Volume 5 Number 5 October-November 2010

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### **Respiratory Therapy**

The Journal of Pulmonary Technique

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# Editorial

### The Consummate Professional

We have heard over and over again how these stressful economic times are having devastating effects. As a healthcare professional, I have always had some sense of job security, knowing that people are always going to get sick and need medical services. I have never really had the sense that my profession would suffer layoffs due to our poor economic times.

Lately, my opinion has been changed. I see and hear from many of my peers that tough times are starting to effect respiratory departments around the country. It seems that almost weekly I hear of some healthcare facility laying off 20, 30 or even 40 RTs at a time. Directors and managers of departments are having to go before executive leadership and prove their existence and worth to warrant their FTEs. It is very disturbing to hear that the very profession I believe in is being threatened.

My fellow RTs, this is a call to arms. This is a wake-up call. We need to make sure that everything we do is valued and well acknowledged among our multidisciplinary team members. It is not a time to lay low and hope this doesn't happen to our departments, it is already here. We *all* need to be the consummate professional. We need to ensure that we are not a side-thought at some executive meeting. We need to make sure that our departments are involved in every aspect of cardiopulmonary care. We also need to use caution in the language we use. Many times I've heard an RT state that, "I need to go do my vent checks." Vent checks, are you serious? Seems to me like we are only going into the room to look at the ventilator. What about that patient lying there in the bed? I think a more appropriate statement would be, "I need to go and do my patient/ventilator assessment." Which one sounds more professional?

We need to bring our profession to a state of perfection. RT departments need to consider expanding the departments' roles. If your state licensure allows RTs to give medications in the bronchoscopy lab, like morphine and Versed... do it. If someone else in the organization is responsible for ECGs, ask about getting those turned over to the respiratory department. Get involved or start rounding in the ICUs. Let's not forget, *we are the cardiopulmonary experts*. I have heard through the years of many organizations doing away with respiratory departments only to bring them back a few years later. Let's not let it get to that point. Become members of our state and national societies. They are there for us, working hard at the state and national levels. I challenge each and every one out there to let it be known that we are an invaluable asset and an integral part of the multi-disciplinary team. We are a voice to be reckoned with and we will not sit idly by and let our profession and, ultimately, our patients suffer.

Cory Daniels BS, RRT-NPS

The author is Advanced Practice Specialist, Respiratory Care Services, Lakeland Regional Medical Center, Lakeland, FL.



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e, John Height: 72100 inches DUB: 127 2222009 Weight: 300.00 Lbs Gender: M Brown BMI: 40.68 Technician: RP Neck Size: 19CM

Total Acquisition Time: 30.5 mil <u>SPIRATORY SUMMARY</u> Agnea Events: 73 O. Apnea Index: Aymea Events: 12 C. Apnea Index: A Wimber of Apnea Events: 85 Total Apnea Index:

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- Hematocrit
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\*"If the variability of the results can be diminished and the measurement accuracy can be improved, the range of normal values for populations can be narrowed and abnormalities more easily detected" (from "ATS/ERS Task Force: Standardization of Spirometry", 2005).

# News

October-November 2010

### WRONG LUNG

The family of a 28-year-old British woman who unknowingly received a lung transplant from a smoker says she would have been "horrified" and has lodged a complaint. Cystic fibrosis sufferer Lyndsey Scott received a double lung transplant from a donor who had smoked for three decades. She died recently of pneumonia. Britain's top transplant official Chris Rudge defended the decision and said patients should be told they are not getting a "brand new" organ. He said on the BBC that "lungs from a smoker can be working perfectly normally." Scott's family called for patients to be told more information about organ donors before accepting a transplant. Reported by the Huffington Post.

### LUNG ON A CHIP

Researchers at Harvard University have successfully created a functioning, respirating human "lung" on a chip in a lab. Made using human and blood vessel cells and a microchip, the translucent lung is, obviously, far simpler in terms of observation than traditional, actual human lungs, in a small convenient package about the size of a pencil eraser. The researchers have demonstrated its effectiveness and are now moving toward showing its ability to replicate gas exchange between lung cells and the bloodstream. Down the road, the researchers hope to produce other organs on chips and hook them all up to the already operational heart on a chip. You can see a video description of the device on YouTube, by going to the site and typing: Lung on a Chip. Reported by engadget.com.

### **BMC UPDATE**

BioMed Central journals now have Impact Factors. Eighteen of these titles received their first official Impact Factor this year including Molecular Neurodegeneration and Biotechnology for Biofuels, while many other titles improved their rankings... The winners of BioMed Central's 4th Annual Research Awards were announced in London last week. The event was attended by shortlisted authors, eminent researchers, publishers, open access advocates and science journalists from around the world... What is life? In a Q&A in BMC Biology, Steven Benner explains, in the light of recent developments in Craig Venter's laboratory, his point of view on the definition of life, and on the dangers of both natural and synthetic forms. In other news, BioMed Central announced that nominations are open for its annual research awards. BioMed Central's awards recognize the most ground-breaking research published in any of its 200+ journals during 2010. For more information or to nominate an article for the Biology and Medicine Prizes or the Open Data Award, please visit the BMC website.

### SCIENCE FOR SECURITY

The Alliance for a Stronger FDA praised HHS Secretary Kathleen Sebelius for her forthright advocacy for regulatory science at FDA. At a press conference, the Secretary highlighted



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regulatory science as part of a long-anticipated report reviewing the development and approval of Medical Countermeasures (MCM) that would protect Americans from a bioterrorism incident or a naturally occurring emerging infectious disease. The HHS press release states: "The review identified a need to upgrade science and regulatory capacity at the FDA. As a result, HHS will make a significant investment to provide FDA scientists with the resources to develop faster ways to analyze promising new discoveries and give innovators a clear regulatory pathway to bring their products to market." The Alliance for a Stronger FDA is a coalition of more than 180 consumer, patient, professional and research groups, companies, trade associations, and individuals who support increased appropriated funding for FDA. The Alliance is the only multi-stakeholder group that advocates for increasing resources at FDA to match the agency's responsibilities.

#### ASTRO-NOMICAL

Braincells named "astrocytes" for their shapes are involved with regulation of breathing, according to researchers at the University College London Department of Neuroscience. Scientists had previously belived that the cells merely acted as a glue between neurons. Researchers hope the discovery of the cells may lead to understanding respiratory failure. The astrocytes, said researchers, are able to sense levels of carbon dioxide in the blood and then activate neuronal respiratory networks by releasing ATP, that increases breathing and leads to exhalation of the carbon dioxide from the blood. The researchers noted that glial dysfunctions (the nerve family involved) may contribute to breathing disorders, SIDS, and Ondine's curse.

#### LAST BREATH

Breathing bad air can lead to suicide, according to researchers in South Korea, who found that an increase in airborne particles correlated with a 9% increase in suicide, with a 19% increase for breathers who also had cardiovascular disease. The researchers correlated particulate matter increases with the 4,341 suicides recorded in 2004. Adolescents with asthma were twice as likely to commit suicide as teenagers without; the more severe the asthma, the higher the suicide rate. For more see AJP in Advance, the online edition of The American Journal of Psychiatry.

#### **MORE SMOKE**

Smokers exposed to smoke from wood used for heating, cooking or campfires and such are more likely to get COPD, according to researchers at the Lovelace Respiratory Research Institute. Not only that, but such smokers also had epigenetic changes in their DNA which further exacerbated their risk of getting COPD. The researchers said smokers exposed to wood smoke have a fourfold risk for COPD. The researchers sent questionnaires to 1,800 current and former smokers between 40 and 75 years old, and obtained demographic and smoke exposure information, as well as sputum samples which were analyzed for epigenetic changes. Most affected were white men. The researchers advised that smokers should try not to heat their homes with wood or cook on wood smoke, and should stay out of smoky neighborhoods.

### **SLEEP EASY**

There are no differences in patient outcomes when anesthesia services are provided by Certified Registered Nurse Anesthetists (CRNAs), physician anesthesiologists, or CRNAs supervised by physicians, according to the results of a new national study conducted by RTI International. The study, titled "No Harm Found When Nurse Anesthetists Work Without Supervision by Physicians," appears in the August issue of Health Affairs. The RTI study examined nearly 500,000 individual cases and confirms what previous studies have shown: CRNAs provide safe, high-quality care. The study also shows the quality of care administered is equal regardless of supervision. For more contact aana.com.

#### **HEALTHY NO MORE**

More than half of swine flu deaths and hospital admissions occurred in people with no apparent health problems, according to researchers at the University of Liverpool. and Nottingham. Their study also found that hospital admissions were highest in children under five and pregnant women. Researchers analyzed data from 55 hospitals during the first wave of the swine flu pandemic, collecting info on 631 people with swine flu, with ages ranged from three months to 90 years. Thirty-six percent were under 16 and 5% were 65 or older. Blacks and other minorities comprised 60% of admissions. Pregnant women were three times as likely to require hospital admission as women who weren't. Typically, two days elapsed between the start of symptoms and admission, with the primary symptoms being fever and cough. One in four people didn't have a fever, however, so researchers wondered if it was a good marker of swine flu. Thirteen percent were admitted to intensive care; 5% (1 in 20) died. Risk factors included obesity and inflammation. Half the patients had asthma but half of these weren't using inhalers or taking steroids. Around one in four adults and children did not have a fever on admission, and more than half did not have a high fever, prompting researchers to question the wisdom of using a high fever as a key symptom of swine flu infection.

### AT RISK

Children with elevated levels of exhaled nitric oxide (FeNO) are at increased risk for developing asthma, according to researchers at the University of California (USC). Researchers said FeNO might thus be a useful biomarker for identifying children at risk. Kids with the highest FeNO levels were twice as likely to get asthma as kids with the lowest levels. The researchers said they believed their study was the first to demonstrate the predictive value of FeNO. Further, results were strongest in kids whose parents never had asthma. They found that children with the highest levels of FeNO were more than twice as likely to develop asthma compared to those with the lowest levels. Higher levels of FeNO were linked with development of asthma most often in children whose parents had no history of the disease. Data was drawn from a previous USC study that measured in FeNO in more than 2,200 asthma cases. The USC study drew upon data from the Children's Health Study (CHS), the longest epidemiologic investigation ever conducted on environmental contribution to children's respiratory health.

#### **INTERFERON AND ASTHMA**

Interferon, currently used to treat multiple sclerosis, hepatitis C and some cancers, might also aid asthma patients, according to researchers at UT Southwestern Medical Center. Researchers said that interferon blocks the development of T lymphocytes (Th2 cells), which protect against infections by reducing inflammation. The researchers showed that interferon blocks the development of nascent Th2 cells and inhibits cells that already have become Th2 cells by interfering with a regulatory protein, and added that if one stopped such a cell from making asthma-causing chemicals, it would be the "Holy Grail" of

asthma treatment. The researchers said it might be time to start a clinical trial, and noted that quick progress could be made, since Interferon's toxicity has already been tested.

### **HEART-STOPPING**

Severe obstructive sleep apnea raises the risk of heart failure in older and middle-aged men, according to researchers at Boston University School of Medicine. Such men with severe OSA had a 58% higher risk of heart failure than those without OSA. Men ages 40 to 70 with severe OSA had a 68% risk of developing coronary heart disease. The study was said to be the first to link sleep apnea with increased risk of heart failure. The study also found no link between OSA and heart problems in women, who in any event are half as likely as men to have sleep apnea. In the study, 1,927 men and 2,495 women were 40 or older and free of heart problems when the study began. Twenty-four percent of the men and 11% of the women had at least moderately severe obstructive sleep apnea. Researchers assessed participants' health for almost nine years. The researchers concluded that, given the apnea/heart disease link, it was time to take a look at studies to treat the apnea, likely with CPAP.

### NOTHING TO SNEEZE AT

During the recent H1N1 outbreak, one in four people didn't cover their mouth when they coughed or sneezed, at least in New Zealand, according to researchers at the University of Wellington. This was at a time when healthcare providers were urging taking simple action to stop the possible spread of the virus. The researchers studied a train station, a hospital, and a shopping mall, where public health announcements had been previously made. They observed five and a half coughs and sneezes per hour, nearly 27% of which went uncovered, and 5% covered by a tissue. Mostly, people covered their mouths with their hands, secondly with a handkerchief or tissue, and lastly using an elbow. The researchers concluded that media campaigns hadn't been very successful. (Or perhaps people got the message but just didn't care.) Information for the above copyright Medical News Today.

### TRANSPLANT SURVIVAL

The five year survival rate of lung transplant patients varies significantly among US transplant centers, according to researchers at the Mayo Clinic, but it was hard to say why, due to the complexity of care. The researchers analyzed data for 15,642 adult patients undergoing lung transplantation between 1987 and 2009 in 61 US transplantation centers. Nineteen (31.1%) performed between 1 and 10 lung transplantations; 18, from 11 to 25; 20 centers (32.8%), from 26 to 50 transplantations; and 4 centers did more than 50 transplantations. Median patient survival was 4.9 years. One-month and 1-, 3-, and 5-year survival rates were 93.4%, 79.7%, 63% and 49.5% percent, respectively. Characteristics of donors, recipients, and surgical techniques varied substantially among centers, but even after adjusting for these factors, the variability of survival rates remained, with risk of death ranging from 30% lower to about 70% higher for low vs high-risk centers, and for 5-year survival rates of 30% to 61%. Higher lung transplantation volumes were associated with improved long-term survival and accounted for 15% of among-center variability; while incenter performance variability was significant. Several lowvolume centers had good outcomes. The research suggests that there's a great deal of variation in survival rates from center to center, but no one can say why some perform better than others, unless, supposedly, more research is conducted.

### COCHRANE CONTROVERSY

A costly treatment for alpha-1 antitrypsin deficiency has no proven clinical benefit, according to a review by Cochrane Researchers, who reviewed data from two trials involving 140 people at a high genetic risk of developing chronic lung disease. According to Cochrane, patients were given intravenous alpha-1 antitrypsin or a placebo every four weeks for three years and in another trial, the protein or a placebo was given weekly for a minimum of two years. Cochrane reported no difference between treatment and control groups in terms of exacerbations of lung disease or quality of life. Combining the results from the trials, the review authors found no evidence of a clinically important effect on lung function; indeed the results suggested modest harm, or at best no effect. The researchers said the treatment, which costs \$150,000 a year, could not be recommended. "The drug has not shown any clinical benefit, is extremely costly and has important adverse effects," said lead researcher Peter Gøtzsche of the Nordic Cochrane Center at Rigshospitalet in Copenhagen, Denmark. "In view of the lack of evidence and high cost of treatment, treating alpha-1 antitrypsin deficiency by replacement therapy cannot be recommended." However, the Alpha-1 Foundation responded that the Cochrane Library was wrong, saying, "The report is so flawed in its methodology that it may threaten the reputation of the Cochrane Library. The report does a disservice to rare disease patients everywhere. We hope that therapies for other rare conditions won't become victims of the same poorly designed analysis." According to a pro-Alpha-1 researcher, Cochrane's conclusion "was based on retrospective analysis of published data from only two small pilot placebocontrolled studies that were not powered to evaluate the effectiveness of augmentation therapy. This flies in the face of carefully crafted guidelines from the American Thoracic Society, the European Respiratory Society, the American College of Chest Physicians, and the American Association for Respiratory Careall prestigious organizations that recommend augmentation therapy for the treatment of patients with lung disease due to Alpha-1. The guidelines are based on the totality of the evidence, scientific understanding of the disease, correcting the biochemical defect, and a wealth of observational studies." The pro-Alpha people went on to say, "[Cochrane's] article also discards an important endpoint of both studies, the evaluation of loss of lung tissue as judged by CT scans, as being of no clinical interest. In fact, CT scans are the most direct method for evaluating the extent and progression of emphysema-the primary lung disease suffered by those with Alpha-1-and now accepted as the best predictor of mortality in this disease." They also argued that larger studies had shown better results.

### FAULTY FILTERS

Breathing filters used in intensive care anesthesia units don't provide protection from bacteria if they get wet, according to researchers in Edinburgh, UK. The researchers noted that testing for effectiveness is only done on dry filters, and doesn't account for what happens when filters become wet from airway secretions or water. For their test, the researchers looked at three hydrophobic pleated filters designed for use as heat and moisture exchanging filters, a hydrophilic unpleated heat and moisture exchanging filter, and two simple filters. The filters were tested using candida albicans and coagulase staphylococcus. Researchers found that all the filters tested permitted substantial passage of bacteria and yeast, and that even in a one microlitre loop of filtered solution, the number of colony-forming units transmitted through the filters was too large to quantify. The researchers noted that in most cases the bacterial cultures from filters could not be distinguished from the samples created using unfiltered bacteria. and that viable organisms pass across all types of breathing systems filters tested under conditions that may occur in clinical practice. However, they also pointed out that this doesn't necessarily result in patient infection, in that "a microbe would have to make a long journey to infect a new patient by this route."

### DON'T PLAY ON THE FREEWAY

Exposure to pollution near Los Angeles freeways, even if brief, is strong enough to exacerbate asthma by boosting allergic inflammation, according to a UCLA study. According to the researchers, even the smallest air pollutants particles, less than 180 nanometers, or about one-thousandth the width of a human hair, incite lung inflammation, and that such pollutants come from car and truck emissions which are strongest by LA's freeways. The researchers explained that pollution particles emitted by vehicles and other combustion sources are coated with a layer of organic chemicals that can be released into the lungs. These chemicals generate free oxygen radicals, which excite the immune system in the lung through cell- and tissuedamaging oxidation, which contributes to allergic inflammation in the lungs of people with asthma. UCLA researchers said theirs is the first study to show that breathing of ultrafine pollutant particles triggers the same reaction as breathing larger particles and may be more damaging, due to the particles' tiny size, insofar as such particles can carry chemicals deep into the lungs. Researchers found that exposure to air containing ultrafine particles for a few hours a day over five days significantly enhanced allergic airway inflammation, which correlated to the changes found in the immune system and expressed genes, and that the most profound allergic inflammation was seen deep in the lung. Exposure was noted to be greater near the freeway than on the freeway, inside drivers' cars.

### PRODUCTS

### PROMOTED

Ed Coombs, MA RRT-NPS has been promoted to Regional Director of Marketing for North America for Draeger. He is a 1986 graduate of SUNY Upstate Medical Center in Syracuse New York where he earned his respiratory care credentials. He served as a respiratory therapist, shift supervisor, and clinical instructor for Stony Brook University Hospital and other Long Island community hospitals for



approximately 18 years prior to becoming involved in the medical device industry. Contact draeger.com.

### PRIZED

At the recent Congress of the European Society of Anaesthesiology (ESA), Euroanaesthesia, in Milan, the ESA presented for the third time the "Dräger Award for Intensive Care Medicine." The 10,000 Euro prize was donated by Dräger. The award went to the working group studying "Effects of ventilation with 100% oxygen during early hyperdynamic porcine fecal peritonitis" in the Department of Anesthesiology, University Hospital Ulm, Germany. The award was presented to Professor Dr Peter Radermacher, representing this working

group. This annual prize honors significant European research in the field of intensive care medicine. The prize is given to the anesthetic or intensive care department that produces the article rather than any one research worker. This year, the Dräger Prize subcommittee of the ESA who judged the prize recognized this working group for their investigation of the effects of pure O<sub>2</sub> ventilation on organ function and tissue injury during septic shock. With this prize, Dräger wishes to honor scientific endeavors and support advances in the field of critical care medicine. Prof Radermacher's working group investigated the effects of pure O<sub>2</sub> breathing as a putative adjunct to early goal directed therapy of septic shock. This had not been done before, since ventilation with 100% O<sub>2</sub> during sepsis is referred to as being potentially harmful as a result of enhanced oxidative stress. In a clinically relevant long-term porcine model of well-resuscitated septic shock resulting from fecal peritonitis, ventilation with 100% O<sub>2</sub> improved organ function and attenuated tissue injury without affecting lung function and oxidative or nitrosative stress. Contact draeger.com.

### SCRUBS

Scrubs Magazine is a magazine and website edited for nurses, with a wide range of nursing features and nurse lifestyle, career and health articles. A sample: How to Fix Your Scrubs in a Crisis, Passing the NCLEX Exam, 5 Movies Featuring Nurses, The Soldier Nurse, Nursing Unions, and Too Tattooed to Be a Nurse? For more information visit scrubsmag.com.

### FDA CLEARANCE

Instrumentation Laboratory (IL) announced that it has received clearance from the FDA to market the first-ever, rapid point-ofcare, lab-quality blood test for measuring total bilirubin (tBili) in newborns. The new tBili assay is performed on IL's GEM Premier 4000 critical care analyzer. It allows clinicians to receive lab-quality test results in 90 seconds from whole blood in the Neonatal Intensive Care Unit (NICU), rather than waiting up to an hour for results from the lab, using traditional chemistry methods. tBili assays performed on the GEM Premier 4000 are not affected by moderate turbidity or hemolysis, ensuring accuracy. Additionally, from a single whole blood sample, a full range of analytes can be measured, including Blood Gas, Electrolytes, Glucose, Lactate and full CO-Oximetry, for an efficient and comprehensive assessment of patient status. IL announced the FDA clearance of the tBili assay at the Annual Meeting of the American Association for Clinical Chemistry in Anaheim, CA. At the meeting, IL also introduced GEMweb Plus Custom Connectivity, software for automated information management. GEMweb Plus is the only software to provide system-wide, bi-directional capabilities from any networked PC or GEM Premier 4000 analyzer. GEMweb Plus provides complete control of all networked analyzers, regardless of location, to enhance quality assurance and regulatory compliance. GEM Premier 4000 critical care analyzer provides blood gas, electrolyte and metabolite analysis with integrated CO-Oximetry testing. It features IL's patented Intelligent Quality Management (iQM), a real-time, automated, quality assurance system that continuously detects, corrects and documents, to assure quality results and compliance, 24/7, regardless of operator or testing location. iQM, coupled with its cartridgebased technology and ease of use, allows the GEM Premier 4000 analyzer to provide consistent, accurate, lab-quality results throughout the hospital. Products mentioned above are trademarks of Instrumentation Laboratory Company and/or one of its subsidiaries or parent companies. Contact ilus.com.

### LUNG PLAYING

Medical Acoustics, Buffalo, NY, introduces the Lung Flute, the only FDA and CE cleared respiratory device that is dualindicated for diagnostic and therapeutic use. The Lung Flute uses patented low-frequency acoustic wave technology to optimize secretion clearance deep in the lungs, a method that is clinically proven to achieve better results than standard vibration and OPEP therapy. Sputum induction with the Lung Flute is also superior to hypertonic saline, according to clinical studies. The Lung Flute is a safe, noninvasive device to induce sputum for diagnostic and pathologic examination, including measuring for genotyping and inflammatory, bio, and DNA markers. It is expected to play a significant role in the treatment, diagnosis of, and drug development for COPD, lung cancer, tuberculosis, chronic bronchitis, asthma and communityacquired pneumonia, and is FDA and CE cleared for both diagnostic and therapeutic use. The Lung Flute was selected by Frost and Sullivan for a Best in Technology Award, Popular Science named the device a Best Innovations of 2009 and MD&DI Magazine recognized Medical Acoustics as one of the Top 50 Companies to Watch. Contact (716) 218-7355, lungflute.com.

