROM THE PRESIDENT

Dear Readers,

It has been a very busy and productive time since our last issue of PAT Signals, and we have a lot of news and interesting items to share with you.

This issue focuses on "PAT-Day", a demonstration of Itamar Medical's PAT™ technology and applications, initiated by our strategic partners, Medtronic, and held at their headquarters in Minneapolis in November. This event was an unprecedented opportunity, as we gained valuable exposure to some of the leading players in the healthcare and scientific community. The participation of so many of our field investigators, from some of the world's leading research institutions and universities, illustrates the magnitude of the PAT Signal's potential and the growing interest it has inspired in the scientific community.

Our Sleep_PAT technology was a highlight at the European Sleep Research Society's (ESRS) 15th Congress, held in Istanbul in September of last year. We are following up on the leads generated at the show, and increasing the momentum Sleep_PAT has gained in this important and rapidly growing market.

Recent developments inside Itamar Medical are worth noting as well. We have nearly doubled our staff, and several members of our senior staff have been promoted. We are particularly happy to welcome a new member to Itamar Medical's Board of Directors, Dr. Glen Nelson, Vice Chairman of Medtronic. We look forward to benefiting from Dr. Nelson's extensive experience in the healthcare industry.

This issue features an interview with Dr. Jacob (Koby) Sheffy. Koby, recently appointed VP and Principal Scientist, has been a key member of our team since the company's establishment in 1997. Our invitation to all our readers to contact us with questions or inquiries is always open and we welcome the opportunity to hear from you.

Sincerely,
I. Schreiber

Israel Schreiber
President and Chief Executive Officer

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PAT™-Day at Medtronic in Minneapolis

On November 20, Itamar Medical's technology and products were presented at a day-long seminar and discussion on PAT™ technology, hosted by Medtronic, Inc. in Minneapolis. Many prominent researchers and industry leaders from different branches of medicine came to hear how PAT technology could affect ease and accuracy of diagnosis in a variety of cardiac and sleep related disorders.

Among the industry leaders who participated in the seminar were: ***GE Medical Systems, Somnus Medical Technologies, WebMD*** and ***Xomed–Medtronic.*** Medtronic's top management attended and Itamar Medical's strategic partner for the marketing of sleep related PAT applications – ***Respironics*** - was also there.

A number of representatives from Itamar Medical were present, both from senior management and from the technical staff. They were joined by members of Itamar's Medical Advisory Board: Professor David White of Harvard (who chaired the sleep session), Professor Jan Hedner of Sahlgrenska University Hospital, Goteborg, Sweden, and Professor Barry Zaret of Yale who chaired the cardiac session. Several other investigators participated, including: Peter Ganz MD, of Harvard, Jeffery Kuvin MD, of TUFTS, Amir Lerman MD, of the Mayo Foundation, Marc Pritzker MD, of the Minneapolis Heart Foundation, and Alan Rozanski MD, of Columbia University.

The agenda focused on discussions and panel sessions regarding the clinical potential of the PAT Signal and how it is being evaluated for application in cardiac and sleep medicine. At sessions held throughout the day, our team of researchers and investigators presented numerous aspects of PAT technology and applications, including: "The Neurophysiology Basics of PAT," "PAT and Peripheral Endothelial Dysfunction," "PAT and Coronary Endothelial Dysfunction," "PAT and CHF – Screening and Monitoring," as well as a number of topics regarding PAT in sleep medicine. Israel Schreiber, Itamar Medical's President and CEO presented an overview of the Company's commercialization strategy for incorporating the PAT Signal in a growing line of products for various medical applications. The day concluded with a demonstration of some of these PAT devices and applications.

PAT-Day in Minneapolis – A Great Opportunity

Current clinical trial sites:

University of Colorado Health Sciences Center, Colorado. Study headed by Professor Robert Ballard • ***Columbia University College of Physicians and Surgeons***, New York. Study headed by Professor Allan Rozanski • ***Harvard University School of Medicine***, Boston. Study headed by Professor Peter Ganz • ***Harvard University School of Medicine***, Boston.

Business Briefs

Dr. Glen Nelson joins Itamar Medical's Board of Directors

Welcome to Our New Director

Dr. Glen Nelson, Vice Chairman of Medtronic, has recently joined Itamar Medical's Board of Directors. While a practicing surgeon and CEO of Park Nicollet Medical Center, Dr. Nelson joined Medtronic's Board of Directors in 1980. In 1986 Dr. Nelson was appointed Executive Vice President of Medtronic. He has served as Vice Chairman since 1988.