### **OPEN ACCESS**

The Open Respiratory Medicine Journal is an Open Access online journal, which publishes research articles, reviews and letters in all areas of experimental and clinical research in respiratory medicine. The Open Respiratory Medicine Journal, a peer reviewed journal, aims to provide the most complete and reliable source of information on current developments in the field. The emphasis will be on publishing quality papers rapidly and freely available to researchers worldwide. Contact bentham.org/open.

### FDA APPROVAL

Epocal, Inc, a leading edge provider of point of care technology, announced today that it has received FDA clearance to market its new lactate test on the epoc Blood Analysis System. Lactate measurements from the epoc System are used to evaluate acid-base status and for diagnosis and treatment of lactic acidosis. The addition of lactate to the epoc BGEM Test Card, which includes in vitro diagnostic tests for pH, pO<sub>2</sub>, pCO<sub>2</sub>, Na, K, iCa, Hct and Glu (plus calculated values), further expands the clinical utility of the company's point of care blood gas and electrolyte platform. Lactate on the BGEM Test Card represents the second metabolite cleared for use on the epoc System in the past 12 months. It is also the ninth measured analyte on the single-use test card, surpassing most competitive point of care systems which may require multiple test devices in order to match the same menu. Epocal, Inc develops, manufactures and markets the epoc Blood Analysis System. epoc (enterprise point of care) is healthcare's first cost effective point of care testing solution to leverage SmartCard technology and the power of wireless communication to provide critical caregivers with real-time, laboratory quality test results at the patient's bedside. Contact epocal.com.

### PACIFIED

The Babi.Plus Pacifier Adaptor from B&B Medical Technologies is a convenient new way to provide aerosolized medication therapy for babies and children who present with breathing difficulties and are reluctant to relinquish their familiar pacifiers or to wear a mask. The Pacifier Adaptor attaches directly onto the child's pacifier and delivers medication via a small port directed at the nose, which minimizes aerosol or gas directed toward eyes. The Pacifier Adaptor's "U" shaped connector is applied to the pacifier with adhesive tabs for a secure connection. It fits and adheres to a wide variety of pacifiers and holds fast, but can easily be removed after treatment, even while the child still is sucking on the pacifier, helping to maintain comfort for the child. The Pacifier Adaptor can be reapplied to the pacifier for subsequent treatments. The Pacifier Adaptor is latex- and phthalate-free. The Pacifier Adaptor comes packaged with a 15 cm (6") length of 10 mm tubing and a nebulizer adaptor for connection to any small volume nebulizer. Contact bandb-medical.com.

### PERFORMANCE

Hamilton Medical announced that it is a winner of the Supplier Performance Award, presented by the Premier healthcare alliance. Premier contracts with more than 800 suppliers and Hamilton Medical is one of 65 contracted suppliers to receive the Performance Award. Winners are recognized for their outstanding management of Premier agreements and drive toward the mutual goal of providing clinical and financial value to the not-for-profit hospital members of the Premier alliance. Annette Dusek, National Accounts Manager, accepted the award at the Premier Annual Breakthroughs Conference and Exhibition in Washington. Premier is a performance improvement alliance of more than 2,300 US hospitals and 67,000-plus other healthcare sites. Owned by not-for-profit hospitals, Premier maintains a comprehensive repository of clinical, financial and outcomes information and operates a leading healthcare purchasing network. Contact hamilton-medical.com.

#### **INFORMATION PLEASE**

Informa Healthcare launched a new website that combines its full journal archive with recently published book content onto the informahealthcare.com web platform. The new service delivers approximately 170 journals and 600 online books. Content includes cardiology, dermatology, neurology, pharmaceutical science, respiratory medicine, toxicology, and urology. Users can save searches, highlight articles and chapters, and link to audio and video resources. Contact informahealthcare.com.

### LINKUP

MDLinx has a new website. Its researchers review over 1,000 new articles, sort them, rank them, and send over a million briefings, saving physicians countless hours of time while keeping users up-to-date on medical literature. MDLinx uses degreed physicians to read, sort, and rank all the articles. They cover all peer reviewed journals without bias and are not influenced by advertisers who are clearly labeled as sponsors on its website and newsletters. Contact mdlinx.com.

### SLEEP TESTING

Nihon Kohden America announced the release of the latest in home sleep testing technology. The Nomad is a Type III wearable portable recording device. With the ability to record 2 effort, 2 flow, snoring, body position,  $SpO_2$ , heart rate and leg movements in a lightweight durable casing, this Type III recording solution will meet your needs in the changing sleep diagnostic marketplace. The Nomad comes with the advantages and power of the Polysmith suite polysomnographic software solutions which include Polysmith, Surveysmith and the optional Polysmith DMS database. Nihon Kohden is Japan's leading manufacturer, developer and distributor of medical electronic equipment with subsidiaries in North America, Europe and Asia and distribution in over 100 countries. Contact nkusa.com.

### ACQUISITION

Olympus Corporation acquired all shares of Spiration, and Spiration will become a consolidated subsidiary of Olympus. Olympus Medical's business focuses on products for endoscopic observation, diagnosis and treatment. It is expanding efforts to address respiratory conditions not related to lung cancer. Spiration develops minimally invasive devices for the treatment of acute and chronic conditions of the lungs. Its IBV Valve System is a device for the bronchoscopic treatment of emphysema and air leaks of the lung. Olympus Medical intends Spiration's full participation in the Olympus Group as a consolidated subsidiary to help accelerate its business related to the IBV Valve System. Contact olympusamerica.com.

### A LIGHT TOUCH

Royal Philips Electronics showcased its new LiteTouch aerosol delivery mask at the annual Association of Asthma Educators (AAE) Conference. LiteTouch incorporates a newly designed soft-seal feature that contours to the patient's face with a minimal amount of applied pressure. LiteTouch is designed to provide greater comfort and easier delivery of aerosol medication. The mask uses a unique composite that fuses a clear, hard shell to an exclusive soft-seal interface. It fits onto the mouthpiece of a Philips Respironics valved holding chamber (VHC) and functions by simply touching the mask seal lightly to the patient's face. LiteTouch contours to the face with a minimum amount of pressure. LiteTouch is being sold to hospitals through CareFusion Corporation and will also be available to asthma clinics. CareFusion currently carries the Respironics OptiChamber VHC devices which may be used with the LiteTouch mask. Contact philips.com.

#### GO ASK ALICE

Philips' Alice PDx portable diagnostic system received a gold award for design excellence during the Medical Device & Manufacturing (MD&M) East Conference and Exposition, in New York. The Alice PDx is easy for patients to set up and use in the comfort and privacy of their home. A logical graphical screen assists the user in the application of the device. A separate step-by-step diagram also is included as reference. Color-coded labels located around the perimeter of the device indicate which sensors to connect and where to connect the sensor leads. The system easily accommodates side sleepers and the sensor leads have been specifically designed to minimize excess length to make it easier for patients to manage them. Contact alicepdx.respironics.com.

#### **TECH ADVANCE**

Covidien announced the integration of its Nellcor BIS X4 brain monitoring software into the Mindray BeneView Series of multi-parameter patient monitors. BIS X4 technology monitors both hemispheres of a patient's brain simultaneously and in real time, providing highly sophisticated data to help physicians make optimal decisions for safe patient care. Covidien's BIS technology provides a direct, real-time measure of the effects of anesthetics and sedatives on the brain. The critical improvement offered by BIS X4 technology is that clinicians can compare activity between hemispheres of the brain, identify imbalances and intervene to achieve the best and safest patient outcomes. Studies indicate that BIS-monitored patients wake up faster, are extubated sooner, are better oriented upon arrival to the post anesthesia care unit (PACU) and are eligible for PACU discharge sooner. Additionally, BIS technology may help clinicians measure anesthesia levels more

precisely, which may decrease costs for surgical procedures and ICU care. Incorporating BIS X4 technology in BeneView Series units enables physicians to adapt treatment to meet the specific needs of their patients, while also managing resource consumption effectively. Contact covidien.com.

#### **DIVERSE SOLUTIONS**

Roche featured a diverse portfolio of diagnostics testing solutions for healthcare professionals at the AACC/CSCC 2010 Clinical Lab Expo. Roche's DreamLab display allowed booth visitors to custom-design analyzer systems-right down to module configurations, reagent channels and system throughputs-to help determine the most effective solutions for their own lab. Roche also featured a variety of new technology for laboratory and point-of-care testing, including integrated clinical chemistry and immunoassay analyzer platforms, automation components, information technology solutions, handheld and mobile point-of-care systems, and chemistry, immunoassay and molecular diagnostics tests. New products included the cobas 800 analyzer series, the ACCU-CHEK Inform II System, the CoaguChek XS Pro System, the cobas p 501 post-analytical unit, the Elecsys Anti-HCV Assay, and the LyghtCycler MRSA Advanced Test. Contact roche.com.

#### TAKE A WALK

COSMED announced the launch of the Spiropalm 6MWT, a new medical device incorporating the latest design for portable spirometry and a unique tool for the standardized Six-Minute Walk Test. The Spiropalm 6MWT provides the customer with a complete testing package with the ability to measure minute ventilation and breathing pattern during walking together with a fully integrated pulse oximeter to monitor  $\text{SpO}_2$  and HR during the test. Spiropalm 6MWT allows full assessment of ventilation limitation due to dynamic hyperinflation and air trapping in patients with pulmonary disease. Fully complies with ATS/ ERS guidelines for the 6MWT (2002). Contact: cosmed.com.

#### EXHALE

An independent clinical study has recently been undertaken by the Department of Pathophysiology at the National Koranyi Institute in Hungary to compare the NObreath monitor by Bedfont Scientific with other commercially available Fractional Exhaled Nitric Oxide (FENO) monitors. The results, published in Respiratory Medicine Journal, have concluded that the NObreath provides reproducible results to the two other units and is suitable for use in clinical practice. The study, carried out on 18 healthy volunteers, showed that the FENO values measured with NObreath are reproducible and in good agreement with those obtained by other commercially available FENO monitors. Contact bedfont.com.

#### MASKED, MAN

Philips Respironics introduced its ComfortGel blue nasal mask, designed for better compliance for obstructive sleep apnea patients. Philips Respironics ComfortGel Blue nasal mask is used in the treatment of obstructive sleep apnea (OSA). Based on the company's popular blue gel masks, this product is designed to help enhance patient comfort and compliance. Retaining the comfort and flexibility features found in previous gel masks, ComfortGel Blue incorporates an improved forehead pad designed to help reduce pressure points, a lower profile exhalation port with an integrated swivel that quietly directs air flow up and away from a bed partner, and a new gel cushion that gently conforms to facial features. Used together with Philips Respironics System One Resistance Control, the mask will help deliver optimum PAP therapy and comfort. The mask is available in four sizes, and FitPacks with two sizes of cushions are available. DuoPacks with multiple cushions of the same size also are offered to support supply replacement initiatives for patients. Contact respironics.com.

### AWARD

Siemens announced that its syngo iFlow has been honored with a 2010 R&D 100 Award by the editors of R&D Magazine. syngo iFlow—Dynamic Flow Evaluation won in the Bioscience category. For use in the interventional suite, syngo iFlow allows the creation of a static image displaying dynamic information that shows the user the history of the contrast media through the vessels, in full color, at the click of a button. This dynamic flow evaluation provides a greater understanding of the contrast flow within the pathology, greater ease in visualizing the success of a procedure and assists the clinician in image review by showing a complete Digital Subtraction Angiography (DSA) run in a single image. Contact siemens.com/healthcare.

### ALL TIED UP

The new Pepper Medical Inc Vent-Tie # 401 and Pedi Vent-Tie #401-P are patented ventilator anti-disconnect devices coupled with a trach tube neckband. This unique combination device offers a margin of safety to ventilator dependent patients and clinicians alike. The easy to use Vent-Tie features a quick release Velcro strap that is compatible with all trach tubes, elbow connectors, and closed suction devices. The integral anti-disconnect strap eliminates the use of rubber bands, shoelaces and tape to secure the ventilator circuitry to the trach tube. The Vent-tie neckband is made of a soft, 100% cotton flannel that offers moisture wicking properties to keep skin dry and cool. This disposable, combination product saves time and money by offering an all-in-one device. The Vent-Tie is individually packaged in boxes of 20 each. Free samples are available upon request. Contact peppermedical.com.

### APPS-PLICABLE

Philips has introduced the world's first app for noninvasive ventilation, offered free to all clinicians involved in critical care ventilation. The interactive Philips NIV Guide is a valuable reference tool to build or expand ventilation skills. The guide contains physician tips, contraindications, predictors of failure, and successful mask fitting tips. The NIV protocol and process map covers everything from patient selection through initiation, adaptation, monitoring, and weaning. The app's NIV IQ test tests your NIV knowledge. The app also offers educational white papers and articles on NIV. It is available for the iPhone, iPod touch and iPad. Go to the apple app store to download the guide.

### **NEWS FROM MASIMO**

Masimo recently announced FDA 510(k) clearance for the **Pronto-7**, a new handheld device designed for quick and easy noninvasive hemoglobin (SpHb)spot-check testing, along with SpO<sub>2</sub>, pulse rate, and perfusion index, in virtually any environment. The palm-sized Pronto-7, with dimensions of just  $5.1" \times 2.8" \times 1"$  and weight of 10.5 ounces, represents a breakthrough solution for measuring hemoglobin in less than one minute. It puts the power of noninvasive hemoglobin spot-check testing into any clinician's hands in almost any environment, without the needles, time-consuming laboratory analysis, risk of blood contamination, hazardous medical waste, and patient discomfort associated with traditional blood

tests. Pronto-7 features embedded 802.11 b/g and Bluetooth communication capabilities that make wireless printing and emailing of test results quick and easy and future capabilities enabling wireless transmission to electronic health record (EHR) systems are planned. It is also the first Masimo device to feature Rainbow 4D-designed for fast and accurate spotcheck SpHb measurements, along with SpO<sub>2</sub> and pulse rate, even in low perfusion conditions. The Pronto-7 also made the World Health Organization's List of Innovative Medical Technologies. The list consists of 15 medical devices that represent accessible and affordable healthcare solutions for use in low and middle-income countries. The WHO stated, "The intended purpose of the transcutaneous anaemia monitoring system is to screen populations for insufficient levels of haemoglobin in the blood and to carry out diagnosis of severe anemia." According to Aryeh Shander, MD, President-Elect of the Society for the Advancement of Blood Management (SABM) and the Executive Medical Director for The Institute for Patient Blood Management & Bloodless Medicine and Surgery at Englewood Hospital and Medical Center in Englewood, NJ, "Noninvasive hemoglobin testing at the point-of-care offers a giant leap forward in our ability to tackle the global burden of anemia... The beauty of immediate, noninvasive hemoglobin testing is that it will allow more patients to be assessed, so their physician can determine additional test options and initiate potentially lifesaving treatment." ... Masimo announced that a new independent study demonstrating the clinical accuracy of Masimo noninvasive and continuous hemoglobin (SpHb) monitoring was presented at the European Society of Anaesthesiology (ESA) Annual Congress in Helsinki, Finland. In the study, titled Comparison Between a New Noninvasive Continuous Technology of Spectrophotometry-based and **RBC** Count for Haemoglobin Monitoring During Surgery with Hemorrhagic Risk, Dr Lionel Lamhaut and researchers from the Department of Anesthesiology and Intensive Care at Necker University Hospital in Paris, France, compared the accuracy of Masimo SpHb with hemoglobin measurements obtained invasively via laboratory blood analysis in 20 patients undergoing high blood-loss surgery. SpHb and invasive hemoglobin measurements were simultaneously recorded at the beginning and end of any clinical intervention and before and after blood transfusion. Results showed a strong agreement between the two (0.88), with a bias of 0.26 g/dL and standard deviation of 1.1 g/dL-leading researchers to conclude that this study, conducted under real-world clinical conditions, "confirms the first tests realized by the manufacturer." Affirming the clinical accuracy and utility of Masimo SpHb, researchers further noted that "the correlation is good, suggesting the possibility of a daily use of this technology."\* Masimo SpHb is available as part of Masimo Rainbow platform that noninvasively and continuously measure total hemoglobin (SpHb), oxygen content (SpOC), carboxyhemoglobin (SpCO), methemoglobin (SpMet), Pleth Variability Index (PVI), and acoustic respiration rate (RRa), in addition to the gold standard Measure-Through Motion and Low Perfusion performance of Masimo SET oxyhemoglobin (SpO<sub>2</sub>), pulse rate (PR), and perfusion index (PI). \* L. Lamhaut, R. Apriotesei, M. Lejay, B. Vivien, P. Carli. "Comparison Between a New Noninvasive Continuous Technology of Spectrophotometry-based and RBC Count for Haemoglobin Monitoring During Surgery with Hemorrhagic Risk" Eur J Anaesthesiol 2010; 27 (Suppl 47): 3AP7-1 Contact masimo.com.

### LANDMARK STUDY

Dartmouth-Hitchcock Medical Center announced the peer-

reviewed publication of an in-depth, 21-month clinical study on the impact of the Masimo Patient SafetyNet remote monitoring and clinician notification system. The study, featured in the February 2010 issue of Anesthesiology, is the first published report to demonstrate that continuous pulse oximetry monitoring and clinician notification in post-surgical patients on the general floor leads to a "significant drop" in key clinical outcome measures, including 65% fewer rescue events, 48% fewer ICU transfers, and reduced annualized ICU time by 135 days.<sup>1</sup> In the study, Dr Andreas Taenzer and a team of clinicians at Dartmouth-Hitchcock Medical Center used Masimo Patient SafetyNet, which combines the gold-standard performance of Masimo SET pulse oximetry at the point of care with remote monitoring and wireless clinician notification via pager-in a 36-bed post-surgical orthopedic unit. When comparing data collected for 11 months before and 10 months after implementing Patient SafetyNet in the 36-bed unit-as well as two other post-operative units with only standard monitoring equipment and protocols in place, researchers found that Patient SafetyNet-monitored patients experienced approximately 65% fewer rescue events (1.2 vs 3.4 per 1,000 patient discharges) and 48% fewer ICU transfers (2.9 vs 5.6 per 1,000 patient days), freeing up 135 ICU days per year, while the two comparison units had no change. "Masimo Patient SafetyNet represents a new approach to detect unrecognized post-operative deterioration-a significant precursor in morbidity and mortality for in-hospital patients," stated Taenzer. "Our study results strongly demonstrate that continuous patient surveillance with Masimo Patient SafetyNet can greatly improve outcomes." In an accompanying editorial about the impact of the study, John P. Abenstein, MSEE, MD, at the Department of Medicine, Mayo Clinic, in Rochester, MN, wrote that the "implications of this study are broad" and its results could "have important implications for hospital wards throughout the country."<sup>2</sup> According to Dr Abenstein, "The literature and each of our own clinical experiences have examples of physicians on rounds, or nurses coming to check patients who have been dead for hours... We believe that Taenzer et al have shown us a glimpse of the future. Not only will such systems allow us to improve the quality of care of our patients, but will also be a key to lowering costs." Joe Kiani, Masimo founder and CEO noted that this is the first such study with adults. [References: 1. Taenzer, Andreas H.; Pyke, Joshua B.; McGrath, Susan P.; Blike, George T. "Impact of Pulse Oximetry Surveillance on Rescue Events and Intensive Care Unit Transfers: A Before-and-After Concurrence Study." Anesthesiology, February 2010, Vol. 112, Issue 2; 2. Abenstein, John P.; Narr, Bradly J. "An Ounce of Prevention May Equate to a Pound of Cure: Can Early Detection and Intervention Prevent Adverse Events?" Anesthesiology, February 2010, Vol. 112, Issue 2.] Contact masimo.com.

### FLEET

Dräger has made available to its customers a fleet of Evita XL ventilators that can be rented under a short term or long term agreement. Whether the need is due to an acute increase in patient census or for continuous use, Dräger can now help better serve the needs of its ventilation customers. The rental fleet of Evita XL ventilators will be delivered with the latest software platform to ensure customers have the newest technology. Contact (800) 437-2437, info.usa@draeger.com.

#### INTRODUCTION

Philips Respironics introduced the Trilogy200 portable lifesupport ventilator. Trilogy200 provides both invasive and noninvasive ventilation with added sensitivity for a wide range of adult and pediatric patients (>5kg) in the home and in alternative care settings. Using a new single-limb circuit and proximal flow sensor, Trilogy200 offers improved triggering and leak compensation that allows for more sensitive delivery of therapy. This added sensitivity decreases work of breathing resulting in greater therapy comfort, better ventilation and improved patient/ventilator synchrony. The ventilator weighs 11 pounds and features a six-hour battery system of internal and easy-to-swap detachable batteries. It has three triggering options, Digital Auto-Trak, flow triggering, and proximal flow triggering. Contact philips.com.

### SPOTLIGHT ON BLOOD GAS

### COLLECTIONS

Sarstedt introduces collection products designed for arterial or capillary blood gas determinations. One ml and 2ml plastic blood gas syringes contain a fine dispersion of calcium-balanced heparin, resulting in a large surface area for solubility and quick mixing to ensure accurate results. A ventilation filter cap for the hygienic and contamination-free removal of air from the syringes after blood collection is available pre-assembled on the 2ml syringe or separately. The ventilation filter cap also serves as a closure for transport to analyzers. Sarstedt blood gas capillaries are manufactured from break-resistant plastic with low gas permeability for safe collection and accurate test results. Contact sarstedt.com, (800) 257-5101.

### CALIBRATION

RNA Medical, Devens, MA, has recently introduced CVC 323, Electrolyte Calibration Verification Controls. CVC 323 is an assayed quality control material used for confirming the calibration and linearity of pH and electrolyte instrumentation. It is available in five distinct levels of pH, Na+, K+, Cl+, Li+ and Ca++, covering the significant range of analyzer performance. When used as a supplement to instrument calibration, daily QC procedures, preventative maintenance, and proper record keeping, CVC 323 will contribute to the laboratory's overall quality assurance program. CVC 323 contains no preservatives, no human or biological ingredients and is stored at room temperature. Contact rnamedical.com, (800) 533-6162.

### SMART!

Epocal, Inc develops, manufactures and markets the epoc Blood Analysis System. epoc (enterprise point of care) is healthcare's first cost effective point of care testing solution to leverage SmartCard technology and the power of wireless communication to provide critical caregivers with real-time, laboratory quality blood gas, electrolyte, and metabolite test results at the patient's bedside. In 2010 Epocal has added Glucose and Lactate to its BGEM (Blood Gas, Electrolyte, Metabolite) Test Card. Contact epocal.com.

### TIME-SENSITIVE

OPTI Medical Systems, Inc manufactures the OPTI CCA-TS analyzer for measuring time sensitive diagnostic assays including blood gas, electrolytes, ionized calcium, glucose and measured tHb and SO<sub>2</sub>. It features patented optical fluorescence technology which virtually eliminates maintenance costs, test delays, and downtime. The OPTI CCA-TS is portable and easy to use with excellent reliability—making it ideal for the point of care. The OPTI CCA-TS analyzer will soon measure lactate (pending FDA approval). Contact optimedical.com, (800) 490-6784.

### SPOTLIGHT ON CPAP

### **OPEN AND DISPOSABLE**

Boussignac CPAP System from Vitaid is the original totally open and disposable CPAP device. It requires no capital equipment, just an oxygen source to power the device. With over 30 peer reviewed and published clinical studies in leading medical journals on over 200 patients, the Boussignac CPAP has proven to be a valuable adjunct in treating patients requiring respiratory support. The Boussignac CPAP is a valuable tool in EMS managing CHF with APE and COPD in Respiratory Therapy for weaning ventilator dependent tracheostomy patients and in anesthesia for managing the hypoxic post operative morbidly obese patients in the PACU. Contact vitaid.com.

### SPOTLIGHT ON SPIROMETRY

### **NEW STANDARDS**

ndd Medical Technologies is committed to setting new standards in pulmonary function testing by offering innovative, easy to use products and excellent customer support. The EasyOne Pro is the first lung function instrument to allow Single Breath DLCO measure ment outside of the lung function laboratory. The EasyOne Plus series of spirometers are based on the best technology, packed with features and easy to use, while the Easy One-PC offers real time curves and pediatric incentives. Contact nddmed.com.

### PORTABLE

nSpire Health, Longmont, CO, offers KoKo Legend portable spirometer with full USB compatibility to the industry standard KoKo PFT spirometry software. KoKo Legend's intuitive color touch screen walks both patient and physician through standard testing procedures promoting superior patient test results. Exceeding ATS/ERS 2005 standards, KoKo Legend utilizes a unique flexible orifice pneumotach for extraordinarily precision at the low flow rates. Optional test grading for increased technician compliance. Choose built-in or external office printing for  $81/2 \times 11$  reports. Easily transfer test results into the KoKo PFT Spirometry software and download new patients to be tested. Contact nspirehealth.com, (800) 574-7374.

### **FULL RANGE**

Vitalograph, a world leader in spirometry, offers over 40 years experience designing, manufacturing and marketing spirometry equipment and accessories. Our full range of spirometry products includes the exciting new hand-held Vitalograph In2itive, the latest version of the popular Vitalograph ALPHA desktop spirometer, the Vitalograph Spirotrac 6800 Windows based spirometry system and the 4000 series of screening and patient self-management devices. Vitalograph also produces peak flow meters and a wide range of spirometry consumables to fit most PFT equipment, including SafeTway, the original one-way valve mouthpiece, as well as Bacterial/Viral Filters, nose clips and other disposable accessories. Contact vitalograph.com.

### SPOTLIGHT ON VENTILATION

### **TOP SCORER**

Hamilton Medical, Inc, a leading global provider of ventilator technology, has once again earned the top composite score

for ventilator manufacturers from MDBuyline. Hamilton Medical has earned this top composite rating for the past nine quarters, beginning in July 2008. In the January 1, 2010 MD Buyline Quarterly User Satisfaction Report and the July 1, 2010 MD Buyline Quarterly User Satisfaction Report, Hamilton Medical not only rates the highest in the top composite score, Hamilton also holds the top score in every rating category. Rating categories include system performance and reliability, installation/implementation, applications training, service response time and service repair quality. Contact hamilton-medical.com, (800) 426-6331.

### INTELLIGENT

Hamilton Medical presents world's first fully closed loop ventilation technology. INTELLiVENT-ASV opens the next era of intelligent ventilation. Hamilton launched universal ventilator HAMILTON-S1 with INTELLiVENT-ASV, the world's first fully automatic application for intensive care ventilation. After 16 years of development a well tested product is ready to be used. Optimized ventilation therapy in intensive care requires permanent adjustment of setting parameters to wean and get patient off the device as quick as possible. INTELLiVENT-ASV is the world's first fully closed loop ventilation technology for oxygenation and ventilation covering all applications from intubation until extubation. The automatic adjustments follow protocolized care, measuring lung physiology, respiratory monitoring, capnography ( $etCO_2$ ) and pulse oximetry ( $SpO_2$ ). (Not available in all countries yet according to approval situation.) INTELLIVENT-ASV and ASV are exclusive trademarks of Hamilton Medical, hamilton-medical.com.

### NEXT GENERATION

Dräger continues to meet the challenges of critical care by working with respiratory therapists in the US with the development of the next generation of mechanical ventilation— The Evita Infinity V500. Designed with the clinician in mind, the Evita Infinity V500 is a highly advanced ventilator used for both acute care hospitals and university medical centers. The V500 offers a comprehensive array of invasive and non-invasive ventilation modes for adult, pediatric, and neonatal patients. Pulmonary monitoring features to provide a complete assessment at the bedside is also featured in the user interface. Contact draeger.com, (800) 427-2437.

### PRODUCT FEATURE

# SmartCare/PS knowledge based weaning system

Phillip Thaut, RRT-NPS, RPFT

The respondent is Adult Respiratory Clinical Specialist, Utah Valley Regional Medical Center. This interview was provided by Draeger.

#### What are the challenges associated with weaning longterm patients from mechanical ventilation?

I would say that creating enough time for therapists to spend with each of their long-term patients is one of the major challenges in a busy ICU. The demands placed upon them severely limit their ability to make the frequent adjustments that a marginal patient can require. As a result, I have witnessed several scenarios where a therapist would prematurely discontinue a weaning trial based on a written protocol, for example if the patient became tachypneic.

# What do you see as being the main advantages of a closed-loop knowledge based weaning system?

One of the most important benefits of a closed-loop knowledge based weaning approach is its ability to frequently make the necessary adjustments in ventilatory support without the interruptions, fatigue and the inherent tedium associated with weaning a poorly conditioned, marginal ventilator patient.

## What are the principal advantages of using SmartCare instead of relying solely on clinical practice?

I have spent hours at the bedside monitoring patients who were being maintained on the SmartCare/PS system and have been amazed with some of the results. It is interesting to observe how SmartCare/PS works in a methodical, consistent, efficient—and in some respects—relentless manner while carefully titrating pressure support for patients that are either severely deconditioned or have near end-stage chronic lung disease.

### Relentless is an unusual term, can you elaborate on this?

When I say that SmartCare/PS is "relentless," I am referring to SmartCare/PS's ability to titrate the level of pressure support on a continual basis. SmartCare/PS constantly monitors patients' respiratory frequency, tidal volume, and metabolics (EtCO<sub>2</sub>), testing their capability for small decreases in pressure support while maintaining them in a "zone of comfort." In other words, maintaining their spontaneous workload at the maximum level the patients can tolerate comfortably. Every few minutes, SmartCare/PS's knowledge base evaluates the patient's potential for a small decrease or, if necessary, an increase in pressure support, minimizing the risk for overwhelming fatigue and respiratory failure. As I mentioned earlier, such frequent and minor adjustments in pressure support would be unrealistic if attempted by a bedside practitioner due to the time required and the tedium involved.

### Can you cite a typical example of this "relentless" approach to weaning?

I have personally been involved with several difficult weaning scenarios that have failed our written weaning protocols but were successfully weaned within 48 hours after initiating SmartCare/PS. I have been very impressed with the consistency and effectiveness of the knowledge based approach in helping us wean very difficult patients. However, rather than being replaced by the automation of this closed-loop protocol, the practitioner is provided with more time to supervise and monitor the process. The most significant realization comes from the fact that the weaning process is continuous and does not necessarily rely on the availability or constant presence of the practitioner at the bedside throughout the weaning session.

## How has the use of SmartCare impacted on your quality indicators?

Our Dräger EvitaXL ventilators have been in service since June of 2006. Our observed patient-ventilator interaction and patient comfort have both improved, especially with patients who have previously been described as "difficult to wean" from mechanical ventilation. As a result, SmartCare/PS has become an essential adjunct to our current ventilator management strategy. As our experience with SmartCare/PS operation increases we see the opportunity to advance care continuing to evolve.

### **Case Study**

- 83 year old female
- Probable Myocarditits
- Possible Aspiration
- Severe Esophagitis
- $\bullet$  Severe COPD with chronic  $\mathrm{CO}_2$  retention
- Total Invasive Mechanical Ventilation: 8 days

After initial intubation and stabilization, cardiac catheterization demonstrated relatively clean coronary arteries with an ejection fraction of approx 22%, probably due to acute myocarditis. After stabilization of hemodynamics and improved ejection fraction with inotropic support, weaning mechanics were obtained and spontaneous CPAP pressure support trials were initiated via written protocols. After six days of mechanical ventilation with limited tolerance for spontaneous CPAP–Pressure Support trials the patient was unable to be weaned. Additionally, it was not possible to sustain a Pressure Support levels <18 cmH<sub>2</sub>O without significant tachypnea or weaning trial failure. The overwhelming ventilatory fatigue required an A/C mode for recovery for more than 24 hours. Concerns regarding the risks for ventilator dependency and continued weaning failures prompted placing the patient on the Dräger EvitaXL equipped with SmartCare/PS.

**Settings:** Body Weight: 58 kg; Type of Intubation: Endotracheal; Humidification: Heated humidifier with heated wire circuit; COPD: Yes; Neurologic Disorder: No; Night Rest: Yes; Pressure Support Goal: 10 cmH<sub>2</sub>O.

With SmartCare/PS the patient was able to sustain extended spontaneous CPAP-Pressure Support trials with Pressure Support titrated from 18 to 10 cmH<sub>2</sub>O and was liberated from invasive mechanical ventilation in less than 48 hours. The patient was thereafter supported with intermittent non-invasive mask ventilation until discharge.

### **PRODUCT UPDATE: SLEEP THERAPY**

Obstructive Sleep Apnea (OSA) is a very serious condition affecting millions of people worldwide. For many of the diagnosed OSA patients, the tongue falls backwards into the throat during sleep, obstructing normal nighttime breathing. Targeted Hypoglossal Neurostimulation (THN) Sleep Therapy is a new therapeutic solution that is being tested for neurostimulation of the tongue during sleep. THN Sleep Therapy works on the principal of targeted stimulation. Not every muscle of the human tongue is involved in the opening of the airway. In fact some muscles when stimulated block the airway. THN Sleep Therapy is able to target and stimulate only those muscles that deliver optimal opening of the airway. THN Sleep Therapy stimulates the nerve that provides motor innervations to tongue muscles. During sleep most muscles relax. This is true of the tongue muscles as well. By providing gentle stimulation to the hypoglossal nerve, normal daytime tongue muscle tone is restored to key muscles and the tongue does not fall into the throat. The airway is kept open and the patient can once again breathe normally during sleep. The procedure involves an implant surgery that is relatively simple utilizing a small electrical device to achieve increased upper airway flow. An ENT surgeon implants the device and later a sleep physician programs the device to produce short bursts of electrical pulses that are delivered to the nerve. An incision is made in the upper neck for the electrode placement and another incision is made in the upper chest for the pulse generator placement. The electrode that is implanted near the lower jaw is attached to the Hypoglossal Nerve (12th cranial nerve). The electrode is then connected to a small pulse generator (IPG) implanted in the upper chest wall. After the surgery has been completed, the system is then programmed, a few weeks after implantation, to achieve best possible results customized to each patient. The implant is recharged through the skin once or twice a week. It is turned on by the patient with a handheld radio-frequency device prior to sleeping. It then runs continuously throughout sleep, and is turned off in the morning requiring no additional sensors or synchronization. The THN Sleep Therapy stimulator can be reprogrammed by the physician as often as required. THN Therapy was recently developed and is in the process of completing European clinical trials. It is designed to help OSA patients who cannot comply with other therapies, such as CPAP. The above information was provided by ImThera Medical. Contact imtheramedical.com.

### **SLEEP ROUNDTABLE**

### CleveMed

### What sleep products do you offer?

CleveMed's current sleep product offerings include complete wireless PSG systems, the 14-channel Crystal Monitor 20-S and 20-B and the 22-channel Sapphire PSG. The SleepScout is a 9-channel type III monitor for home sleep testing. All four systems include Crystal PSG software, a sophisticated software package for data acquisition, scoring and reporting.

## What are the latest developments in sleep testing and diagnostics?

Our latest product SleepView is the smallest, lightest home sleep monitor following AASM guidelines for portable monitoring. It is ergonomically designed for patients to perform a self test at home. SleepView works hand in hand with the eCrystal PSG Web Portal, where sleep studies are uploaded for review and scoring by sleep technologists and interpreted by a board certified sleep physician. This practical and efficient patient monitoring system allows physicians to provide a continuum of care.

## How do your sleep products integrate with hospital, sleep lap and/or home testing?

Our wireless PSG systems are easy to set up and portable. These features make the systems ideal for hospital based labs and expansion of existing labs. The DreamPort added to the Sapphire PSG system is used for remotely attended sleep studies allowing patients to have a full PSG study in their home. The SleepView with eCrystal PSG webportal combines a small patient friendly home sleep monitor with a scoring and interpretation service allowing a broad range of physicians to conduct home sleep tests.

# How do you foresee the next several years in sleep related reimbursement?

Over the next several years in sleep and healthcare as a whole I believe there will be an emphasis on cost effectiveness of procedures. This may not lead to cuts in reimbursement but more restrictions on which patients may have an in lab study and how often a full PSG study may be performed. I believe that new products will be introduced that are designed to make HST easy to perform but to provide more diagnostic information with fewer sensors.

### Embla

# What diagnostic and/or therapeutic sleep products do you offer?

Embla is the largest company in the world focused only on Sleep Diagnostic solutions. We offer a complete range of products from our Embletta home sleep testing device, to in-lab and portable PSG systems with a choice of three PSG software platforms: Sandman, REMbrandt, and RemLogic. Embla also offers the Enterprise Sleep Business Management system, which supports all areas of the sleep business from referral through post study follow up. Our Cardio Pulmonary Coupling (CPC) Module can phenotype sleep disorders, predict patient success or failure on PAP therapy, and allow technicians to immediately apply the proper PAP treatment during a split study. Through the development of products like Enterprise and CPC, Embla provides innovative and time saving tools that help customers do their job effectively and efficiently.

# What are the latest developments in sleep testing and diagnostics?

The field of sleep medicine has, in the past relied on subjective self reporting methods, interviews, and psychological variables to assess sleep quality. Sleep questionnaires like the Pittsburgh Sleep Quality Index and Epworth Sleepiness Scale are used universally, but because they are fundamentally subjective, do not offer truly consistent measures of disturbed sleep. Current standards used to score sleep do not always differentiate normal sleepers from poor sleepers. Using the Embla CPC Module, clinicians and medical professionals can add complementary information to PSG data by providing information to distinguish between good and poor sleep. The analysis also identifies what type of SDB a patient may have. Future developments with the CPC Module will allow us to provide very easy and effective ways to track patients' sleep over time, providing constant feedback to the clinician on treatment efficacy. Frequent tracking could allow clinical decisions to be made earlier when a patient is not responding to current treatment. Other applications of the CPC Module could facilitate the intervention of therapy and identify those at risk for heart disease.

### What is the range of applications for your products?

Embla offers solutions ranging from Home Sleep Testing with the Embletta, to standard or complex PSG studies with our three PSG systems. We even have a solution to help lab owners operate their sleep business more efficiently with our Enterprise Sleep Business Software. Embla also features an online sensor shop at shopEmbla.com, which contains competitively priced sleep sensor and accessories as well.

## How do your products integrate with hospitals, sleep labs and/or home testing?

Embla products are used by sleep clinicians worldwide in the home, sleep lab, and hospital environment to collect the data that medical practitioners require to analyze and diagnose sleep disorders. The collected data can be managed and reviewed by sleep medicine clinicians either on site or remotely. Our product offering ranges from full multi-channel PSG systems to portable lightweight home testing equipment. The equipment is supported by a complete range of software applications that allows caregivers to collect, review, interpret and report information both locally and remotely. Beyond the data collection, Embla Enterprise Sleep Business software allows users to manage and track patients throughout the continuum of care from the point of referral, through the scheduling, study, and patient follow up process. Enterprise reports are customizable and can provide otherwise time-consuming information on demand, including patient demographics, referral patterns, occupancy metrics, and report turnaround time. Enterprise is compatible with any PSG system, interfaces with hospital HL7 systems, and provides a paperless environment for your sleep facility.

# How do you foresee the next several years in sleep related reimbursement?

The Health Care Reform Act of 2010 takes effect in 2014 and we are just beginning to hear discussions regarding how it will all work. What is clear is the mandate to reduce costs and it is doubtful that any field of medicine will be spared cuts. Medicare payments to physicians continue to be reduced. There are rumors circulating in the industry regarding cuts to laboratory based PSG as well as Home Sleep Testing, however these remain mostly rumors with no documented evidence. Private carriers typically follow suit with CMS. Again because of the coming changes to how healthcare will be funded, we speculate that private carriers will wait to see what the new parameters will be before revealing their strategies.

### **Itamar Medical**

### What sleep products do you offer?

Itamar-Medical offers WatchPAT, the most convenient, portable sleep testing device on the market for diagnosing Obstructive Sleep Apnea. It is easily installed by patients in the comfort of their own home with over 250,000 tests worldwide. WatchPAT provides AHI, RDI, ODI based on actual sleep time and sleep stages (REM/Wake/Deep/Light) without electrodes attached to the head and without a cumbersome nasal cannula or belt around the chest or abdomen. This gives the patient greater comfort, more natural sleep, as well as an amazingly low failure rate which minimizes the "first night effect."

## What are the latest developments in sleep testing and diagnostics?

With increased demand for solutions in Electronic Medical Records (EMR) and ambulatory trucker sleep testing, WatchPAT is ideally positioned to provide solutions for these latest developments in sleep testing and diagnostics. Itamar-Medical now offers WatchPORTAL for one-step automatic sleep study uplink into EMR and remote interpretation by sleep experts. WatchPAT also provides the only tamper-proof ID solution for positive chain of command & identification in an ambulatory environment to enable conveniently easy trucker testing while on the road. For those labs requiring multi-night testing, WatchPAT supports that as well.

### What is the range of applications for your products?

WatchPAT covers a wide range of clinical applications from the diagnosis of sleep-related breathing disorders, to sleep architecture assessment, to follow-up CPAP and oral appliance adjustments. WatchPAT is the most effective way to monitor CPAP settings since no nasal airflow is required to interfere with sleep or CPAP measurement. It is at the frontier of scientific research as well. WatchPAT is the most medically and scientifically investigated ambulatory testing device in the industry with over 35 peer-reviewed papers and over 3,000 simultaneous PSG studies showing that WatchPAT's accuracy is at least as good as a PSG.

# How do your sleep products integrate with hospital, sleep lab and/or home testing?

WatchPAT is widely used and well integrated within private, national, and international sleep labs, in ENT facilities and dental clinics. It is used extensively by Kaiser, and the VA system to provide patient-friendly, cost-efficient sleep testing for all. Physicians use Itamar's intuitive, EMR-friendly software to review sleep data channels and manually override the automatic suggested scoring (the actual sleep data cannot be altered). Sleep Labs are finding that WatchPAT actually enables them to increase their business and focus their in-lab testing on the more complex patient cases.

## How do you foresee the next several years in sleep related reimbursement?

With the general trend of health-care reimbursement cuts, the lower cost of ambulatory testing will make sleep testing more ubiquitous. The long-term cost savings in treating sleep apnea will become evident as more patients are treated earlier in the process with outcome studies showing the prevention of sleep-related complications such as cardiovascular disease, depression, erectile dysfunction, obesity, etc.

### Nihon Koden America

### What sleep products do you offer?

Nihon Kohden offers several platforms for both in lab and home sleep testing. In lab testing devices come in two platforms; dedicated PSG and Combination EEG/PSG. Dedicated PSG Platforms: **Polysleep 921** – Total 40 Channels (32 AC, 8 DC) available internal mainstream EtCO<sub>2</sub>. **Polysleep 912** – Total 37 Channels (27 AC, 10 DC). Combination Platforms – **EEG**-**1200 EEG/PSG** is available in 27, 32, 64, 128, 192 AC channel platforms. Up to 16 DC channels. Home Sleep Testing – **Trackit Ambulatory** Type II recorders for EEG or PSG available in 18+8 channels, 24 Channels, 32 Channels. Built in SpO<sub>2</sub> available. Nihon Koden also offers the **Track-it Sleepwalker** dedicated type II recorder and **Nomad Type III** recorder 11 channels.

## What are the latest developments in sleep testing and diagnostics?

Our most recent development showcased at the Sleep 2010 in San Antonio is the Polysmith PQ electronic patient questionnaire. This new product allows a pure paperless system securely integrating patient questionnaires into email and the Polysmith DMS database. Polysmith Version 8 will be out later this year and showcases many new features allowing streamlining of sleep lab operations and integrating new features for home sleep testing.

### What are the range of applications for your products?

Our sleep products can be used for PSG, EEG, Epilepsy monitoring and Home Sleep Testing. Nihon Kohden Neurology products also encompass EMG and Inter-operative monitoring as well. Nihon Kohden America provides solutions for the patient monitoring and cardiology markets as well.

# How do your sleep products integrate with hospital, sleep lap and/or home testing?

Nihon Kohden America offers an HL7 module that will allow our systems to integrate with HL7 compatible electronic medical record systems. Thus far we have successfully integrated into many different systems performing bi-directional interfaces. All of our latest software also integrates with our home sleep testing devices for initialization, download, analysis and reporting. This gives our customers a single interface if they use both PSG and HST or they can configure systems one or the other.

# How do you foresee the next several years in sleep related reimbursement?

Unfortunately it appears that reimbursement will likely decline over the coming years. This is for a variety of reasons not the least of which is the new Federal Healthcare changes. It is important for the market and our development to create solutions that lower the daily cost of performing sleep studies and allow our customers to maintain as much positive revenue as possible. If there was a main mission for the coming years it would be to find ways to lower daily overhead for our customers. The positive news is that it appears that more private insurance are now paying for home sleep testing. Although the CMS reimbursement is not sufficient this trend does show a positive direction.

### ResMed

### What sleep products do you offer?

ResMed offers a full line of CPAP, APAP and VPAP bilevel flow generators, as well as adaptive servo-ventilation devices for the treatment of central and complex sleep apnea. Key products include the S9 Elite, S9 AutoSet and VPAP Adapt SV. Our devices are the quietest and most comfortable on the market in each of their respective categories.<sup>1-2</sup> Additionally, our S9 devices have been shown to increase patient average daily usage by up to 30 minutes.<sup>3</sup> Complementing our range of devices is a full line of masks. ResMed's nasal pillows systems, nasal masks and full face masks accommodate a wide range of patient needs, preferences and lifestyles. Our masks also feature a number of innovative comfort technologies, such as our dual-wall cushion technology and specially designed vents, to deliver quiet, comfortable and effective therapy.