We look forward to benefiting from Dr. Nelson's extensive healthcare experience to assist us in advancing PAT™ technology and applications. In addition to Medtronic, Dr. Nelson served as Chairman and Chief Executive Officer of American MediCenters, Inc. and as Chairman, President and Chief Executive Officer of the Park Nicollet Medical Center, a large multi-specialty group practice in Minneapolis, Minnesota. Dr. Nelson serves on the Board of several other major corporations.

A graduate of Harvard College, Dr. Nelson received his Doctor of Medicine degree from the University of Minnesota in 1968 and was certified by the American Board of Surgery in 1970.

We extend a hearty welcome to Dr. Nelson and look forward to working closely with him.

Employee News

Itamar Medical's staff is growing steadily and is currently made up of over fifty professionals. In addition the following senior management changes have occurred since our last issue of PAT Signals.

Israel Schreiber, President of Itamar Medical, has been appointed President and Chief Executive Officer.

Noam Levy, Vice President Finance has been appointed Chief Financial Officer and Vice President for Finance.

Dr. Jacob Sheffy has been appointed Vice President and Principal Scientist.

Shlomo Ayanot has been appointed Vice President Operations.

Dr. Giora Yaron and ***Martin Gerstel*** now serve as co-chairmen of the Board.

Itamar Medical Board Approves Facility Expansion

Itamar Medical's Board of Directors approved a 300 square meter expansion to the company's corporate headquarters at the meeting held in Caesarea on September 20th 2000.

This new section will house our Operations Department and enable us to increase the size of our software and signal processing teams, as well as the clinical teams.

In addition the company's growth and latest product developments were reviewed at length and a new round of promotions and additions to the staff were approved.

Itamar Medical's Board of Directors reviews the Company's progress

Itamar Medical's ISO-9001 certification testifies to the highest quality standards in research, development and manufacturing

Itamar Medical Continues to Maintain ISO Certification

Itamar Medical has maintained its ISO-9001 certification for the third consecutive year, following our annual ISO audit, which took place in August 2000. We have also been granted EN 46001 again, an extension of ISO 9001 certification specifically for medical equipment.

ISO standards for Quality Assurance are currently accepted by ninety countries as their national standard. The most comprehensive of the ISO standards is ISO 9001, which applies to industries engaged in the design, development, manufacture, installation and service of products or services.

Ori Lubin, Itamar Medical's Quality Assurance Manager says: "Itamar Medical is committed to delivering the highest levels of quality and customer satisfaction, and has been operating in compliance with the strictest international quality standards since January 1997, when the company was established. At Itamar Medical quality is a priority requiring management and employees at all levels to continuously strive for excellence and improvement."

Study headed by Professor David P. White • ***Johns Hopkins School of Medicine***, Baltimore. Study headed by Professor Alan R. Schwartz • ***University of Louisville School of Medicine***, Louisvi
Professor Marc Pritzker • ***Philipps-University Hospital***, Marburg, Germany. Study headed by Thomas Penzel, Ph.D. • ***Sahlgrenska University Hospital***, Goteborg, Sweden. Study headed by Pro

Marc Pritzker: "What really fascinated me was the potential of PAT™ technology to provide real-time insight into the physiology and treatment of a number of important medical conditions."

Dr. Marc R. Pritzker, Director of the Heart Failure, Transplantation and Investigational Therapeutics Department at the Minneapolis Heart Institute Foundation, directs current PAT studies on endothelial function, tilt table testing, collagen vascular disease digital flow and endothelial function, endothelial function in pulmonary hypertension, and endothelial function in patients with erectile dysfunction. Dr. Pritzker's training includes a Fellowship with training in intervention, electrophysiology and heart failure. Dr. Pritzker shares some of his thoughts on the progress of his work with the PAT Signal and Itamar Medical.

"I first had the opportunity to investigate PAT technology four years ago. At that time, I was impressed by the results that we obtained in using the device to enhance the accuracy of exercise stress testing for the diagnosis of myocardial ischemia."

> *"Our preliminary experience suggests that the technology provides a useful, historically consistent and physiologically relevant response."*

"However, what really fascinated me was the potential of PAT technology to provide real-time insight into the physiology and treatment of a number of important medical conditions. We began an exciting series of tests looking at its potential utility in a number of situations including: tilt testing for syncope, the response of heart failure patients to various drugs, and endothelial function."