## What are the latest developments in sleep testing and diagnostics?

ResMed recently released the VPAP Tx lab system, the newest all-in-one titration solution for the sleep lab. Easy to use and versatile in every way, it was designed to increase patient comfort in the sleep lab to increase the likelihood of overnight titration success. The VPAP Tx includes all ResMed therapy modes to titrate the simplest to most complex sleep apnea patients, is compatible with all PSG systems, and enables use of ResMed's algorithms and comfort technologies in the sleep clinic.

### What are the range of applications for your products?

Our products are indicated for the treatment of a wide range of sleep-disordered breathing conditions, including obstructive sleep apnea, central sleep apnea, complex sleep apnea, overlap syndrome and chronic obstructive pulmonary disease. They may also be used for noninvasive ventilation, titration in the lab setting and home sleep testing.

# How do your sleep products integrate with hospital, sleep lap and/or home testing?

ResMed's diagnostic solutions for home sleep testing include the ApneaLink and ApneaLink Plus. ApneaLink devices offer an affordable portable testing option that minimizes the cost of each test. Because these devices are so simple to use, our customers get very high first-time success rates. They may also be used in the hospital and other clinical settings to easily and costeffectively diagnose patients with sleep apnea. The ApneaLink devices, in addition to the VPAP Tx lab system, are a perfect fit for sleep labs that diagnose and titrate patients for CPAP therapy. ResMed also offers a full range of quick-fitting, high-performance masks for the titration of patients in the sleep lab.

# How do you foresee the next several years in sleep related reimbursement?

We see payors taking a variety of approaches in the sleep reimbursement market. Some payors are looking at cost mechanisms that may not always factor in the value of the service that HMEs provide to ensure patient care. Other payors are also increasingly interested in focusing on compliance and the capture of data. As an industry, we can all continue working together to invest in educating payors on the importance of managing sleep apnea. In doing so, we can efficiently adapt to these changing reimbursement dynamics and use data to better understand patient symptoms and measure long-term outcomes. [References: 1. User testing 2009 and 2010; 2. Testing per ISO 17510-1: 2002 and 2007; 3. details at clinicaltrials.gov ID NCT01013207.]

### Salter Labs

### What sleep products do you offer?

Salter Labs offers an extensive line of sleep diagnostic products including: The **BiNAPS Nasal Airflow Pressure and Snore Transducer**, a wide array of *Salter-Style* **Sleep Diagnostic Cannulas**, the **ThermiSense Oral/Nasal Thermal Airflow Sensing System** and cannula/holders, **PneumoTHERM** disposable and reusable thermocouples and unique and inexpensive **SnoreTAC** Snore sensing Adapters for use during patient titration.

# What are the latest developments in sleep testing and diagnostics?

Recent changes to AASM guidelines call for both nasal pressure and oral/nasal thermal airflow sensing. Salter Labs has developed a solution to this with their ThermiSense and BiNAPS products.

### What are the range of applications for your products?

The concurrent use of of Salter Labs' BiNAPS Nasal Airflow Pressure and Snore Transducer with their ThermiSense Oral/ Nasal Thermal Airflow Sensing System or PneumoTHERM disposable and reusable Thermocouples allow sleep professionals to easily and inexpensively meet the new AASM guidelines requiring both nasal pressure and oral/nasal thermal airflow sensing.

# How do your sleep products integrate with hospital, sleep lab and/or home testing?

All of Salter Labs' sleep diagnostic products can be used in the hospital, in sleep labs, or during home testing and are specifically designed to function with most of the PSG systems available.

### **PRODUCT REPORT**

### Monitoring SpO<sub>2</sub> During Conditions Involving Low Peripheral Perfusion

This article, a white paper, was provided to Respiratory Therapy by Masimo Corporation.

Masimo Corporation was the first company to receive FDA clearance for the ability to accurately and continuously read SpO<sub>2</sub> values through motion. It was also the first company to receive FDA clearance to claim the accurate measuring of SpO<sub>2</sub> during low peripheral perfusion with its Masimo SET pulse oximeter. Masimo was able to accomplish this feat through its proprietary algorithm, hardware and sensor design. Through the use of specially designed low noise sensors (LNOP), cables designed to minimize electrical interference, and circuit boards designed to lower noise, Masimo engineers were able to obtain the signal during very weak pulsations to acquire accurate readings of SpO<sub>2</sub> and pulse rate. Masimo SET algorithms assist in picking up the pulsations in the midst of artifacts caused by motion and other artifacts. The result was a system that was able to monitor at low perfusion levels approximately 10 fold lower than the conventional pulse oximeters that were on the market. Today, Masimo continues to be the leader in read-throughmotion and low perfusion technology.

The earliest report of Masimo's enhanced ability to read in low perfusion was in an abstract and poster presented at the 1995 Society for Technology in Anesthesia.<sup>1</sup> Researchers compared Masimo to several then current pulse oximeters during low perfusion caused by brachial artery clamping. They found that a Masimo SET prototype device had the lowest total error compared to 5 pulse oximeters: Nellcor (with and without C-Lock), Novametrix, Criticare, Ohmeda. In fact the total error for the Masimo was less than 2% while the best of the other competitors was greater than 32%. Total error was defined as percent of time the device was unable to give a reading plus the percent of time the device was greater than 3% from the control.

Since that report, Masimo has continued efforts focusing on maximizing sensitivity for detecting pulsation and  $SpO_2$  values in patients suffering from extremely low cardiac output and/or low local perfusion levels. An important clinical advantage of increased sensitivity is that the Masimo pulse oximeter provides valuable information (when other pulse oximeters can not) in critical environments and situations where very low perfusion can occur such as: ICU, Trauma, Cardio-Pulmonary Bypass and resuscitation.<sup>3-17</sup> The improved low perfusion capabilities of Masimo SET technology have been shown to be capable of monitoring  $SpO_2$  and PR during extremely low perfusion and in fact have been reported to correctly monitor adequacy of chest compression during resuscitation in neonatal patients.<sup>17</sup>

It is important to understand the concept of "signal to noise ratio" when considering the problem of monitoring  $\text{SpO}_2$  during low perfusion. Low perfusion results in a very small amplitude signal, which can become so low as to be difficult to distinguish from the background noise. Detecting the actual  $\text{SpO}_2$  signal during low perfusion situations is made more difficult during periods of motion. In effect, the motion raises the background noise level thereby making it even more difficult to distinguish the small amplitude SpO<sub>2</sub> signal during low perfusion. The clear advantage of Masimo SET is in the ability to accurately measure SpO<sub>2</sub> during the worst of all situations, periods of low perfusion and motion. Numerous studies have shown the Masimo's SET technology is clearly superior to all other pulse oximeters during conditions of motion and low perfusion.<sup>2,3,5,6,9,14,15,16</sup>

Critically ill patients are at risk of developing low peripheral perfusion. Clinicians may not always be able to reliably predict when patients may develop this condition. Therefore, reliable pulse oximetry needs to function accurately whenever presented with conditions of low perfusion. Masimo SET provides just that; accurate and reliable pulse oximetry during conditions of low perfusion.

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### **TECHNOLOGY REVIEW**

### Medical Acoustics Diagnostic and Therapeutic Lung Flute

This new innovative technology is a first for receiving FDA approval for both diagnostic and therapeutic sputum induction applications. The Lung Flute is an effective diagnostic modality providing an effective option for sputum induction without the effects and risks associated with hypertonic saline aerosols. The therapeutic application for secretion management and pulmonary hygiene is ideal for the hospital and home setting. It is simple in its application, requiring minimal teaching and equipment maintenance, offering a cost effective alternative for the clinician and home care patient.

Unique to the Lung Flute is the acoustical sound waves that target lower distal airways. Flow that is generated by the user results in a low frequency acoustic wave that travels retrograde into the lower more distal airways and lung parenchyma. This low frequency is very similar to the rhythmic beat of the cilia and creates a vibration between 15-25Hz. This frequency induces a mucus phase change from its viscous state to a more liquid state, aiding the mucocillary activity and secretions to move more freely.

Before its official hospital debut, news of the device spread quickly in the private sector. Patients sought out the device from their physicians following articles highlighting the award winning technology in Popular Science. With a strong following of users who suffer from chronic conditions, it was no surprise that the Lung Flute won the Frost and Sullivan Excellence in Medical Devices Award and was honored for Innovative Technology with North American Pulmonary Therapeutic and Diagnostic Devices Excellence in Technology of the Year.

With the Lung Flute's abilities to be used for sputum induction for a specimen in place of hypertonic saline and for therapeutic purposes, there is now a new potential for one device to save time, resources, and product cost. The Lung Flute for diagnostic use has billable/ procedural code for diagnostic sputum induction. The Lung Flute for therapeutic use is separate and follows the same guidelines as other vibratory secretion clearance devices.

# The physics behind sound and vibration for secretion clearance

Understanding the differences behind sound and vibration for therapeutic use will help clinicians make that connection for patient need and therapeutic choice. An effective way to identify differences is to look at the simple physics.

Starting with simple principles and physics, use an analogy of a ball at the edge of a bookcase. At rest, the ball has potential energy—a potential energy that cannot do anything. However, if the ball falls from the top of the bookcase, the potential energy changes because the force of gravity accelerates it towards the ground. The potential energy is converted to kinetic energy. Kinetic energy has the ability to be transferred to other objects. If the ball encounters another object, the kinetic energy can be transferred to that object. The ball then loses this energy and comes to rest. The object that received the energy transfer expresses this energy through movement. The effectiveness of the energy transfer and the amount of movement is dependent on the resistance, to movement, of the object. This is how it works with the mechanisms that help give a push or a running push to mobilize secretions.

Creating a division of top and bottom with the lungs may help make an easy separation and distinction of needs for therapy. In the larger airways, there is a greater shear force with the air moving through the larger airways with turbulent flow, and the main mechanism of secretion clearance is flow and the cough reflex. As you progress deeper into the lungs, there are many significant changes in size of airways, laminar flow, temperature, secretions, and the mechanism for secretion clearance is the mucocillary escalator, expansion, and flow. This helps explain how and why therapy will respond differently depending on location and mechanism for improving secretion mobility.

With the top half it would make sense that a more intense vibration would be the mechanism that would be needed to overcome resistance and reinstate secretion mobilization for this type of airway. Thinking of the lower half of the lungs, the mucociliary escalator is the mechanism that helps mobilize secretions. As conditions change in the gel/sol layer of the cilia or with the viscosity of the secretions, the ciliary movement becomes ineffective in secretion mobilization. At this point, what is needed is a mechanism to transfer additional energy to the secretions. A well chosen therapy will provide that mechanism aiding the cilia, by changing the viscosity of the secretions and provides a push to once again mobilize secretions. The Lung Flute generates sound waves optimal for the cilia beat and that is why this device works in the lower half of the lung so well. What differentiates the device is the type of sound and vibration it generates. This is done by a flexible reed generating an increasing sound wave that is like a drop of water falling into a pool and creating a ripple. The sound moves through and around the secretions generating energy, converting the potential to kinetic. Sound wave

progressively builds, transferring more and more kinetic energy to the secretions. The Lung Flute has the ability to vary the intensity

and amplitude simply by changing the push (pressure) behind the flow. This is beneficial for varying needs with secretions and airways. Viscous mucus is resistive to energy applied to it at a regular frequency. It needs a progressive, increasing transfer of energy to break free the surface tension that is holding it in place (shearing force). The progressive application of force/energy provided through the lung flute mechanism allows the transfer of a progressively larger amount of mobilizing force.

What is different about the Lung Flute is the range of sound waves. Being accustomed to feeling the vibration in your upper airways, you won't likely feel them in your lower airways. If you are healthy, you will still feel it, but you won't necessarily produce secretions. If secretions are present in your airways, you are likely to vibrate them loose.

Essential to good quality care for our patients, it is important to recognize that one size does not fit all when it comes to technology and therapy. With so many factors and processes involved with patient care, there is a reason there are choices in technology for therapy. It all comes down to the right technology for the right person, for the right job, at the right time.

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Early Technology Validation—Bench Test Acoustic Analysis & Comparison

- Conducted in 2003 at the Acoustics Laboratory within the Department of Physics at Northern Illinois University
- Investigation focused on the efficacy of Sound Waves versus Pressure Waves by comparing the Lung Flute to a FDA cleared PEP device sold by Axcan Scandipharm as the "Flutter"

Completed Studies/Trials:

- Northern Illinois University acoustic bench test 2003
- UB/VA diagnostic clinical trial 2004
- Perceptronix/St. Mary's Lung Cancer diagnostic trial 2007
- Japan TB diagnostic clinical trial 2007
- UB/VA therapeutic COPD 2009

Univ of Buffalo/VA Clinical Study—Diagnostic Application

- Three clinical patient groups were evaluated: 20 and 15 COPD subjects respectively and a group of 10 healthy individuals.
- Safety and efficacy of sputum induction with the *Lung Flut* was compared with sputum induction with hypertonic saline and saliva
- Biological markers were measured which indicate the presence of lower respiratory secretions.

Univ. of Buffalo/VA Diagnostic Clinical Study-Summary Results

- Sputum induction with Lung Flute was as good as hypertonic saline on all four measures
- No statistical difference
- Lung Flute was statistically better than saliva on three of four characteristics
- Gram stain
- Fibrinogen content
- Interleukin-8 content
- No statistically significant difference was observed in free Neutrophil Elastase activity

UB/VA Therapeutic Clinical Trial 2008-2009 Conclusions

- The study hypothesized that the Lung Flute, used on a twice daily basis will provide clinical benefit to patients with COPD with chronic bronchitis.
- The study found no statistical difference in the dry sputum weight between the Lung Flute and the predicate device.
- The study included a quality of life questionnaire (CCQ). The

CCQ is an objective validated tool to assess COPD symptoms. There was a significant improvement in the CCQ in patients who were using the Lung Flute. There was no statistically significant improvement in the CCQ in patients using the predicate device.

- The Lung Flute is safe for patient use. There were no serious adverse events or mortality in this study.
- Received FDA 510(k) clearance in Jan 2010

#### Planned Trials:

- Tokyo, Japan multi site TB 100 patient diagnostic trial 2010
- Biomoda- NM multi site Lung Cancer 1200 patient diagnostic trial 2009
- S. Africa TB diagnostic trial 2010
- Nepal CDC/IOM 300 patient TB diagnostic trial 2010

The diagnostic Lung Flute is covered by the following CPT codes for insurance reimbursement:

- CPT 94640 \* Pressurized or non-pressurized inhalation treatment for acute airway obstruction or for sputum induction for diagnostic purposes (eg. with an aerosol generator, nebulizer, metered dose inhaler or intermittent positive pressure breathing [IPPB] device)
- CPT 94664 \* Demonstration and/or evaluation of patient utilization of an aerosol generator, nebulizer, metered dose inhaler or IPPB device

\*The therapeutic Lung Flute has already been assigned DME E0484 for Medicare/Medicaid reimbursement which provides a reimbursement rate which is favorable to the company.

### The Effects of CPAP on Cardio-Respiratory Function

Donald Pell, MD, FCCP

While speaking about the effects of CPAP on Cardio-Respiratory Function, CPAP is an ideal remedy as it corrects abnormal respiratory physiology. Before discussing the advantages of CPAP, let's compare physiology between normal and abnormal respiratory function.

### **Normal Physiology**

Under normal breathing, respiratory effort is handled by the diaphragm. Air is drawn into the lungs when the diaphragm contracts. As the diaphragm contracts, pressure falls in the chest and rises in the abdomen, pressurizing venous blood to return to the right heart, (the thoracic- abdominal pump). Air is drawn into the lungs while reduced pressure in chest draws venous blood to the right side of the heart (pre-load). The expanding lung acts as a pump which pulls returning venous blood into the lung circulation and decreases left heart filling. When the lung exhales, work is done by previously stretched elastic tissues and vessels-and consequently, there's no cost. The lung expands and contracts, air spaces (alveoli) are kept open by surfactant made by the lining cells. Negatively charged, walls repel each other, preventing total collapse of the alveoli when in a nearempty air position. This synchronized effort allows air and blood to flow through the lungs, achieving CO<sub>2</sub> transfer and acquiring oxygen at the same time.

### **Abnormal Physiology**

During abnormal physiology, most illnesses involve the left heart, such as Acute Heart Failure (Pulmonary Edema). The right heart is the receiving chamber. It's thin and distensible, accommodating returning blood volume. The left heart is 6 times thicker than the right as it pumps higher pressure, ie, 120 systolic, 80 diastolic. Therefore, it is less easily distended. When heart failure occurs as stroke volume (number of cc's blood/ per beat) falls, to make up for decreased cardiac output, heart rate rises. Additionally, an increased rate/sympathetic tone increases oxygen demand and myocardial work. Usual causes of left heart failure include: arterial sclerosis, hypertension and vascular disease. Other contributors can also be cardiomyopathy due to alcohol, thyrotoxicosis, viral and familial. The left heart is thick and can't distend. The right heart continues to pump making lungs become stiff and rigid, making it harder to ventilate, gas space is reduced, water fills air sacs, gas transfer of oxygen is

The author is Clinical Assistant Professor of Medicine, University of South Florida; Board Certified/Recertified, Internal Medicine and Pulmonary Disease, Inventor and Patentor of Related Respiratory Devices. This article was provided by Mercury Medical. decreased, and  $O_2$  level falls. The rapies to improve left heart performance reduce pre-load (blood getting to the heart) or after load (resistance to blood flow leaving from the left heart). Inhibitors under these instances are nitroglycer in (pre-load) and ACE. A drug to reduce sympathetic tone (autonomic vaso constriction/ fluid retention, cardiac arrhythmogenicity) is Aldactone.

There are many types of CPAP systems available today. Some use flow generators, while others do not. The new disposable CPAP systems are cost-efficient, lightweight, convenient, and reliable. Most are available with accessories such as: masks, head straps, T- piece & nebulizers, filters, valves and connectors. Some examples of CPAP disposables include Flow-Safe (Mercury Medical), Boussignac (Vitaid), O2-RESQ (Pulmodyne) and WhisperFlow (Philips Respironics).

CPAP therapy provides the following: 1) improves abnormal work of breathing, 2) corrects hypoxia, 3) decreases myocardial  $O_2$  consumption, 4) reduces pre-load/afterload, 5) decreases sympathetic tone, reducing cardiac risk and cardiac arrhythmia.

### What is CPAP (Continuous Positive Airway Pressure)?

CPAP pressurizes  $O_2$  with a mixture to the lungs through a sealed mask device with titratable pressures and flow. CPAP provides fast attainment of work reduction and cardiac stability. Equally important, it also decreases the need for intubations. Possible consequences of intubation (driving in ambulance) may be misplacement, tissue damage and/or bleeding, cardiac arrhythmia, and dental damage.

As tomorrow's disposable technology is here today, pressure/ flow generators are no longer necessary. Disposable CPAP systems require no pressure flow generators; they only require oxygen flow. The CPAP systems are titratable from 2 1/2 cm  $H_2O$  to 10 cm  $H_2O$ . With improved head straps, coaching, and the ability to attain  $O_2$  saturation, CPAP can seamlessly be transferred to ER along with  $O_2$  flow/pressure settings for continued optimal care and minimal downtime for transport personnel. To understand CPAP better, a simple analogy of CPAP is like blowing up a balloon and allowing it to inflate the lungs. A set level of pressure is applied to raise airway pressure and expand alveoli. It will also restrict air flow out of the lung (like pursed lip breathing). Expiratory work done by the elastic recoil of the lung doesn't require muscle effort once CHF improves. This can be done passively. The respiratory goals of CPAP are:

- 1. to increase alveoli gas volume, as well as  $PO_2$  and  $O_2$  transfer;
- 2. decrease the work of breathing;
- 3. lower respiratory muscle oxygen requirement;
- 4. satisfy the patient's respiratory flow needs; and
- 5. to improve the patients comfort, clinical status and level of consciousness.

CPAP systems dramatically and beneficially affect pressure and flow. Air is positively pressurized and pushed into the airway, reducing inspiratory muscle work, decreasing venous blood flow returning to right heart as venous flow has to be at higher level than pressure resisting blood return (CPAP). Other benefits of CPAP are less blood pooling in lungs and less fluid transferred into air space, decreasing sympathetic tone, afterload on the left heart, as well as cardiac rate reduction. All these benefits mentioned result in lowered cardiac work/  $O_2$  consumption and reduced cardiac arrhythmia risk.

### When to Use CPAP?

CPAP should be used when an O<sub>2</sub> saturation at 92%/4 liters can't be maintained, the patient's respiratory distress is increasing; the level of consciousness is decreasing; cardiac arrhythmia isn't responding to drugs; respiratory acidosis is increasing (rising  $PCO_2$ ); cardiac rate of 120+ isn't responding to oxygen therapy; and, the respiratory rate of 36+ isn't responding to oxygen therapy. Before using CPAP, you need to make sure you know how to use it correctly. Allow the patient to hold device in place to feel improvement in inspiratory ease-of-breathing. Once the patient is comfortable, attach the head strap and titrate inspiratory pressure upward for desired results. Make sure the mask fits comfortably on the patient to maintain an adequate seal. Once attained, this seal should be kept and protected from attempts of unintentional displacement or suctioning in CHF as recurrent pulmonary edema will quickly occur. Then adjust the head strap once the patient is comfortable. Stay with the patient, display the improvements attained (O<sub>2</sub> saturation, heart rate, etc). Next, adjust the flow for patients inspiratory flow rates. If the needle gauge drops to negative values, then flow is inadequate. A positive attitude coupled with an easy to use CPAP device can relieve consequences of CHF. The goals of CPAP consist of the following:

- 1. to attain  $O_2$  saturation of 92%;
- 2. decrease work-of-breathing and improve patient's respiratory status;
- 3. decrease cardiac rate of 120 or less;
- 4. decrease respiratory rate below 30;
- 5. improved  $PCO_2$  level if elevated;
- 6. improved cardiac arrhythmia;
- 7. reduced need for in-the-field intubations;
- 8. improved mental status/cooperation; and
- 9. to leave the CPAP equipment settings with the patient when transferred from transport to the ER.

### **Contraindications of CPAP**

CPAP has the following contraindications: facial trauma/ fractures, recent gastric surgery, dense, copious respiratory secretions and frequent suctioning. Also, the patient is unable to tolerate the mask, respiratory arrest, PCO<sub>2</sub> is greater than 50 in CHF patient/ monitor (relative), near lethal cardiac arrhythmia (ventricular tachycardia, ventricular fibrillation). Other contraindications of CPAP include decreased level of consciousness, persistent vomiting, and pneumothorax. Possible side effects of CPAP are nasal bridge skin necrosis (rare), hypotension due to decrease in venous return (rare), claustrophobic (coaching proper technique may eliminate this).

What if diagnosis is incorrect? In spite of usual over-inflation of lungs, the  $CO_2$  is lowered,  $O_2$  saturation is improved, LOC improves as  $PCO_2$  falls, respiratory effort is enhanced and  $CO_2$ production is decreased. While in the ER, excess  $PO_2$  can be titrated downward (decrease pressure slowly and you'll see an increased  $PCO_2$  and low  $O_2$  will be corrected.) Due to dry state, low blood pressure occurs (rarely); however, to correct this, use rehydration and adjust CPAP pressure downward. If the patient has asthma while using CPAP, there will be a reduction in inspiratory work, better expansion of previously collapsed alveoli with reduced  $CO_2$  level and increased  $O_2$  level and there will be a reduced need for intubations.

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# The Use of Non-Invasive Ventilation on COPD Patients

There are times in which our patients need extra help in breathing. Sometimes that support is to rouse them or sit them up in bed or to provide them extra oxygen to breathe. Sometimes it requires a greater level of care. That care can be provided by putting your patient on non-invasive positive pressure ventilation, NPPV. This means that positive pressure helps create a breath rather than the physiologic negative pressure that occurs when the diaphragm drops allowing our lungs to expand.

NPPV comes generally in two forms: either bi-level positive airway pressure or continuous positive airway pressure, CPAP. Bi-level positive airway pressure, frequently called BiPAP, is a type of NPPV that provides two different pressure settings that help stent open your patients' airways during exhalation and during inhalation. CPAP provides a constant level of pressure that functions in the same role.

### **Methods of Administration**

Non-invasive positive pressure ventilation can be delivered via oral interface, nasal pillow, nasal mask or full face mask. No patient machine interface has been shown to be superior and patient comfort is for the most part the determining factor in choosing a patient interface. It is important to note that these methods of patient treatment are not designed for total ventilatory support, which means that a NPPV machine cannot breathe on behalf of the patient; it provides support while the patient breathes on his or her own. Some of the most common uses of CPAP is in the treatment of Obstructive Sleep Apnea and Chronic Obstructive Pulmonary Disease. The most common acute indication is the treatment of cardiopulmonary edema and respiratory failure.

Respiratory failure is another indication for NPPV. The etiology of respiratory failure can be ventilatory, hypoxic or a combination of the two. The therapies for these two forms of compromise are different but can overlap. Hypoxemic respiratory failure is generally treated with oxygen therapy but may also improve with NPPV. Ventilatory respiratory failure frequently requires NPPV but can progress to require mechanical ventilation.

The use of NPPV in acute respiratory failure due to COPD has been shown to improve several measures of outcome, including the need for intubation and mortality. In the setting of cardiogenic pulmonary edema, the use of NPPV remains controversial because of a possible increase in myocardial infarction associated with NPPV in this patient population. In this discussion of NPPV, we will focus on the COPD population.<sup>2</sup>

# Quick review of the important pathological facts concerning Chronic Obstructive Lung Disease

COPD is a spectrum of diseases that incorporates emphysema, asthma and chronic bronchitis. In all cases damage to your lungs from these diseases can lead to poor exchange of oxygen and carbon dioxide and poor air flow in and out of your lungs. These diseases are also associated with an increase in airway resistance which causes a greater pressure change from the alveoli to the bronchi which can lead to an increased work of breathing.<sup>8</sup> The lung changes associated with COPD also create an increased potential for negative intrathoracic pressure resulting in narrowed or collapsed airways.<sup>4</sup> In addition, the history of inflammatory change associated with these diseases can reduce the structural integrity of these airways leading them to close more readily for any given lung volume or transluminal pressure change.<sup>5</sup> In emphysema in particular, the elastic recoil of the lung is reduced from inflammation, the air passages are poorly supported by the scarred lung parenchyma and the transmural change in pressure can become negative quickly. All of the above processes, the reduced air flow, the increased pressures, air trapping, the scarring and the greater likelihood of small airway collapse, contribute to the signs and symptoms of COPD patients that are so evident.

These characteristics include shortness of breath, barrel chest and cyanosis and can lead ultimately a poorer quality of life. Another classic symptom associated with COPD is wheezing, the result of air flow through these narrowed and scarred airways. These symptoms often force a COPD patient to breathe with pursed lips thus increasing the pressure in their airways which allows better air flow. This increased flow encourages better gas exchange and is a natural response to their pathology.

# Quick review of the important physiologic benefits of CPAP

**What does CPAP do?** A COPD lung has a natural tendency to collapse, trap air and have poor gas exchange. CPAP provides a constant pressure to the airways to prevent this collapse and improve gas exchange. This pressure produces two well described, salutary effects on the pulmonary system and thus oxygenation:

- 1) The redistribution of the extra vascular water leads to resolution of VQ mismatch
- 2) Alveolar recruitment which increases FRC. FRC = (Residual volume + expiratory reserve volume).

Thus, continuous positive pressure ventilation provides improved oxygenation, ventilation and lung compliance in those patients that need it most.

This article was provided to Respiratory Therapy by Oridion.

**Requirements for NPPV:** Not every patient that has COPD, however should be administered NPPV. The candidate for NIPPV should have no facial fractures and no risk of aspiration—remember these patients have to be able to breathe on their own and as such must be able to protect their own airway. In addition, they should have the mental status to cooperate with a pressurized face mask. In 2001, Antonelli et al captured the characteristics of patients who were most likely to fail CPAP therapy and require intubation. These characteristics include: Pneumonia, ARDS, >40 years old and PaO<sub>2</sub>/FiO<sub>2</sub> ration less than 146 after one hour on NPPV.<sup>1</sup>

### Monitoring your patient while on NPPV

It is important to recognize that your patients have been placed on this ventilatory aide to improve not only their oxygenation but also their ventilation. For that reason, it is important to monitor the patient's ventilatory and oxygenation status by measuring oxygen and carbon dioxide levels in the blood. During NPPV, frequent measurements may be required, especially during early titration of the pressure settings. One method of monitoring the efficacy of the NPPV is the use of arterial blood gas measurements. This allows the clinician to monitor to the concentration of oxygen and carbon dioxide as well as the hydrogen concentration. However this method of patient monitoring may require multiple arterial punctures or an indwelling arterial catheter, the costs and trauma of which increase the level of acuity of your patient.

Rather than arterial cannulation, a preferred method of monitoring this patient population is one that is continuous and noninvasive. This allows the clinician to monitor the patient's ventilatory status over time and the immediate response to adjustments in therapy as well as avoiding the potential pain and complications of arterial sampling. Pulse oximetry works well for monitoring oxygenation status while the measurement of end-tidal CO<sub>2</sub>, also known as capnography, serves as this crucial measure of ventilation.

Capnometry involves the application of a nasal/oral cannula similar to an oxygen cannula that monitors the concentration of carbon dioxide exhaled with each breath. Capnometry has been shown to be more effective in early discovery of respiratory compromise than oximetry "... by allowing early detection of respiratory compromise, prompting intervention to minimize hypoxemia."<sup>9</sup>

A recent publication by Nuccio et al demonstrated that "the readings from the (Nasal-Oral) sampling cannula proved to be the most reliable in trending  $etCO_2$  values in all scenarios with different ventilator modes, settings and leak rates in the normal patient. This method correlated most closely with changes in minute volume that occurred under differing testing conditions."<sup>6,7</sup>

Repeatedly, the use of pulse oximetry as the sole marker of oxygenation and ventilation is coming into disrepute and the monitoring of exhaled carbon dioxide is the necessary element to keep your patients safe.

### **Benefits of CPAP – Hospital setting**

We have seen that CPAP stents open the collapsed airways of our COPD patients and that it also decreases the amount of edema that COPD patients sometimes suffer from. It has also been shown that fewer serious complications (38% vs 66% lower incidence of PNA or sinusitis 3% vs. 31%) plus shorter periods of ventilation and shorter stays in the ICU occurred when patients are trialed on NPPV. Immuno-compromised patients with acute hypoxic respiratory failure and pulmonary infiltrates were studied by Hilbert et al and when compared to the control, intubated group the NIPPV group had significantly decreased ICU mortality and hospital mortality. CPAP then is a fantastic tool in the clinical armament and one in which the hospital setting is relying on more consistently.<sup>3</sup>

These studies demonstrate that NPPV is an ever increasing tool for keeping patients safe, infection free and helping them to return to their lives faster than before. We also see that the effective use of this tool requires careful titration of settings to maximize clinical benefit while minimizing hemodynamic complications and failure rates. Successful use of NPPV can be most accurately achieved with the use of non-invasive carbon dioxide and oxygen concentration monitoring thus reducing hospital cost and improving patient outcomes.

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## Implementing NAVA Using Prediction Tools for Facilitating Training and Utilization

Jacylyn Thrush, RRT-NPS, AAS; William Brown, RRT, BS

**Introduction:** When implementing a new ventilation mode, educating the staff and providing support materials are vitally important. Recently, the Respiratory Therapy Department at Washington Regional Medical Center in Fayetteville, AR, began using the "Neurally Adjusted Ventilatory Assist" mode (NAVA) available on the SERVO-i ventilator.

NAVA is a spontaneous mode that provides pressure and flow based on the electrical activity of a patient's diaphragm (also known as Edi, which is measured in microvolts). When in NAVA mode, the patient has a direct communication to the ventilator from his or her respiratory center—which controls the diaphragm's electrical activity (Edi). Therefore, the communications between patient effort and mechanical delivery of support are in unison. During NAVA ventilation, the depth and rate of ventilation are determined by the patient's own drive to breathe, as any spontaneous mode allows.

**Background:** When setting up the ventilator for NAVA, the operator has four parameters that can be adjusted (Figure 1). These settings include the NAVA level (cm  $H_2O$ /microvolt); the PEEP level (cm H2O); the  $O_2$  concentration (%); and the Trigger Edi (microvolts).

**Ventilator Settings:** Of the four NAVA parameters, two are familiar to respiratory therapists and physicians: the PEEP level and the  $O_2$  concentration. The parameters that are new to most practitioners are the NAVA level and the NAVA trigger (Trigger Edi).

The NAVA level establishes how much pressure the ventilator will instantaneously deliver within the patient's current breath (current Edi signal). The NAVA level is the setting that helps determine the amount of work shared between the patient and the ventilator.\*

The NAVA trigger is similar to the flow and pressure trigger (sensitivity setting). However, the NAVA trigger senses diaphragm activation (expressed as a change in Edi), rather than a change in pressure or flow, to trigger inspiration.

**Monitored Values:** In addition to the two new ventilator settings, two new measured values are available on the ventilator once NAVA mode or the preview screen has been initiated. These values are the "Edi min" and "Edi peak" (Figure 2). Edi min is the lowest Edi value measured during a breath cycle and Edi peak is the highest Edi value measured during a breath cycle.

Jacylyn Thrush is Coordinator of Respiratory Therapy and William (Bill) L. Brown, BS, RRT, CPFT is Director of Respiratory Care, Physical Therapy, ECG, EEG, and the Sleep Disorders Center, Washington Regional Medical Center, Fayatteville, AR. This article was provided to Respiratory Therapy by Maquet. **Training Guides:** Because the NAVA mode and the associated ventilator settings' measured values are relatively new to our staff, we wanted to provide tools they could use when they first start to ventilate a patient with NAVA. For this purpose, we designed a tool the staff could use for determining the proper NAVA level setting. Table 1 provides the estimated amount of pressure that the ventilator would deliver during a NAVA breath (assuming no change in Edi). The amount of pressure immediately applied by the ventilator during inspiration is determined by the following equation: Estimated peak pressure (Pest) in NAVA = NAVA Level × (Edi peak – Edi min) + PEEP.

For individuals unfamiliar with NAVA, we have found that using the table, which estimates the amount of pressure above PEEP during a NAVA breath, is helpful to our medical staff. The table was calculated using the above formula for estimated pressure (Pest). The x-axis (horizontal) represents the delta  $Edi_{peak}/Edi_{min}$  and varies with each breath, based on the patient's response. The y-axis (vertical) represents the NAVA level set by the clinician. Values within the table represent the estimated pressure that the SERVO-i would potentially deliver, assuming the Edi value does not change significantly. Our staff has found this information useful when initially setting a NAVA level, since it represents a parameter (pressure) that they understand.

It is important to emphasize that these pressures are estimated values. While the NAVA level remains constant, unless it is changed by the operator, the patient's Edi changes. For example, a patient may have an initial Edi of 10 microvolts, but that value can change within the breath.

**Factors that Influence Edi:** A question that frequently arises with new users is: What are normal values for the Edi? Individuals with relatively normal lung function have an Edi of about 3 to 10 microvolts.<sup>1</sup> Patients with COPD tend to have Edi values that are much higher (43% of peak Edi values; eg, the Edi signal is more than five times higher in patients with COPD).<sup>2</sup>

When a sedative or pain medication is administered, this may reduce the Edi from its current value.<sup>3</sup> The use of a NAVA level that is too high for the patient, ie, one that is attempting to deliver a high amount of pressure, may stimulate the stretch receptors in the lungs. Those receptors then signal the respiratory center in the brain to lower the phrenic nerve signal to the diaphragm and, consequently, lower the Edi and the amount of pressure delivered from the ventilator.<sup>4</sup> Alternatively, a NAVA level that is set too low for a patient might result in an increase of the Edi from its current value in an effort by the patient to receive more support.<sup>5</sup>

**NAVA Level Sliding Scale:** To help our staff understand the NAVA level control values, we used a visual sliding scale with verbal cues indicating a low level of support versus a high level of support (Figure 3).





**NAVA Trigger Sliding Scale:** The fourth control parameter with NAVA is the NAVA trigger. We designed a visual sliding scale illustrating a more sensitive trigger level versus a less sensitive trigger level (Figure 4). Once NAVA mode has been activated, the respiratory therapist or physician can evaluate the appropriateness of the trigger level. We strive to avoid auto-triggering if the NAVA trigger is too sensitive. We also will attempt to increase the NAVA trigger value (less sensitive) if the ventilator is triggering from a pneumatic trigger rather than the NAVA trigger. (Note: During NAVA, the SERVO-i operates on a first-come, first-served basis using either the Edi signal or the pneumatic signal to trigger the breath.)

**Summary:** The estimated pressure table and the two sliding scales are placed near the ventilators so they are readily accessible. These tools have been found to be beneficial by the staff in their early experiences initiating the NAVA mode on



**Figure 1.** Displayed is the "Set Ventilation Mode" screen on the SERVO-i. Note that the patient is currently on the pressure support mode (upper left corner). The operator has selected the new mode (NAVA). In the NAVA "Set Ventilation Mode" screen, the NAVA parameters that can be adjusted within that mode are displayed. The adjustable NAVA parameters (left side of screen) include the NAVA level (cm H2O/microvolt), PEEP (cm H<sub>2</sub>O), O<sub>2</sub> concentration (%) and the NAVA trigger (microvolts). On the right side of the "Set Ventilation Mode" screen are the Pressure Support and Backup ventilation parameters.



**Figure 2.** The screen display shown contains the graphic and monitored data information visible during NAVA ventilation. The scalars (top to bottom) show pressure, flow, volume and Edi (diaphragm's electrical activity). The right-hand column of data represents monitored values; the last two values (at bottom right) are Edi peak and Edi min (microvolts).



**Figure 3.** A sliding scale showing the available range of NAVA levels, from 0.3 to 3.0 cm H2O/microvolt (Version SW 4.0), with 0.3 cm H2O/microvolt being the least amount of support available, based on the Edi signal.



**Figure 4.** A sliding scale illustrating the range of NAVA trigger, from 0.0 to 1.0 microvolts (Version SW 4.0). A NAVA breath will trigger when the SERVO-i detects an increase in Edi signal from the preceding Edi min value.

patients, and the initial designs are constantly being modified as we gain more experience with NAVA. Hopefully this information will be beneficial to other NAVA users as well.

\*The SERVO-i provides a NAVA preview screen during initial setup. Generally, the first NAVA level attempted should produce the same pressure as that used in the current ventilator mode, or perhaps slightly lower.

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# **Spirometer Calibration**

Skloot et al recently reported on portable spirometry in their paper, "Four-Year Calibration Stability of the EasyOne Portable Spirometer,"\* concluding that The EasyOne retained inhalation and exhalation volume accuracy of better than 3% for the four years of the study, and that routine multiple-speed volume calibration checks may not be necessary using that product. They also noted that "the acceptability and repeatability of patient efforts should be the primary focus of quality-assurance programs with spirometers that have been demonstrated to remain accurate for long periods."

The EasyOne ultrasonic flowsensing spirometer was employed by the World Trade Center Worker and Volunteer Medical Screening Program, which required that the accuracy of each spirometer for inspiratory and expiratory volume be checked each day, and that its flow accuracy should be checked each week. Thirty-four spirometers were tested, with 5000-plus calibration-check results collected between 2003 and 2007.

Recommended spirometer calibration standards suggest that the spirometer should have at least a 3% volume accuracy, calibrated with a 3-L syringe. In the primary care setting, most spirometers have tested accurately. The value of such calibration had not been established in a field setting. As such, it had been recommended that accuracy be validated in actual practice. The spirometer to be tested would ideally retain accuracy for an extended period, minimize the risk of crosscontamination when employed in an inspiratory and expiratory capacity, provide automated quality checks and updates, and be able to store the results and allow easy access. The spirometer employed was the EasyOne, from ndd Medical Technologies, Zurich, Switzerland. A dedicated spirette was used for checking calibration at the various sites, and the calibration syringes were stored near the spirometers so temperature differences would be minimal. The weekly linearity check methodology was to empty the syringe into the spirometer at three speeds. More than 10,000 people were tested at six sites during the length of the study, and 4,109 single-speed and 1,189 three-speed calibration checks were collected. The mean volume error was 2 mL and about 98% of the inhalation calibration checks were accurate within 3%. Syringe emptying time goals were 1, 3 and 6 seconds, and the percentage of checks with results at 3% accuracy were 97.6%, 98.6% and 97.6%. ndd helped technicians familiarize themselves with the spirometers so that they could comfortably perform the three speed calibrations.

The researchers reported very low error rates on calibrationcheck results. They noted that the weekly three-speed linearity checks weren't necessary to verify the inspiratory or expiratory volume. Emptying the calibration syringe in one second generated a maximum flow of under 4L/s, confirming that daily single calibration checks can stand in for three-speed linearity checks. The authors noted that several factors could affect accuracy, including those due to the calibration syringe. Other affective factors noted that may contribute to measurement errors are body temperature of the tested, differences in mouthpiece diameter, and flow difference due to users biting on the mouthpiece. Therefore, the researchers stated that it is necessary to measure ambient temperature when measuring forced inspiratory flow, and subsequently converting that measurement to inspiratory FVC.

The World Trade Center program was set up to note subtle spirometry variations over an extended period of time—several years. As such the researchers chose an ultrasonic flowsensing spirometer to avoid cross-contamination, since it uses a disposable flow sensor, is compact, and allows for easy maintenance. While the accuracy of the EasyOne had been bench-tested, this would not naturally insure long-term field applications. The authors recommended that users follow ATS guidelines for field use and verify the spirometer's accuracy each day it's used. The authors concluded that the EasyOne "retained inspiratory and expiratory volume accuracy of better than 3% for at least four years." They noted that daily checks are important, but perhaps more important is "vigorous coaching of patients for maximal breathing efforts."

\*Gwen S. Skloot, MD; Nicole T. Edwards, MSc; Paul L, Enright, MD, Respir Care 2010;55(7):873–877. © 2010 Daedalus Enterprises. The paper on which this article is based was provided to Respiratory Therapy by ndd.

# Economic Results of a Palivizumab Seasonal Prophylaxis Using a Cohorting Software and Vial Sharing

Elio Coletta, Salvatore Coppolino, Febronia Federico, Francesco Fulia

### Abstract

**Background:** Respiratory syncytial virus is the most important pathogen in lower respiratory tract infection in infants and young children. In high-risk populations it may develop severe, sometimes fatal, lower respiratory tract infections. A proportion of these infants require admission to intensive care units due to the severity of the condition and the level of care needed. Furthermore, we must consider the possible increased risk of asthma following RSV infection in infancy.

**Methods:** The aim of this work is to show how we strictly coordinated, during the 2008-2009 RSV season, the delivery of prophylaxis while minimizing drug cost through vial sharing and cohorting infants with a software performed through Visual Basic programming system.

**Results:** By using this method we have been able to obtain a saving of the 29.2% compared to the theoretical amount. No infant requested hospitalization for a RSV infection.

**Conclusions:** Such a model ensures all patients to receive appropriate immunization and thus positively influencing the cost-benefit of palivizumab prophylaxis. We hope that our model of care delivery will be of use to other hospitals.

#### Introduction

Respiratory syncytial virus (RSV) is the most important pathogen in lower respiratory tract infection in infants and young children.<sup>1</sup> It causes coughs and colds in winter season. The virus belongs to the same family as the human parainfluenza viruses and mumps and measles viruses. By 2 years of age, approximately 80% to 90% of children experience at least one episode of RSV infection. Although the majority of RSV infections are mild, high-risk populations such as premature infants (gestational age <33 weeks) or children with hemodynamically significant heart disease or with lung abnormalities or with immunodeficiency may develop severe, and sometimes fatal, lower respiratory tract infections.<sup>2</sup> In Italy, about 4-5000 RSV infected high-risk infants are hospitalized every year. A proportion of these infants require admission to

Autors Coletta and Fullia are with UOC Pediatria e UTIN; Coppolino is with the Dipartimento del Farmaco, Cittadella della Salute, Federico is with Servizio di Farmacia, Messina, Italy. Reprinted from BioMed Central, Italian Journal of Pediatrics, © 2010 Coletta et al., licensee BioMed Central Ltd. This is an open access article distributed under the terms of the Creative Commons Attribution License. intensive care units due to the severity of the condition and the level of care needed<sup>3</sup> and have higher mortality rates than healthy infants.

Furthermore, as potential long-term sequelae, we must consider the possible increased risk of asthma and allergies following RSV infection in infancy and its impact on life quality.<sup>4</sup> Palivizumab, an intramuscular humanized mouse monoclonal antibody, is used to reduce the risk of hospitalization secondary to RSV infection.<sup>5</sup> Seasonal prophylaxis with this antibody demonstrated clinical efficacy and satisfactory tolerability and it doesn't interfere with the administration of other vaccines.<sup>6,7</sup> The aim of this work is to show how we strictly coordinated, during the 2008-2009 RSV season, the delivery of prophylaxis while minimising drug cost through vial sharing.

#### **Materials and Methods**

The 2008-2009 RSV prophylaxis started in November 2008 and ended in April 2009. The vaccination program was designed to ensure that every eligible infant received RSV prophylaxis and his or her parents received necessary education to prevent RSV-related hospitalisation. The 4 bed UTIN unit at "Barone I. Romeo" Hospital, Patti (Messina) accepts 249 admissions per year. During the RSV prophylaxis season to 24 high-risk eligible children was administred the prophylaxis with palivizumab. High-risk criteria indicating the prophylaxis are reported in Table 1. The current recommended palivizumab dosage is 15mg/kg intramuscular injections (once per month for a total of 5 -6 doses during the RSV season). The cost of 50mg and 100mg vials of Synagis (Abbott Laboratories Limited) were 490.37€ and 814.35€

Table	1.	High-risk	criteria
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Evidence grade I	Infants born from 32 weeks of gestation or earlier to 12 months at the beginning of RSV season.
Evidence grade I	Infants and children younger than 24 months with CLD who required medical therapy (supplemental oxygen and/ or drugs).
Evidence grade I	24 months old or younger children receiving medication to control hemodybamically significant heart disease or diagnosed with moderate to severe pulmonary hypertension or diagnosed with cyanotic heart disease.
Evidence grade III	Infants, born at 32 to less 35 weeks of gestation, who are 12 months old, or younger, at the start of RSV season with at least two of the following risk factors: low weight at birth (<2.5Kg), exposure to environmental air pollutants or tobacco smoke, lack of breast-feed, twin birth, chest malformation, hematologic diseases, cystic fibrosis, school- aged siblings, congenital abnormalities of the airways, cancer, severe neuromuscular diseases, immunodefiency or living where the access to a hospital is difficult.