"At the time we first used the device for endothelial function, the notion that endothelial function could be tested in patients to assess risk of coronary disease was just emerging. It seemed that the PAT Signal could be used for this type of testing in a simple way, which would avoid the high costs and technical expertise required for brachial artery ultrasound studies. Our preliminary experience suggests that the technology provides a useful, historically consistent and physiologically relevant response. The implication to us was that with an easy-to-use, portable device one could evaluate patient risk, not only at large research centers, but also in 'real world' clinical settings. Early diagnosis of vascular dysfunction no longer need be confined to research centers or large medical centers equipped with the ability to detect coronary calcification."

"One very dramatic use of the device was in a female patient with severe scleroderma-associated Raynauds and digit ulcerations. A number of medications had been tried empirically with little effect. We decided to use PAT technology to assess her digital blood flow in response to prostacyclin (IV) and high dose oral persantine. In the baseline state we could detect no pulsatile digital blood flow. With the fingertip device on, we began the infusion of prostacyclin and could see an immediate restoration of pulsatile digital blood flow, even before the patient reported 'tingling and increased warmth.' We then showed that high dose oral persantine had the same effect, paving the way for a successful therapy which spared the patient amputation of several digits."

"Our work here at the Minneapolis Heart Institute is leading us in many directions, like this one where a useful therapeutic solution was found, and to other potential applications for screening and diagnosis in cardiac care." ■

Koby Sheffy: "I have always been interested in the questions we uncover in research—and by the new areas these questions lead us to."

Dr. Jacob (Koby) Sheffy, Vice President and Principal Scientist, joined Itamar Medical in 1997, along with the founders and colleagues from the Technion-Israel Institute of Technology. A native Israeli, Koby has a B.Sc. in Electrical Engineering from the Technion, and a Ph.D. in Biomedical Engineering from Oxford. Koby currently lives in Tel Aviv, with his wife and son. He and his family will soon be moving to the Haifa area, where he will continue to pursue his avid interest in film, music… and creating innovative ideas in his favorite laboratory—the kitchen.

Like so many others at Itamar Medical, you have a multidisciplinary background in science. How does an electrical engineer end up in physiology research?

"I have always been interested in the questions we uncover in research—and by the new areas these questions lead us to. After I received my undergraduate engineering degree, I worked for RAFAEL - The Israel Armaments Development Authority, as a development engineer. I also began graduate work in biomedical engineering and medicine at the Technion. Then I was granted a research fellowship at Oxford in biomedical engineering and medicine to do research on the control of the respiratory muscles during anesthesia. I was offered a research grant and invited to continue towards a Ph.D. That led to seven fascinating years at Oxford."

What was your research focused on?

"My thesis was on 'Recording of Diaphragm Activity During Anesthesia.' Our goal was to detect and measure physiological signals from the diaphragm. The diaphragm is the most important respiratory muscle accounting for more than 90% of the respiratory work, and without which life cannot be sustained. We recorded the spontaneous activity of the diaphragm in anaesthetized patients and stimulated the diaphragm under various conditions to better understand its innervation and control. We had to solve the problem of stimulating it under various clinical conditions and developed probes that were able to record a variety of physiological signals from the diaphragm via the esophagus. We also developed a novel technique using a variable high magnetic field that could induce sufficient current, in the main nerves that innervate the diaphragm."

> *"The nature of the research creates a synergy all its own, and has created an unprecedented level of multidisciplinary collaboration."*

So a background in electrical engineering came in handy?

"Yes, the project was so multi-dimensional that it didn't fit into one, or even two, scientific disciplines. My Ph.D. was granted by the School of Engineering and the Departments of Anesthesia and Clinical Neurophysiology."

How did you arrive at Itamar Medical?

"When I returned to Israel, I was invited to join Professor Lavie as the R&D Director of the Technion Sleep Medicine Center, in Wolfson Hospital. Our sleep lab collaborated fully with many departments in the hospital. This is where I met and worked with Dr. Bob Schnall on several projects, including non-invasive blood pressure monitoring during sleep. This eventually developed into the first prototype device that could measure the PAT™ Signal."

What does your job at Itamar Medical entail?