**Figure 1.** Screen of the developed software – This figure shows the main screen of the software used to schedule young patients during treatment. It automatically evaluated the amount of drug to be administered and then it sorts infants by weight suggesting the best way to minimize waste.

respectively. Synagis requires storage in a refrigerator (2 to  $8^{\circ}$ C) and once reconstituted, the palivizumab shelf life is estimated at six hours<sup>8</sup> and multidose use of single-use vials is proven safe.<sup>9</sup>

We used a collaborative framework for the delivery of RSV prophylaxis. The multidisciplinary team (pharmacists, physicians, nurses) collaborated to create a RSV prophylaxis program logic model, ensuring that each discipline's perspective of the program process was considered. For each program component, the team identified process and program objectives and outcomes.

Before the beginning of the prophylaxis all infants were visited and weighted and the obtained data were recorded on a database. In order to start the administration infants were grouped in four cohorts of five and one of four with a software performed by Coppolino S. through Visual Basic programming system. Visual basic is used to write Windows-based computer programs; by doing so you are not bound by the limitations of a particular "off-the shell" computer program. What is more you are able to design applications to meet your own specific needs.<sup>10</sup> This software requests only to insert infants names and their weight. By the clicking of a button the software calculates the palivizumab dosage, in mg, to be administrated to each infant, and following to the vial selected (50mg or 100mg one) automatically divide infants in groups, evidenced by different colours, to use as few vials as possible to minimise waste (Fig 1). Children marked with the same colour were scheduled to be vaccinated within the same day.

All data were automatically collected in a ".txt" file created to generate reports to be analyzed afterwards with common softwares. For each dose, infants attended the Ambulatory

 Table 2. Use of palivizumab and resources saving during 2008-2009

 campaign

	Theoretical single use	Real use with vial sharing	Saving
50mg vials	67	16	51
100mg vials	58	60	-2
mg wasted	3.176,88	777,08	2.399,80
Value	80.087,09€	56.706,92€	23.380,17€

Ward on five consecutive afternoons. The second dose was administred after 3 weeks and subsequent ones at 4 weekly intervals. In total 6800mg were bought and 6200mg were given to patients. During the season, adverse events following immunization did not occur.

#### Results

All infants successfully completed their full course of RSV prophylaxis and were followed for 150 days after the last scheduled injection. No one requested hospitalisation for RSV infection. We calculated theoretical vial usage if every infant had been individually dosed with one vial and compared this with our real use, obtained by using the cohorting software and vial sharing. The aggregate seasonal drug cost for the season was  $56.706,92 \in$  instead of  $80.087.19 \in$  with a saving of  $23.380,17 \in (29.2\% \text{ of theoretical amount})$ . At the individual partecipant level the average seasonal palivizumab prophylaxis cost was  $2372,69 \in$ . All data are reported in Table 2.

### Discussion

During all past seasonal prophylaxis with palivizumab we treated an almost constant number of high-risk eligible children for every year.

By using vial sharing and the above described software we obtained a drug cost saving of 25% compared to 2007-2008 season. Regarding the 2009-2010 campaign, in which we used vial sharing and software again, the cost saving was of about 2%, more or less the same of 2008-2009 season and linked to the children weight.

There are main other considerations besides costs in clinical decision making, but the careful use of resources must always be considered. In-hospital interdisciplinary communication and working relationships were a program strength point, particularly the relationship between pharmacy and "Pediatria e UTIN" staff. This strength was attributed to the ongoing opportunity for dialogue.

Like any expensive healthcare intervention, palivizumab immunization must be used judiciously. Our experience shows that it is possible to minimize the cost by an accurate cohorting and by multidose distribution with a maximising use of 100mg vials in preference to the more expensive 50mg vials for cost saving with no increased risk to patients. This does, however, required tight coordination between hospital pharmacist and ward and patient selection to discard ineligible children.

### Conclusions

The use of palivizumab can be optimized through a model in which children are prospectively identified and vials are shared. Such a model ensures all patients to receive appropriate immunization and thus positively influencing the cost-benefit of palivizumab prophylaxis. We hope that our model of care delivery to high-risk infants will be of use to other hospitals who seek to optimise delivery of their RSV immunization programs.

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# Spirometric Reference Values from a Sample of an Urban Greek Population

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### Abstract

**Background:** The need for updated spirometric reference values taking into account race/ethnic factors is widely accepted. The aim was to compare measured spirometric values with those predicted from the European Community for Steel and Coal statement and develop new lung function reference equations for the Greek population.

**Methods:** Measured values and reference equations were derived from 235 normal subjects (113 males, 122 females), aged 20-65 originated from the metropolitan area of Athens, Greece. Comparisons between predicted and measured values were performed using a repeated measures multivariate analysis of variance-MANOVA (Wilks'  $\lambda$  value).

**Results:** ECSC equations significantly overestimates/ underestimates spirometric values compared to measured values except for FEV<sub>1</sub> in females. In males measured FEV<sub>1</sub> was  $96.8\pm12.1\%$  and FVC was  $97.1\pm13.0\%$  and in females FEV<sub>1</sub> was  $102.3\pm11.3\%$  and FVC was  $104.3\pm13.1\%$  compared to predicted values according to ECSC/ERS statement. The FEV<sub>1</sub>/ FVC ratio was  $102.4\pm2.8\%$  and  $103.3\pm2.6\%$  of those predicted for males and females respectively. Based on stepwise multiple regression analyses we derived prediction equations for spirometric values in the Greek population from age and height. Weight and BMI was not found as a significant predictor of spirometric values.

**Conclusions:** The ECSC reference values are not applicable for the Greek population. Spirometric prediction equations should be derived from local population of the same ethnicity/race.

**Keywords:** Spirometry; Ethnicity/Race; Reference equations; Forced expiratory volume in 1 s; Vital capacity; General population.

### Introduction

Spirometry is the most important and most frequently performed pulmonary function test measuring inhaled and exhaled volumes of air as a function of time which are necessary for diagnosis, monitoring, evaluation of disability/impairment and public health purposes.<sup>1</sup> Spirometry includes forced vital capacity (FVC), forced expiratory volume in one second (FEV<sub>1</sub>), and ratio FEV<sub>1</sub> / FVC.<sup>1</sup>

The authors are with Athens University School of Nursing, ICU at "KAT" General Hospital, Athens, Greece. The study was partially funded by OPAP (Greek Organization of Football Prognostics). The study sponsors had no involvement in the study design, in the collection, analysis and interpretation of data; in the writing of the manuscript; and in the decision to submit the manuscript for publication.

Currently in Europe, the reference equations for spirometry published by European Community for Steel and Coal (ECSC) statement are used for people aged 18-70 yrs, with a height range of 155-195 cm in males, and 145-180 cm in females.<sup>2</sup> The recent American Thoracic Society/European Respiratory Society (ATS/ ERS) Task Force committee does not recommend any specific set of equations for use in Europe, but suggests the need for a new Europe-wide study to derive updated reference equations for lung function.<sup>3</sup> Also, suggests that the subjects being tested should be asked to identify their own race/ethnic group and even nation, and recognises and encourages the continuing interest of worldwide researchers in deriving and using race/ethnic/ nation-specific reference equations.3 Also, there are unexplained differences in lung function between ethnically similar nonsmoking symptom-free populations and centre variation between several European countries was found more likely to be due to true population differences.<sup>4</sup>

The purpose of the present study was to compare normal lung function values measured in a sample of an urban Greek population to the currently used prediction equation in Greece.<sup>2</sup> Also, to develop new prediction equations for  $FEV_1$  and FVC for the Greek population and to analyze the possible effect of miscalculation by the use of non-suitable pulmonary prediction equations.

### **Material and Methods**

The study protocol was approved by the local Ethics Committee Board. Informed consent was obtained from all subjects for the study purposes.

**Study subjects:** An urban population of Greece living in Athens (700 m above sea level) aged 20-65 years old were invited to participate in the study. These included students of Athens University, employees of our hospital and their families and individuals visiting our outpatient clinic for check up. We explained the purpose of the study and the procedure and then a clinical examination was performed based on a combination of the ECCS questionnaire on respiratory symptoms, physical examination, conventional chest radiograph and 12-lead resting electrocardiography.<sup>5</sup> A standardized questionnaire was used by the interviewing physician to identify eligible participants.

Exclusion criteria were: unacceptable spirometry, previous or current smoking habit, history of chest injuries; chest, abdominal, oral or facial pain, presence of denture; exposure to substances known to cause lung injury; known respiratory disease (asthma, pulmonary tuberculosis, emphysema or chronic bronchitis); respiratory symptoms during the last 12 months; hypertension; abnormal chest radiographs; major

**Table 1.** Distribution of age and sex in the reference sample. Data are presented as n (%).

Age yrs	М	F
20-29	30 (26.5)	25 (20.5)
30-39	28 (24.8)	27 (22.1)
40-49	29 (25.7)	29 (23.8)
50-59	19 (16.8)	27 (22.1)
60-65	7 (6.2)	14 (11.5)
Total	113 (100)	122 (100)

M: males; F: females

ECG abnormalities; history of myocardial infarction; diabetes; dementia or confusional state, and the use of any drug and especially diuretics, cardiac glycosides or *b*-adrenergic blocking agents.<sup>6</sup>

### Methods

Spirometry was performed following ATS/ERS Task Force recommendations.<sup>1,3,6</sup> All tests were performed by two physicians well educated and experienced in spirometry. Spirometry was performed using a Schiller SPIROVIT SP-1 spirometer (Schiller, Switzerland). This spirometer is ATS/ERS approved, fulfilling the criteria for minimal recommendations for spirometry systems and calibrated regularly.<sup>1</sup>

Height was measured at the nearest 0.5 cm without shoes, in a standing position with the feet together, with the patient erect and looking straight ahead (Frankfort position). Subjects were weighted without shoes wearing indoor clothing. Age was also recorded according to birthday to the nearest 0.5 year. BMI, and BSA were derived from height and weight.

Spirometry was performed in sitting position in armed chairs in our outpatient clinic wearing a nose clip. Subjects were relaxed did not smoke, exercise, consume alcohol, wear heavy clothing or eat large meal before testing. The procedure was performed at the same room between 8.00 – 10.00 am and barometric pressure, temperature and relative humidity were registered every morning. Hygiene and infection control measures were undertaken as recommended.

Spirometry flow/volume loops were conducted in accordance with ATS recommendations.<sup>1</sup> At least three acceptable trials were required, defined as a good start of test (extrapolated volume of <5% of FVC or 0.15 L, whichever was larger), at least 6 s of expiration and a plateau in the volume/time curve (change in volume <30 mL for  $\geq$ 2 s). As recommended by the ATS, data that did not meet reproducibility criteria were not excluded, but subjects were asked to perform up to a maximum of eight manoeuvres in an attempt to obtain reproducible results. The highest FEV<sub>1</sub>, and FVC from tests of acceptable quality were used for analysis.<sup>7</sup>

### **Statistical Analysis**

Numerical data are expressed as mean  $\pm$  standard deviation. Statistical significance was considered at the level of p<0.05. Measured spirometric values of FEV<sub>1</sub>, FVC and the ratio FEV<sub>1</sub>/ FVC, were compared to those obtained from the ECSC prediction equation using a paired sample t-test. Stepwise multiple regression analyses were used to develop prediction equations for FEV<sub>1</sub>, FVC and FEV<sub>1</sub>/FVC (dependent variables), from age, height and weight (independent variables) separate across gender. The variables inclusion criterion in the equation was based on the R<sup>2</sup> change and was assessed in the 0.05

Table 2. Summary statistics for males and females

Variable	Mean	SD	Min	Max
Males (n=113)				
Age (years)	38.3	12.9	20	65
Weight (kg)	86.1	13.2	56	130
Height (cm)	177.7	6.6	162	191
FEV <sub>1</sub> (ml)	3876	621.1	2360	6120
FVC (ml)	4715	744.5	3150	7140
FEV1/ FVC (%)	82.3	5.8	78.8	89.9
FEV <sub>1</sub> (ml)*	4006	515.5	2680	4910
FVC (ml)*	4856	572.8	3370	5900
FEV1/ FVC (%)*	80.4	2.1	73.2	85.0
Females (n=122)				
Age (years)	41.7	13.9	20	64
Weight (kg)	66.5	10.5	48	108
Height (cm)	161.4	7.2	143	180
FEV <sub>1</sub> (ml)	2779	605.1	1360	4940
FVC (ml)	3294	686.4	1860	5660
FEV <sub>1</sub> / FVC (%)	84.3	6.5	80.2	88.4
FEV1 (ml)*	2717	532.3	1700	3890
FVC (ml)*	3157	572.1	1910	4430
FEV <sub>1</sub> / FVC (%)*	81.60	2.5	74.10	92.10

FVC=forced vital capacity, FEV<sub>1</sub>=forced expiratory volume in one second \*: Values obtained from the prediction equation of Quanjer

Table 3. Ratios of measured/predicted values for  $\mathsf{FEV}_1,\,\mathsf{FVC}$  and  $\mathsf{FEV}_1/\mathsf{FVC}$  for males and females

Parameter	Males measured/predicted (%)	Females measured/predicted (%)
FEV <sub>1</sub>	96.8±12.1	102.3±11.3
FVC	97.1±13.0	104.3±13.1
FEV <sub>1</sub> / FVC	102.4±2.8	103.3±2.6

FVC=forced vital capacity, FEV<sub>1</sub>=forced expiratory volume in one second

significance level. The statistical package for the social sciences (SPSS) was used for statistical analysis.

The lowest standard error of the estimate (SEE) was determined and the lower limit of normal (LLN) was calculated as the lower fifth lung function percentile. The LLN for each pulmonary function test was calculated as the mean predicted value minus 1.645 times the SEE. The McNemar statistical analysis was used to compare the percentages of individuals classified differently as above or below the LLN by the two prediction equations used.<sup>8</sup>

The difference between measured values from the present study and those predicted from ECSC equation are given as Bland-Altman plots as difference vs average.<sup>2,9</sup>

### Results

**Descriptive statistics:** Of the 550 individuals approached 235 met the inclusion criteria and divided according to sex which resulted in two groups of 113 males and 122 females. Distribution of age and sex of the reference sample is shown in Table 1. The summary statistics, separate for males and females, are shown in Table 2 along with predicted values for FEV<sub>1</sub> & FVC and FEV<sub>1</sub> & FVC according to Quanjer et al.<sup>2</sup> Data distribution, tested with the Kolmogorov-Smirnov test, showed non significant results indicating normality for all measured variables, separate across gender (p>0.05).

**Comparisons with existing reference values:** For males FEV<sub>1</sub> and FVC predicted from Quanjer equation were significantly

Table 4. Prediction equations coefficients derived from the present study	
versus the ECSC norms.	

	Ethnic	Intercept	Age(y)	Height (cm)	R <sup>2</sup>	SEE
Males						
FVC	ECSC	-4.345	-0.026	5.757	N.A	0.610
	Greeks	-3.454	-0.017	0.050	0.336	0.607
FEV <sub>1</sub>	ECSC	-2.492	-0.029	4.301	N.A	0.510
	Greeks	-1.256	-0.020	0.033	0.367	0.484
FEV <sub>1</sub> /FVC	ECSC	87.21	-0.179		N.A	7.170
	Greeks	117.53	-0.130	-0.169	0.091	5.327
Females						
FVC	ECSC	-2.887	-0.026	4.426	N.A	0.430
	Greeks	-2.134	-0.022	0.039	0.556	0.411
FEV <sub>1</sub>	ECSC	-2.604	-0.025	3.953	N.A	0.380
	Greeks	-1.008	-0.023	0.029	0.540	0.378
FEV <sub>1</sub> /FVC	ECSC	89.10	-0.192		N.A	6.510
	Greeks	108.43	-0.111	-0.122	0.065	4.968

ECSC=European Community for Steel and Coal, SEE=standard error of the estimate, FVC=forced vital capacity, FEV<sub>1</sub>=forced expiratory volume in one second, R<sup>2</sup>=higher explained variance, SEE = Standard Error of the Estimate, N.A = Not available

**Table 5.** Bias, SD and the 95% limits of agreement according to Bland-Altman analysis. FVC = forced vital capacity,  $FEV_1$  = forced expiratory volume in one second.

	Bias	SD	95% limit of agreement		
Males					
FEV <sub>1</sub> (ml)	-146.9	447.5	-1024.1 to 730.3		
FVC (ml)	-158.8	559.7	-1255.8 to 938.3		
FEV <sub>1</sub> /FVC (%)	2.2	5.4	-8.5 to 12.9		
Females					
FEV <sub>1</sub> (ml)	47.4	328.1	-595.7 to 690.6		
FVC (ml)	120.9	353.3	-571.6 to 813.5		
FEV <sub>1</sub> /FVC (%)	2.9	5.8	-8.5 to 14.3		

higher (p=0.004, p=0.009, respectively) compared to those measured in the present study. Also, measured FEV<sub>1</sub>/ FVC were significantly higher than those predicted from the equation of Quanjer (p=0.000). For females FEV<sub>1</sub>, measured were no significantly different compared to those predicted by Quanjer equation. However, FVC and FEV<sub>1</sub>/ FVC measured were significantly higher compared to those predicted from Quanjer equation [p=0.000, p=0.000, respectively). A comparison of measured/predicted values for FEV<sub>1</sub>, FVC and FEV<sub>1</sub>/ FVC is shown in Table 3. In males measured FEV<sub>1</sub> and FVC were by 2.9-3.2% lower and in females were 2.3-4.3% higher than predicted values. The differences were statistically significant. Figure 1 shows mean observed FVC and FEV<sub>1</sub> values in 5-yr interval with SEM. From the age of 35-39, FEV<sub>1</sub> and FVC declined with age in both sexes.

**Derivation of new reference equations:** Stepwise multiple regression analyses were used to predict the spirometric measures from age, height and weight separate across gender. For males, the results were as follows: a) The FEV<sub>1</sub> was significantly predicted from age ( $R^2$  change=0.250, F=35.740, p=0.000) and height ( $R^2$  change=0.117, F change=19.568, p=0.000), while weight ( $R^2$  change=0.005, F change=0.788, p=0.377) did not emerge as a significant predictor. b) The

FVC was significantly predicted from age ( $R^2$  change=0.161, F change=20.571, p=0.000) and height ( $R^2$  change=0.175, F change=27.892, p=0.000), while weight ( $R^2$  change=0.004, F change=0.710, p=0.401) did not emerge as a significant predictor.

For females, the results were as follows: a) The FEV<sub>1</sub> was significantly predicted from age (R<sup>2</sup> change=0.424, F=78.90, p=0.000) and height (R<sup>2</sup> change=0.115, F change=26.58, p=0.000), while weight (R<sup>2</sup> change=0.000, F change=0.041, p=0.841) did not emerge as a significant predictor. b) The FVC was significantly predicted from age (R<sup>2</sup> change=0.386, F change=67.23, p=0.000) and height (R<sup>2</sup> change=0.170, F change=40.67, p=0.000), while weight (R<sup>2</sup> change=0.001, F change=0.231, p=0.632) did not emerge as a significant predictor. The respective regression equations for FEV<sub>1</sub>, FVC and FEV<sub>1</sub>/FVC for both sexes as well as the commonly used equation in Greece of the ECSC are summarized in Table 4.

Figure 2 presents the Bland-Altman plots of the difference vs. average separately by sex for FEV<sub>1</sub>, FVC and FEV<sub>1</sub>/FVC. Bias  $\pm$ SD and the 95% limit of agreement according to Bland-Altman analysis for FEV<sub>1</sub>, FVC and FEV<sub>1</sub>/FVC is shown in Table 5. The plots for FEV<sub>1</sub> and FVC for both sexes were symmetrical and unbiased and the magnitude of difference ranged from 47.4 to 158.8 ml which could be clinically significant. For FEV<sub>1</sub>/FVC ratio the variability was not consistent. The scatter around the bias line was larger as the average was higher or lower. Also, the difference between the two equations tends to get larger as the average increased.

To further evaluate the differences in the estimation and the effect of miscalculation, which may lead to the misclassification of individuals, we calculated the LLN according to the ECSC equations as well as the present study equations for each individual and compared the percentage of individuals misclassified.<sup>2,8</sup> The results are shown in Table 6 and indicate that a significant percentage of normal individuals are misclassified as abnormal while they are normal (column 4).

### Discussion

Predicted values and reference equations should be obtained from studies of a representative sample of "normal" or "healthy" subjects of a general population with the same anthropometric (sex, age and height) and ethnic characteristics.<sup>3</sup>

	, ,				
	ECSC>LLN Local>LLN	ECSC <lln Local<lln< td=""><td>ECSC&gt;LLN Local<lln< td=""><td>ECSC<lln Local&gt;LLN</lln </td><td><math>\chi^2</math> p value</td></lln<></td></lln<></lln 	ECSC>LLN Local <lln< td=""><td>ECSC<lln Local&gt;LLN</lln </td><td><math>\chi^2</math> p value</td></lln<>	ECSC <lln Local&gt;LLN</lln 	$\chi^2$ p value
Males					
FVC	105 (96.3%)	1 (0.9%)	0 (0%)	3 (2.8%)	26.493 < 0.001
FEV <sub>1</sub>	104 (95.4%)	1 (0.9%)	0 (0%)	4 (3.7%)	20.993 < 0.001
FEV <sub>1</sub> /FVC	109 (100%)	0 (0%)	0 (0%)	0 (0%)	N.A
Females					
FVC	102 (93.6%)	4 (3.7%)	0 (0%)	3 (2.8%)	60.506 < 0.001
FEV <sub>1</sub>	101 (92.7%)	4 (3.7%)	0 (0%)	4 (3.7%)	52.424 < 0.001
FEV <sub>1</sub> /FVC	109 (100%)	0 (0%)	0 (0%)	0 (0%)	N.A

**Table 6:** Numbers and percentages of individuals classified as below the LLN by the ECSC and our prediction equations. FVC=forced vital capacity, FEV<sub>1</sub>=forced expiratory volume in one second



**Figure 1.** Mean observed FVC and FEV<sub>1</sub> in 5-yr interval with SEM in males and females. FVC = forced vital capacity,  $FEV_1$  = forced expiratory volume in one second.