"My responsibilities include leading the R&D group, and the ongoing clinical research that is defining new applications and technologies. It is a wonderful combination of physiologists, MDs and specialists in signal processing. This also includes supervising the clinical trial sites and research around the world. We are doing research with the best, and that makes it very exciting. The nature of this multidisciplinary collaboration creates a synergy all its own. My only wish is that we could adopt this kind of interdisciplinary cooperation to other aspects of our lives… especially in our troubled part of the world." ■

Itamar Medical Exhibits at ESRS in Istanbul

At the ESRS 15th Congress in September, held in Istanbul, Turkey, Itamar Medical displayed its Sleep_PAT™ technology for sleep related breathing disorders.

Over 1,000 participants attended the 15th Congress of the European Sleep Research Society (ESRS) held in Istanbul, Turkey. Itamar Medical was there to exhibit PAT™ technology and sleep related applications and attracted a great deal of attention and interest among congress participants.
At our booth, visitors heard how Sleep_PAT™ technology identifies apneic episodes and sleep disorders by non-invasively monitoring Peripheral Arterial Tone (PAT), the window to the autonomic nervous system discovered by Itamar Medical. Visitors viewed demonstrations about how Sleep_PAT will open new channels to support the screening, diagnosis and follow-up of patients suffering from sleep related breathing disorders.

Itamar Medical's booth at ESRS, Istanbul,Turkey

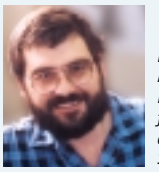
Upcoming Events

Look for Itamar Medical at...

APSS - Annual meeting of Associated Professional Sleep Societies
June 7 – 9
Chicago, Illinois, USA

AHA – American Heart Association
November 11 – 14
Anaheim, CA, USA

PAT FAQs



Dr. Bob Schnall, Itamar Medical's Chief Physiologist, answers frequently asked questions about the PAT™ Signal and Technology

How is it that the PAT Signal is able to recognize both sleep apnea during sleep studies and myocardial ischemia during exercise studies?

Admittedly, it appears rather strange that the PAT Signal can do both jobs when the two conditions appear so different. In reality, it is not that surprising at all.

The PAT Signal is designed to provide an index of sympathetic nervous system activation, and it does this from the vascular beds of the fingertips, which are ideally suited for that purpose. Sympathetic activation is the human body's way of rapidly adapting to potentially threatening situations—in a reaction that has been aptly described as the "fight or flight response."

Basically this response prepares us to cope with life threatening situations by making sure that the brain, heart and necessary large muscles are very well supplied with blood and equipped with what it takes to get out of life-threatening situations—whether it is a rapid getaway or thwarting off an attack. Physiologically, this means increasing heart rate and blood pressure, breathing deeper, increasing blood sugar level, and diverting blood supply away from parts of the body that do not immediately need it, like the fingertips.

It is fairly easy to understand why a sudden awakening in the middle of sleep would trigger this sort of response. During exercise, things are a bit more complex, but basically, if the heart muscle is being taxed to the point where parts of it become depleted of sufficient oxygen the same type of sympathetic response is brought into play.

Exercise is a particularly interesting case because the body generates and needs to offload a considerable amount of heat in order to avoid increasing core body temperature. The surface of the fingers and hands, as well as the toes and soles of the feet, are prime sites for this heat offloading process, and usually exercise causes considerable increases in the blood supply to those regions. Therefore a healthy response to exercise shows a progressive increase in the PAT Signal. If however the PAT Signal begins to fall during exercise, this could be a possible sign of trouble.

Progress Report

Clinical Trials—Focus on the Mayo Clinic

Itamar Medical is conducting clinical trials at some of the most prestigious research and medical centers in the world. In this issue, we focus on the clinical research being conducted at the Center for Coronary Physiology and Imaging of Cardiovascular Diseases and Internal Medicine Division at the Mayo Clinic, Rochester, Minnesota. There, Dr. Amir Lerman is investigating the association between reactive hyperemia using the PAT™ device and the assessment of coronary endothelial function by coronary catheterization and administration of acetylcholine and adenosine, which serves as a gold standard for detecting endothelial dysfunction. The results of this study may support a role for the PAT device as a non-invasive test to identify patients with early atherosclerosis and endothelial dysfunction. The clinical testing at the Mayo Clinic commenced in October 1999.

Dr. Christian Guilleminault • ***Technion Faculty of Medicine***, Haifa, Israel. Study headed by Professor Peretz Lavie • ***TUFTS - New England Medical Center***, Boston. Study headed by Professor James Udelson and Dr. Jeffrey Kuvin • ***Yale University School of Medicine***, New Haven. Study headed by Professor Barry Zaret.