In this study we found that ECSC prediction equations significantly overestimates  $FEV_1$  and FVC in males but underestimates FVC in females. Also that ECSC prediction equation significantly underestimates  $FEV_1/FVC$  ratio for both sexes which may affect the diagnosis of airway obstruction which is in accordance with the literature.<sup>10</sup>

These differences may be attributed to cohort effects (changes in general health status, lung function over time, measurement devices). Also, to the fact that the ECSC prediction equations were derived from subjects including smokers in the years 1954-1980, from different study populations and data sets.

However, differences observed in our study may be attributed in part to racial differences and validate the hypothesis that lung function may vary according to ethnicity/nation as pointed out by the ATS/ERS Task Force.<sup>3</sup> These findings further support the need for adding racial/nation contribution to lung function prediction equations. It has been suggested that racial/ethnic group could be an important source of inter-individual variations in studied populations and an estimated variability due to racial/ ethnic factor is around  $\pm 10\%$ .<sup>11,12</sup> This makes sense since 27% of inter-individual variations for spirometric values still remain unexplained.<sup>13</sup>

However, differences in the normal lung function parameters due to ethnicity/nation are not well defined and there is currently not known valid explanation.<sup>14,15</sup> It has been suggested that these differences may be explained, in part, by differences in trunk length relative to standing height, but there are also differences in alveolar size, airway dimensions, fat-free mass, chest dimensions and strength of respiratory muscles.<sup>3,16-19</sup>

Also, it has been suggested that the use of ethnicity adjustment factors is not as good as the creation of specific race/ethnic reference equations.<sup>20</sup> For this purpose ethnic/race specific equations are recommended.<sup>1,3</sup> Also, the ECSC and the ATS/ ERS have both published comprehensive listings of published reference equations for spirometry.<sup>2,10</sup>

A large number of studies examining the effect of ethnicity/ race on lung function values and prediction equations have been published in the last 15 yrs showing the ethnicity effect on spirometric values.<sup>21-28</sup>

By comparing the classification of individuals as "normal" or below the LLN using the present study prediction equation and the commonly used ECSC, we found that by using the ECSC prediction equation, there is a significant proportion of individuals that are misclassified as normal compared with the present prediction equation for the lung function parameters tested in both sexes. Also, a significant proportion of individuals could be classified as below LNN according to ECSC prediction equation but normal with the present prediction equation for the lung function parameters tested in both sexes (Table 6). These findings may have significant clinical implications for diagnostic purposes.

Our sample of 113 males and 122 females was appropriate and representative of healthy subjects in Greek general population. The ATS/ERS Task Force committee suggest that for spirometry, a relatively large number of subjects (ie n=100) is necessary to be confident that a significant difference between the published reference equations and the values from the local community does not exist.<sup>3,10</sup>

Another finding of our study is that according to stepwise multiple regression analyses, weight may be not an important parameter in predicting spirometric values. However, we derived equations including body weight or body mass index (BMI); (data not shown) for both sexes and we found that adding weight or BMI in the equations does not significantly improves the predictive value of the equations. We compared predicted spirometric values using Quanjer et al and our equations with or without body weight or BMI. We found significant differences in spirometric values between those predicted by Quanjer et al and our equations but not between our equations with or without body weight/BMI. Our findings suggest that the coefficients of gender, age and height but not weight nor BMI were highly significant to predict lung volumes are in accordance with previous published data and the commonly used equations.<sup>2,20,26,27</sup> Our finding may reflect the increased prevalence of overweighed in the Greek population of these ages which may eliminate the significance of body weight on spirometric values.<sup>29,30</sup> In a previous publication by ours regarding reference equations in Greek elderly, we found that the variable with the highest contribution to the FVC and FEV<sub>1</sub> prediction equation was height and age followed by weight having the less contribution.<sup>22</sup>

Several limitations of our study include: Due to the crosssectional nature of our study, our data are subject of cohort bias due to host and environmental factors. Also, the relatively small number of subjects compared to other studies and the method of selection of participants may affect the validity of our results. Our sample size is sufficient to determine whether the ECSC prediction equations are appropriate for the testing population but the validation of our study derived prediction equations requires larger population.

#### Conclusions

In conclusion, we found that ECSC equation significantly overestimates/underestimates normal lung function values in a sample of Greek urban population leading to misclassification of a significant percentage of individuals. We also developed



**Figure 2.** Bland-Altman plots showing the difference for FEV<sub>1</sub> (A, B), FVC (C, D) and FEV<sub>1</sub>/FVC (E, F) for males (A, C, E) and females (B, D, F) between the developed equation versus those of Quanjer et al.<sup>2</sup> FVC = forced vital capacity, FEV<sub>1</sub> = forced expiratory volume in one second.

new prediction equations for common lung function parameters which however cannot be generalized out of Athens. Our data further support the necessity of new prediction equations worldwide which should be derived from large local population based survey of the same ethnicity/race/nationality because they may have important clinical implications both for the diagnosis and management of patients with obstructive lung disease and healthcare systems.<sup>28</sup> The participation and support of organizations (eg lungfunction.org) may help for this purpose.

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## Risk of Postoperative Hypoxemia in Ambulatory Orthopedic Surgery Patients with Diagnosis of Obstructive Sleep Apnea

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#### Abstract

**Background:** It is unclear when it is safe to discharge patients with a diagnosis of Obstructive Sleep Apnea (OSA) after ambulatory surgical procedures due to concern for postoperative respiratory compromise and hypoxemia. Our OSA patients undergoing ambulatory-type orthopedic procedures are monitored overnight in the PACU, thus we reviewed patient records to determine incidence of complications.

**Methods:** Two hundred and six charts of patients with preoperative diagnosis of OSA based on ICD-9 codes were reviewed for outcomes including episodes of hypoxemia. Univariate analysis followed by logistic regression and propensity analysis was performed to determine independent risk factors for hypoxemia and association with adverse outcomes.

**Results:** The majority of patients had regional anesthesia (95%). Thirty four percent of patients had hypoxemia in the PACU. Initial risk factors for hypoxemia identified by univariate analysis were BMI  $\geq$  35, increased age, history of COPD, upper extremity procedure, and use of peripheral nerve block. Independent risk factors identified by logistic regression were history of COPD (OR 3.64 with 95% CI 1.03-12.88) and upper extremity procedure (2.53, 1.36-4.68). After adjustment with propensity scores, adverse events were rare, and unplanned hospital admission after PACU stay was not increased with hypoxemia (11% vs 16%).

**Conclusions:** Episodes of postoperative hypoxemia in OSA patients undergoing ambulatory surgery with regional anesthesia are not associated with increased adverse outcomes or unplanned hospital admission.

#### Background

Ambulatory anesthesia is increasing in worldwide popularity, and approximately 60% of procedures in the United States in 2007 were performed on an ambulatory basis.<sup>1</sup> However, it remains unclear whether it is safe to immediately discharge patients with a diagnosis of obstructive sleep apnea (OSA) immediately home after ambulatory procedures. OSA is associated with increased morbidity due to hypoxemia, and

The authors are with the Department of Anesthesiology, Hospital for Special Surgery, Weill College of Medicine of Cornell University, New York. Reprinted from BioMed Central, Patient Safety in Surgery, © 2010 Liu et al; licensee BioMed Central Ltd. This is an Open Access article distributed under the terms of the Creative Commons Attribution License. estimates for prevalence of OSA range from 10-64%.<sup>2</sup> Postoperative apnea may be more severe due to perioperative disturbances in sleep architecture3 and respiratory depressant effects of postoperative analgesics.<sup>4</sup> Current clinical guidelines for OSA are based only on expert opinion,<sup>2,5,6</sup> and incidence of respiratory compromise after ambulatory procedures in OSA patients is unknown.<sup>7</sup> Hospital for Special Surgery is an orthopedic surgical hospital and has had a policy since December, 2005 that patients with a diagnosis of OSA spend the night in our post anesthesia care unit (PACU) for continuous monitoring including pulse oximetry after ambulatory surgical procedures. Thus, we retrospectively reviewed charts of patients with a preoperative diagnosis of OSA to determine if there was an association with hypoxemia and adverse outcomes including unplanned subsequent hospital admission.

### Methods

After obtaining Institutional Review Board (IRB) approval, 206 patients with a preoperative diagnosis of OSA undergoing ambulatory surgery from December, 2005 to March, 2009 were identified by using ICD-9 codes 327.23 and 780.57 for OSA. Their charts were reviewed and retrospective data abstracted. Since the research did not present more than minimal risk of harm to the subjects or their privacy, the IRB granted waivers for informed consent and Health Insurance Portability and Accountability Act (HIPAA) authorization. All patients spent at least the first postoperative night in the PACU with initially 2 liters/min oxygen delivery via nasal canula. All patients were continually monitored with pulse oximetry and other standard non-invasive monitors. Collected data included patient characteristics, type of procedure, type of anesthetic, intraoperative data, postoperative course and complications during hospitalization, and type of postoperative analgesia. Hypoxemia was defined as a Spo2 <95% on pulse oximetry.

#### **Statistical analysis**

Episode of hypoxemia was the primary outcome. Descriptive analysis was initially performed to determine if any differences in perioperative characteristics (Table 1) were apparent between groups that had at least one episode of hypoxemia (mild or severe) versus those who did not. Perioperative characteristics that appeared to differ between groups were then compared with univariate analysis (t test or chi square test) to screen for potential risk factors for hypoxemia. Potential risk factors that had a p<0.05 on univariate analysis were then used for multivariate logistic regression to determine independent risk factors for hypoxemia (mild

#### Table 1: Selected perioperative characteristics

Characteristic	No hypoxemia (n = 135)	Hypoxemia (n = 71)	
Age *(yrs, mean/SD)	55 ± 11	58 ± 12	
Gender (M/F, %)	79%/21%	77%/23%	
BMI (mean/SD)*	32 ± 6	35 ± 7	
ASA physical status (1/2/3/4, %)	1/61/37/1	1/47/52/0	
Past Medical History			
CPAP at home (%)	53%	54%	
COPD (%)*	3%	11%	
Procedure*			
Knee arthroscopy (%)	25%	18%	
Knee ACL Repair (%)	3%	3%	
Hand/Forearm (%)	12%	20%	
Shoulder arthroscopy (%)	33%	47%	
Foot/Ankle (%)	12%	7%	
Other upper extremity (%)	4%	4%	
Other lower extremity (%)	11%	1%	
Anesthesia*			
General only (%)	6%	4%	
General + regional (%)	3%	3%	
Regional only	91%	93%	
Spinal/Epidural (%)	46%	28%	
Interscalene block (%)	25%	35%	
Other nerve block (%)	21%	31%	
Postoperative Analgesia			
Oral Opioids (%)	85%	92%	
NSAIDs (%)	36%	39%	
IV Opioids (%)	24%	32%	

\* = Identified as potential risk factor by univariate analysis Upper extremity vs lower extremity. Regional vs General

or severe). Logistic regression was performed with both discrete and continuous predictors and was adjusted for type of procedure. A combination of forwards and backwards stepwise methods was used for logistic model selection.

Unadjusted association between hypoxemia with adverse outcomes was tested with either Chi square or T test. Adjusted association between hypoxemia with adverse outcomes was examined with propensity analysis to reduce bias between groups with and without hypoxemia. Propensity scores for each patient were created based on the above identified risk factors for hypoxemia.<sup>8</sup> A propensity score is the probability of assignment to a particular condition based on a set of known covariates, and propensity analysis performs statistical adjustment with propensity scores to reduce selection bias by equating patients based on these covariates. Thus,

#### Table 2: Incidence and risk of hypoxemia for individual and combinations of risk factors

Number of risk factors	Risk factors combinations	Incidence of hypoxemia (% and number of pts)	Odds
0	None	22% (20)	0.35
1	COPD	33% (1)	0.5
	Upper extremity procedure	41% (43)	0.71
2	COPD + Upper extremity procedure	78% (7)	2.59

Odds were calculated from logistic regression. Individual odds ratios can be calculated for any pair. For example the odds ratio for both risk factors versus just COPD is (2.59/0.5 = 5.18)

Table	3:	Adverse	outcomes
	•••		

Outcome	No hypoxemia (N = 135)	Hypoxemia (N = 71)
CPAP at home + subsequent routine PACU use (%)	33	41
Emergent CPAP (%)	0	0
Increase in oxygen delivery (%)	16	37*
Incidence of postoperative hypertension (%)	33	41
Need treatment for hypertension (%)	4	4
Need for postoperative hospital admission from PACU (%)	16	11
Reasons for hospital admission		
Physical Therapy (%)	45	13
Intravenous antibiotics (%)	9	13
Pain Control (%)	14	13
Infectious Complication (%)	18	38
Radiation therapy (%)	0	13
Other (%)**	14	13

\* = P < 0.05. \*\* No patients admitted for persistent hypoxemia

propensity analysis was performed by logistic regression with propensity scores and hypoxemia as independent variables against any adverse outcome that had unadjusted statistical differences between groups with and without hypoxemia.<sup>9,10</sup> P<0.05 was considered as significant for all analyses.

#### Results

Table 1 displays selected perioperative characteristics. As expected in an exclusively OSA population,<sup>6</sup> our patients were predominantly male (78%), older (mean age 56), overweight (101 kg mean), and 54% used CPAP at home. The majority (95%) of patients underwent regional anesthesia. In the PACU, thirty four percent of patients had at least one episode of hypoxemia. Potential risk factors for hypoxemia identified by univariate analysis were BMI  $\geq$  35, increased age, history of chronic obstructive pulmonary disease (COPD), upper extremity procedure, and use of peripheral nerve block. From these, independent risk factors identified by logistic regression were history of COPD (OR 3.64 with 95% CI 1.03-12.88) and upper extremity procedure (2.53, 1.36-4.68). The Hosmer and Lemeshow test was performed and indicated a good fit of the data for the regression model (p=0.87). Incidences of hypoxemia (22-78%) varied with combinations of risk factors (Table 2).

None of our patients suffered from major complications. Incidences of postoperative hypertension, need for continuous positive airway pressure (CPAP), and need for hospital admission after required PACU stay were not associated with hypoxemia (Table 3). Only a need for increased oxygen flow was significantly associated with hypoxemia which remained significant after propensity analysis.

#### Discussion

Episodes of postoperative hypoxemia in OSA patients undergoing ambulatory surgery were not associated with increased adverse outcomes or unplanned hospital admission. The only previous study of OSA patients undergoing ambulatory surgery was a retrospective case series that matched 234 patients with OSA (diagnosed with polysomnography) against an equal number of normal patients,<sup>11</sup> but did not perform overnight respiratory monitoring as in our study. No patients suffered from a serious adverse event, and similar rates of unplanned hospital admission (24% vs 19%) were reported for the two groups. Our rates of adverse outcomes and unplanned hospital admission were similar to this previous study,<sup>11</sup> which suggests external validity for our data. As neither a diagnosis of *Continued on page 58...* 

### **Computed Tomography Assessment of Exogenous Surfactant-Induced Lung Reaeration in Patients With Acute Lung Injury**

Qin Lu, Mao Zhang, Cassio Girardi, Belaïd Bouhemad, Jozef Kesecioglu, Jean-Jacques Rouby

### Abstract

**Introduction:** Previous randomized trials failed to demonstrate a decrease in mortality of patients with acute lung injury treated by exogenous surfactant. The aim of this prospective randomized study was to evaluate the effects of exogenous porcine-derived surfactant on pulmonary reaeration and lung tissue in patients with acute lung injury and acute respiratory distress syndrome (ALI/ARDS).

**Methods:** Twenty patients with ALJ/ARDS were studied (10 treated by surfactant and 10 controls) in whom a spiral thoracic computed tomography scan was acquired before (baseline), 39 hours and 7 days after the first surfactant administration. In the surfactant group, 3 doses of porcine-derived lung surfactant (200 mg/kg/dose) were instilled in both lungs at 0, 12 and 36 hours. Each instillation was followed by recruitment maneuvers. Gas and tissue volumes were measured separately in poorly/nonaerated and normally aerated lung areas before and seven days after the first surfactant administration. Surfactant-induced lung reaeration was defined as an increase in gas volume in poorly/non-aerated lung areas between day seven and baseline compared to the control group.

**Results:** At day seven, surfactant induced a significant increase in volume of gas in poorly/non-aerated lung areas  $(320\pm125)$  ml versus  $135\pm161$  ml in controls, P=0.01) and a significant increase in volume of tissue in normally aerated lung areas  $(189\pm179)$  ml versus  $-15\pm105$  ml in controls, P<0.01). PaO2/ FiO2 ratio was not different between the surfactant treated group and control group after surfactant replacement.

**Conclusions:** Intratracheal surfactant replacement induces a significant and prolonged lung reaeration. It also induces a significant increase in lung tissue in normally aerated lung areas, whose mechanisms remain to be elucidated.

#### Introduction

Acute respiratory distress syndrome or acute lung injury

Authors Lu, Bouhemad and Rouby are with the Multidisciplinary Intensive Care Unit, Department of Anesthesiology and Critical Care Medicine, Assistance Publique-Hôpitaux de Paris, La Pitié-Salpêtrière Hospital, France; Zhang is with the Department of Emergency Medicine, Second Affiliated Hospital, Zhejiang University, School of Medicine, Hangzhou, China; Girardi is with the Department of Anesthesiology, Federal University of Sao Paulo, Brazil; Kesecioglu is with the Department of Intensive Care Medicine, University Medical Center Utrecht, The Netherlands. Reprinted from BioMed Central, Critical Care, © 2010 Lu et al, licensee BioMed Central Ltd. This is an open access article distributed under the terms of the Creative Commons Attribution License. (ARDS/ALI) is characterized by hypoxemia, high permeability type pulmonary edema, decreased lung compliance and loss of aeration. Inactivation or deficiency of surfactant is directly involved in ARDS pathophysiology.<sup>1</sup> Pre-clinical experiments show that mechanical ventilation itself can also have a deleterious impact on endogenous surfactant.<sup>2,3</sup>

Currently, intratracheal replacement of surfactant is recognized as the standard therapy for premature neonates and children with acute respiratory failure.<sup>45</sup> In patients with ARDS/ALI, despite the efficacy of surfactant on arterial oxygenation and lung compliance,<sup>6</sup> randomized trials have failed to demonstrate a decrease in mortality.7,8 Inadequate dose of surfactant and short treatment duration may account for the lack of beneficial effect on mortality rate.9,10 Administration of natural surfactant rather than synthetic surfactant increases the treatment efficacy and decreases mortality rates in neonates.11 A recent randomized multicenter trial, however, failed to demonstrate any improvement in mortality following the bolus administration of exogenous natural porcine surfactant in patients with early ALI/ARDS.<sup>12</sup> Moreover, oxygenation was not improved by surfactant replacement in this trial. In ARDS/ALI, loss of lung aeration does not have a uniform distribution. In supine position, aeration loss largely predominates in lower lobes as a result of external compression by abdomen and heart.<sup>13,14</sup> The deficiency of surfactant also contributes to the loss of lung aeration. As a result, in a vast majority of patients fulfilling the ALI/ARDS criteria, upper lobes remain entirely or partly normally aerated.<sup>15</sup> During mechanical ventilation with positive end-expiratory pressure (PEEP), alveolar recruitment and lung overinflation occur simultaneously in different parts of the lung.<sup>16,17</sup> If natural surfactant administered by intratracheal route reaches the distal lung, it should logically reaerate nonaerated lung regions, induce a more homogenous regional distribution of tidal volume and PEEP, and consequently result in a reduction of mechanical ventilation-induced lung injury.

Computed tomography (CT) is the reference method for measuring alveolar recruitment<sup>18</sup> because it provides the possibility of performing a regional analysis taking into account normally and poorly/nonaerated lung regions, separately. Alveolar recruitment can be defined as the volume of gas penetrating into poorly and nonaerated lung areas following various therapies such as PEEP, recruitment maneuver or surfactant administration. Based on this CT method, we undertook a prospective randomized study aimed at evaluating the effect of porcine-derived lung surfactant administered by intratracheal route on lung reaeration in patients with ARDS/ALI.



**Figure 1.** Representative computed tomography (CT) sections of upper and lower lobes obtained at baseline and day 7 in a patient with acute respiratory distress syndrome. CT sections at baseline and day 7 are at the same lung region as attested by the anatomical landmarks present on the rough images at baseline and day7 (aortic arch and vascular divisions for upper lobe CT sections). As previously described [18], poorly and nonaerated lung areas of right and left upper and lower lobes are manually delineated (dashed line) at baseline (before HL-10 administration) with the aid of the software Lungview) that identifies poorly and nonaerated lung areas in light gray and red, respectively. Delineation performed at baseline is manually "transposed" to the CT section corresponding to the same anatomical level obtained at day 7. Surfactant-induced lung reaeration is defined as the increase in gas volume within the delineated zone between day 7 and baseline. The same process is repeated on each CT section in order to assess overall surfactantinduced lung reaeration.

#### **Materials and Methods**

Study design: The present study is a part of an international, multicenter, randomized, controlled, open, parallel group study conducted between January 2003 and May 2004.12 Twenty mechanically ventilated critically ill patients admitted to the multidisciplinary intensive care unit of La Pitié-Salpêtrière hospital (University Pierre et Marie Curie of Paris 6, France) for ALI/ARDS were included in the study and randomized either to the surfactant group (3 doses of surfactant in addition to usual care, n=10) or to the control group (usual care alone, n=10). Inclusion was restricted to the first 60 hours from the start of mechanical ventilation. Exclusion criteria were: age ≤ 18, acute bronchial asthma attack or suspected pulmonary thrombo-embolism, daily medication for chronic obstructive pulmonary disease at time of admission, need for mechanical ventilation for more than 48 hours continuously within 1 month prior to the current ventilation period, pneumonectomy or lobectomy, untreated pneumothorax, tracheostomy, surgical procedures under general anaesthesia performed within 6 hours, mean arterial blood pressure <50 mmHg in spite of adequate fluid administration and/or need for vasoactive drugs, PaO2 <75 mmHg with a FiO2=1.0 not responding to adjustment of PEEP, head injury, life expectancy less than 3 months due to primary disease and treatment with any investigational drug within the previous 4 weeks. The institutional review board of La Pitié-Salpêtrière approved the study protocol. Two informed consents were obtained from each patient or their next of kin: one for inclusion in the international, multicenter, randomized, controlled study conducted between January 2003 and May 2004<sup>12</sup> and another for the present study.

**Surfactant administration:** A freeze-dried natural surfactant isolated from pig lungs (HL-10, Leo Pharmaceutical Products, Ballerup, Denmark; Halas Pharma GmbH, Oldenburg, Germany) composed of approximately 90-95% phospholipids, 1-2% surfactant hydrophobic proteins (surfactant proteins SP-B and SP-C) and other lipids was administered to the patients. The product was delivered as a solution containing 50 mg/ml of HL-10 (100 ml vials containing 3 g of HL-10 dispersed in 60 ml

warm 37-40°C saline). Baseline was defined as the time after randomization preceding the first large bolus of surfactant. Up to three doses of HL-10, totalling a maximum cumulative amount of 600 mg/kg (200 mg/kg/dose) were instilled at 0 hour, 12 and 36 hours thereafter. Before each large bolus, patients were sedated and paralyzed. HL-10 was then placed in two 300-ml syringes, with half of the total dose in each. The mechanical ventilator was set on volume control mode with a tidal volume of 6 ml/kg predicted body weight (PBW), FiO2 1.0 and PEEP left unchanged. The patient was turned to one side, the endotracheal tube was clamped at expiratory hold, the mechanical ventilator was disconnected from the patient, and the HL-10 injected into the endotracheal tube as fast as possible. The patient was reconnected to the ventilator, the tube was unclamped and the tidal volume was temporarily increased to 12 ml/kg PBW with PEEP reduced to 5 cmH2O to optimize the pulmonary distribution of HL-10. After 5 breaths, PEEP was set 5 cmH2O above pre HL-10 administration values for 30 minutes, to avoid



**Figure 2.** PaO<sub>2</sub>/FiO<sub>2</sub> ratio at baseline, 39 hours after baseline (H39) and day 7 in control (open circles) and surfactant groups (closed circles) of patients with acute lung injury/acute respiratory distress syndrome.



**Figure 3.** Volumes of gas and tissue at baseline before HL-10 instillation (upper part of the figure) and changes in volume of gas and tissue between H39 (within 3 hours following the third bolus of HL-10) and baseline (lower part of the figure) in right upper and middle lobes (RUL), left upper lobe (LUL), right lower lobe (RLL) and left lower lobe (LLL) in patients with acute lung injury/acute respiratory distress syndrome instilled with 200 mg/kg of HL-10. Comparisons were performed by Friedman repeated measures analysis of variance on ranks followed by a Tukey test. P values above the horizontal brackets indicate significant difference between RUL, LUL, RLL and LLL using Friedman repeated measures analysis of variance.\* p < 0.05 versus RUL, § p < 0.05 versus LUL.

transient hypoxemia. After all the HL-10 had disappeared from the tube, the patient was turned back to the supine position and the tidal volume was put back to 6 ml/kg PBW. After a steady state was obtained, the patient was turned to the opposite side and the administration process was repeated to the other lung.

Computed tomography measurement of lung reaeration: Each patient was transported to the Department of Radiology by two physicians. Spiral CT sections were acquired from the apex to the diaphragm using a spiral Tomoscan SR 7000 (Philips, Eindhoven, The Netherlands) at PEEP 10 cmH2O at baseline, 39 hours (H39) or within 3 hours after the third bolus of HL-10 for surfactant group and day 7. During the acquisition, airway pressure was monitored to ensure that PEEP 10 cmH2O was actually applied. Contiguous axial 5-mm thick sections were reconstructed from the volumetric data using standard filter in order to avoid an artifactual increase in the hyperinflated compartment.<sup>19</sup>

Computed tomography measurement of lung, gas and tissue volumes: CT data were analyzed using a specifically designed software (Lungview, Institut National des Télécommunications, France) including a color coding system.<sup>20</sup> The following lung compartments were identified: hyperinflated, made up voxels with CT numbers between -1000 and -900 HU; normally aerated made up voxels with CT numbers between -900 and -500 HU; poorly aerated made up voxels with CT numbers between -900 and -500 HU; poorly aerated made up voxels with CT numbers between -100 and +100 HU; nonaerated made up voxels with CT numbers between -100 and +100 HU. Using the color coding system of Lungview, each nonaerated voxel was colored in

red, each poorly aerated voxel in light gray, each normally aerated voxel in dark gray and each hyperinflated voxel in white. The overall volume of gas present in both lungs at PEEP 10 cmH2O was defined as end-expiratory lung volume. Volumes of gas and tissue and hyperinflated lung volume of the whole lung were measured as described in the additional file at baseline, H39 and day 7 (see additional file 1).

Computed tomography measurement of surfactant-induced lung reaeration: Surfactant-induced lung reaeration was computed on all CT sections according to a method proposed by Malbouisson et al. for measuring PEEP-induced alveolar recruitment.<sup>18</sup> Such a method is based on the concept of measuring reaeration not only in nonaerated but also in poorly aerated lung regions on the whole lung. Accordingly, surfactant-induced reaeration was defined as the increase in the volume of gas entering nonaerated and poorly aerated lung regions after 3 doses of surfactant administration (day 7) compared to baseline. In the control group, lung reaeration was computed as the increase in gas volume within poorly and nonaerated lung regions between day 7 and baseline. The detail regional CT analysis is described in figure 1.

Computed tomography assessment of lung distribution of surfactant: In both surfactant and control patients, right upper and middle lobes, right lower lobe, left upper lobe and left lower lobe were analyzed separately at baseline and H39. By referring to anatomical landmarks such as pulmonary vessels, fissures, and segmental bronchi, the different pulmonary lobes were identified on each CT section obtained at baseline





and H39 and manually delineated using the roller ball of the computer. Because the CT scan at H39 in the surfactant group was performed within 3 hours following the third bolus of HL-10, the increase of volume of tissue at H39 provided an estimated volume of the third bolus of HL-10. Therefore, the increase in volume of tissue at H39 was compared to the volume of HL-10 intratracheally administrated. The distribution of surfactant between upper and lower lobes was computed as the increase in lung tissue in each lobe.

Statistical Analysis: The normal distribution of data was verified by a Kolmogorov-Smirnov test. Patients' characteristics and regional changes in volumes of gas and tissue between day 7 and baseline were compared by Chi2 test or an unpaired bilateral student test. Gas and tissue volumes at baseline and their changes between H39 and baseline within the lobes were compared by Friedman repeated measures analysis of variance on ranks followed by a Tukey test. Correlations between instilled volume of HL-10 and increase of tissue volume were made by linear regression. Cardiorespiratory and CT variables measured at different days were compared between the two groups using a two-way analysis of variance for a repeated factor and a grouping factor. The statistical analysis was performed with Sigmastat 3.1 (Systat Software Inc., Point Richmond, CA). Data were expressed as mean ±SD or median and interguartile range (25-75%) according to the data distribution. The statistical significance level was fixed at 0.05.

### Results

**Patients:** Among the 20 patients, one in the surfactant group died at day 4 from severe hypoxemia. Thirty percent of ALI/ARDS were related to extrapulmonary sepsis. The overall mortality rate was 30%. As shown in table 1, the clinical characteristics and cardiorespiratory parameters at baseline were not different between the control and urfactant patients.

### Cardiorespiratory changes in control and surfactant groups:

As shown in figure 2, PaO2/FiO2 ratio increased significantly from baseline to H39 and day 7 in both groups and in similar proportions. All other cardiorespiratory parameters remained unchanged between baseline and day 7 in both groups.

**Distribution of HL-10 in the lungs:** The mean volume of HL-10 instilled into the lungs per instillation was  $240 \pm 30$  ml. In the surfactant group, between H39 (immediately after

the third administration of HL-10) and baseline, CT tissue volume increased by  $311 \pm 200$  ml. The increase in tissue volume correlated linearly with the instilled volume (R=0.81, p=0.008, Y=-987+5.4X). As shown in figure 3, at baseline, CT gas volume was significantly less in lower lobes than in upper lobes whereas tissue volume was significantly greater in right upper lobe than in left lower lobe. At H39, gas volume remained unchanged whereas tissue volume significantly increased in similar proportion in upper and lower lobes. In the control group, gas volume was not different between baseline and H39. Tissue volume of right lower lobe decreased significantly at H39 compared to the value of baseline (table 2).

#### Assessment of lung reaeration after HL-10 replacement:

At baseline and PEEP 10 cmH2O, total lung volume, gas volume and tissue volume were not different between control and surfactant groups. As shown in figure 4, total gas volume did not change significantly between baseline, H39 and day 7 in control and surfactant groups. In contrast, HL-10 induced a significant increase in tissue volume at H39

Table 1. Baseline clinical characteristics of the patients.

Variables	Contro	)i	Surfactant	P value
	(n = 10	)	(n = 10)	
Male/Female	9/1		8/2	NS
Age (years)	59 ±	16	62 ± 1	12 NS
SAPS II	40 ±	10	41 ± '	10 NS
LISS	2.3 ±	0.4	2.6 ± (	).5 NS
Septic shock (%)	80%		70%	NS
Survival (%)	70%		70%	NS
Cause of ALI/ARDS:				
Bronchopneumonia	4		6	
Aspiration pneumonia	1		1	NS
Lung contusion	2		0	
Sepsis	3		3	
PaCO <sub>2</sub> (mmHg)	38.4 ±	8.2	37.9 ± 7	, NS
PaO <sub>2</sub> /FiO <sub>2</sub> (mmHg)	200 ±	63	201 ± 6	4 NS
TV/kg (ml)	5.7 ±	0.8	6 ± 0	0.9 NS
RR (breaths/min)	23 ±	4	20 ± 6	, NS
Ppeak (cmH=0)	32 ±	5	32 ± 6	, NS
Pplat (cmH <sub>2</sub> O)	23 ±	4	23 ± 5	, NS
PEEP (cmH <sub>2</sub> O)	9.7 ±	0.9	9.4 ± 1	NS
Crs (ml.cmH <sub>2</sub> O <sup>-1</sup> )	38 ±	12	41 ± 2	NS NS
HR (beats/min)	110 ±	23	88 ± 2	A NS
MAR (mmHa)	00 ±	15	07 ± 0	NS NS

Definition of abbrevations: Surfactant = Porcine-derived lung surfactant; SAPS II = Simplified acute physiology score II; LISS = Lung injury severity score; ARDS = Acute respiratory distress syndrome. ALI= Acute Lung Injury. TV = Tidal volume; RR = Respiratory rate; Ppeak = Peak airway pressure; Pplat = Plateau airway pressure; PEEP = Positive end-expiratory pressure; Crs = Compliance of respiratory system; HR = heart rate; MAP = Mean arterial pressure. Data are expressed as mean±SD.



Figure 5 Individual and mean changes in volume of gas and tissue in poorly/nonaerated lung regions (upper part of the figure) and normally aerated lung regions (lower part of the figure). Volume changes were measured on computed tomography scans acquired at baseline and 7 days in patients who received either usual care (control, open circles) or usual care plus intratracheal porcine-derived surfactant (HL-10, closed circles). In surfactant group, each patient is identified by a specific symbol.

that persisted at day 7 (interaction p<0.001). The increase in tissue volume between day 7 and baseline correlated linearly with the instilled volume of HL-10 (R=0.72, p=0.03, Y=-1594+7.6X). Hyperinflated lung volume was not different between both groups at baseline, H39 and day 7.

As shown in figure 5, in poorly/nonaerated lung regions, gas volume significantly increased at day 7 compared to baseline in both control and surfactant groups. The increase in gas volume at day 7 was significantly greater in the surfactant group than in the control group  $(320\pm125 \text{ ml versus } 135\pm161 \text{ ml}, p=0.01$ , figure 5A). In the control patients, tissue volume of poorly/nonaerated lung regions significantly decreased (figure 5B, p=0.04) between day 7 and baseline whereas it remained unchanged in surfactant group. In normally aerated lung regions, gas volume did not change between day 7 and baseline in both groups (figure 5C). However, HL-10 induced a significant increase in tissue volume at day 7 (189±179 ml versus -15±105 ml, p=0.007, figure 5D).

#### Discussion

The present study demonstrates that intratracheal administration of porcine-derived surfactant to patients with ALI/ARDS induces a significant lung reaeration of poorly/nonaerated lung regions. This beneficial effect, however, is associated with a significant increase in lung tissue in normally aerated lung areas at day 7 whose mechanisms remain to be elucidated. Distribution

of surfactant within the lung is likely an important factor that determines the efficacy of surfactant therapy. Delivery technique and lung morphology influence surfactant distribution. In a previous randomized clinical trial,7 the unsuccessful surfactant treatment was related to the technique of aerosolization that provided less than 10% distal lung deposition.<sup>21</sup> Intratracheal instillation by a catheter positioned just above the carina has been shown to be much more effective in animals and patients with ARDS.6,22 In patients with ARDS/ALI, the loss of lung aeration does not have a uniform distribution and, in the supine position, dependent and caudal lung regions are virtually nonaerated as a result of external compression by the abdomen and heart.<sup>13,14</sup> Exogenous surfactant's distribution in aerated and nonaerated parts of the distal lung has never been assessed and it is unknown whether instilled surfactant does penetrate into nonaerated lower lobes. In the present study, the CT scan at H39 in the surfactant group was performed within 3 hours following the third administration of HL-10. Based on the fact that the tissue volume didn't change at H39 compared to its baseline value in the control group, we can assume that the increase in lung tissue between baseline and H39 in the surfactant group is representative of instilled exogenous surfactant. The present data show that the overall volume of instilled HL-10 was homogeneously distributed between upper and lower lobes and between normally and poorly/nonaerated lung regions (figure 3). This result demonstrates that the procedure of instillation

 Table 2. Volumes of gas and tissue at baseline and H39 in the control group of patients

	Ba	selin	e		H39		P value
Volume of gas (ml)							
Right upper and middle lobe	864	±	440	934	±	411	NS
Left upper lobe	752	±	321	722	$\pm$	295	NS
Right lower lobe	178	±	206	241	±	244	NS
Left lower lobe	14	2 (4	7 <b>-2</b> 77)	111(	23-	296)	NS
Volume of tissue (ml)							
Right upper and middle lobe	317	±	115	313	±	105	NS
Left upper lobe	281	±	69	272	±	71	NS
Right lower lobe	321	±	106	275	±	87	0.02
Left lower lobe	299	±	89	267	±	49	NS
Data are averaged as mean C	) or modi		nd 05 75	0/ intergue	et la	rongo	LI20 CT and

Data are expressed as mean $\pm$ SD or median and 25-75% interquartile range. H39 = CT scan performed 39 hours after baseline.

(successive bolus in right and left lateral positions followed by consecutive recruitment maneuvers) resulted in uniform bilateral surfactant distribution. A predominant distribution of HL-10 in normally aerated lung regions can be ruled out.

Although several randomized trials have failed to demonstrated beneficial effects of exogenous surfactant in adults patients with ARDS in terms of mortality and ventilatorfree days,<sup>7,8,23</sup> the effect of surfactant therapy on lung aeration had never been evaluated. In the present study, using CT regional analysis of normally and poorly/nonaerated lung regions, a significant higher lung reaeration was evidenced at day 7 in patients treated by surfactant replacement as compared to control patients (figure 5A). This finding provides evidence that tracheal instillation of HL-10 induces a substantial and prolonged reaeration of poorly/ nonaerated lung regions and more specifically of nonaerated lower lobes. This encouraging result supports the rationale for exogenous surfactant replacement as indication for lung reaeration in adult patients with ALI/ARDS. HL-10 induced lung reaeration was, however, associated with a long lasting increase in lung tissue in previously normally aerated lung areas. Its mechanism remains unknown and several hypotheses can be discussed. A delayed alveolar clearance of the large doses of HL-10 administered to aerated lung regions, where endogenous surfactant is already present, is a possible mechanism that could explain the sustained increase in lung tissue. In newborn infants, the surfactant half life is around 35 hours.<sup>24</sup> In patients with ARDS treated by recombinant surfactant, components of exogenous surfactant were retrieved in bronchoalveolar lavage (BAL) 2 days after initial administration, but were no longer detectable 5 days later.<sup>6</sup> The dose of surfactant used in the present study was orders of magnitude beyond what was commonly used in neonates, older children and adults. The high volume of phospholipids administered may have prolonged the turn-over time, explaining the persistent increase in lung tissue. Another hypothesis explaining increase of lung tissue could be an inflammatory reaction resulting from the interaction of HL-10 with active endogenous surfactant present in aerated lung regions.<sup>25</sup> As illustrated in the present study, normally aerated lung regions in ARDS/ALI are characterized by an excess of lung tissue<sup>15</sup> and an increased vascular permeability,<sup>26</sup> 2 abnormalities increasing lung parenchyma's vulnerability to external aggressions. In these regions, saline diluted HL-10 could induce depletion of endogenous surfactant,<sup>27</sup> increased release of TNF and IL-6 in response to overinflation<sup>28</sup> and a resulting increase in lung micovascular permeability. The consecutive influx of albumin into the alveolar space could inactivate further endogenous surfactant,<sup>29</sup> and aggravate lung injury. In addition, 720 ml of saline (4 ml/kg/bolus) containing HL-10 were instilled in both lungs over 36 hours. By itself, such an amount of liquid could induce lung injury in experimental normal lungs. Lastly, breakdown products of the phospholipids

in surfactant, specifically lysophosphatidylcholine, can provoke inflammation. In this study, BAL after surfactant replacement was not performed. Further study is required to explore the correlation between the presence of inflammatory mediators, components of exogenous surfactant, protein and cells in BAL, and the CT increase in lung tissue in normally aerated lung areas.

Exogneous surfactant has strong immunomodulatory properties.<sup>30-32</sup> In patients with ARDS, exogenous surfactant therapy decreases interleukine-6 concentrations in plasma and bronchoalveolar lavage of patients with ARDS, suggesting either a direct anti-inflammatory effect or a reduction of ventilator-induced lung stretch.6 However, in the present study, despite surfactant-induced recruitment of poorly/ nonaerated lung regions, CT lung hyperinflation was similar in both groups. Unexpectedly, HL-10-induced reaeration was not associated with a significant improvement in arterial oxygenation. Very likely, HL-10 instillation in normally aerated lung regions worsened regional ventilation/perfusion ratios through an increase in lung tissue. In other words, benefit in terms of aeration of poorly/nonaerated regions of the lung was likely counteracted by a negative impact of HL-10 on aeration of previously normally aerated lung.

### Conclusions

Even though the rationale for exogenous surfactant replacement in patients with ARDS /ALI is strong with some phase II studies showing positive responses,<sup>33,34</sup> all clinical phase III studies failed to demonstrate a beneficial effect in terms of mortality and duration of ventilation.<sup>7,8,12</sup> Our study demonstrates that non selective tracheal administration of porcine-derived surfactant reaerates poorly/nonaerated lung regions, but induces a prolonged increase in lung tissue in regions remaining normally aerated; therefore, gas exchange is not improved. Further studies are needed to examine whether a more selective instillation of exogenous surfactant in poorly/nonaerated lung regions would be beneficial in terms of improvement of oxygenation, reduction of mortality and ventilator-free days.

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### Random Variation of Inspiratory Lung Function Parameters in Patients with COPD

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### Abstract

**Background:** In chronic obstructive pulmonary disease (COPD), the response of the forced expiratory volume in 1 second (FEV1) after bronchodilator application is weak. Inspiratory parameters like the forced inspiratory volume in 1 second (FIV1) and inspiratory capacity (IC) can be responsive to bronchodilators. In an individual patient with COPD, a significant bronchodilator response must at least exceed the random variation for that parameter. Therefore, it is important that the type of scatter is homoscedastic, as the chance of underestimating or overestimating the random variation for low or high parameter values is minimized. The aim of this study is to investigate the random variation (type and quantity) of inspiratory parameters.

**Methods:** In 79 stable COPD patients, spirometry was performed. The forced inspiratory volume in 1 second (FIV1), inspiratory capacity (IC), maximal inspiratory flow at 50% (MIF50) and peak inspiratory flow (PIF) were measured five times in one day and again within two weeks of the first measurement. The values of these parameters, taken within one hour, within one day and between two different days, were compared. The coefficient of repeatability (CR) was calculated, and, in addition, linear regression was performed to investigate the type of scatter (homo- or heteroscedastic) of the measured parameters.

**Results:** The type of scatter was heteroscedastic for all of the parameters when the differences were expressed as absolute values; however, when the differences were expressed as the percent change from the initial values, we found a more homoscedastic scatter. The CR within one hour of each parameter expressed as the percent change from the initial value was: IC, 19%; FIV1, 14%; PIF, 18%; MEF50, 21%.

**Conclusions:** To obtain a more homoscedastic scatter, percentage changes in FIV1, IC and MIF50 are more appropriate than absolute changes. In an individual patient with COPD, a significant improvement for a particular parameter must at least exceed the above-mentioned CR.

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#### Background

The severity of chronic obstructive pulmonary disease (COPD) is defined by the degree of expiratory airflow limitation. It is essential for diagnosis and provides a useful description of the severity of pathological changes in COPD.<sup>1</sup> It is, however, well known that the correlation between the subjective improvements in dyspnea and the increases in Forced Expiratory Volume in 1 second (FEV1) after inhalation of bronchodilators is low.<sup>24</sup>

Many COPD patients do not show significant reversibility of FEV1 after bronchodilators, as defined by a 12% improvement from the initial value and at least 200 ml,<sup>5</sup> but may experience less dyspnea from their use. Taube and co-workers<sup>4</sup> demonstrated that this change in dyspnea may be related to improvements in inspiratory flow rates. These authors found that in patients with severe COPD (FEV1 mean was 38% of the predicted normal value), the reduction in dyspnea after the inhalation of a beta (2)-adrenoreceptor agonist was closely correlated to the change in parameters of forced inspiration, particularly for the forced inspiratory volume in 1 second (FIV1), but not with changes in parameters of forced expiration. They also concluded that, "In less severe COPD or asthma, the reduction in dyspnea was associated with the improvements in both FIV1 and FEV1, but in severe COPD with the improvement in FIV1 only."6

O'Donnell et al found a correlation between the change of the Inspiratory Capacity (IC) after bronchodilator administration, dyspnea and duration of exercise.<sup>7,8</sup> In 2005, a published ATS/ ERS statement on clinical pulmonary function testing<sup>9</sup> made no recommendations on the measurement of inspiratory parameters including FIV1. Therefore, it is unclear how FIV1 and other inspiratory parameters should be measured and which improvements in a patient are beyond random variation for these parameters after the use of bronchodilators or other interventions.

How FIV1 should be measured in patients with COPD was the subject of a previous study by our group. We found that the optimal FIV1 was obtained immediately after a slow expiration (in contrast to a forced expiration) and that at least five forced inspiratory maneuvers should be performed.<sup>10</sup>

However, there is no clear consensus about how to express reversibility in subjects with airflow limitation.<sup>5</sup> The two most commonly described methods are the percent change of the initial value and the absolute change in the parameter value. As the percent change from the initial value is too sensitive at very low values, as measured in severe obstructive patients, a third method uses the percent change from the predicted normal value.<sup>5</sup> For the inspiratory parameters under study, no accepted predicted normal values are available; hence, we used the first two methods.

For an individual patient with COPD, a significant bronchodilator response must at least exceed the random variation for the parameter of interest. Therefore, it is important to know which type of variation or scatter exists for that parameter. Figure 1 shows a theoretical dataset of a test-retest lung-function parameter with different types of scatter. In the left panel, we made the amount of scatter the same for each value of the parameter, called "homoscedastic" scatter. For the whole range of the parameter, we can use the same value for the random variation, and a difference of more than 0.2 is beyond the random variation. The same dataset is used in the right panel, in which the differences are related to the (average) parameter value (percent difference) but now

the amount of scatter depends on the parameter value: the higher the value, the less (in this example) scatter or random variation there is; this type of scatter is called "heteroscedastic." Therefore, it is important to know the type of scatter of the parameters in which we are interested. A more homoscedastic scatter is desired when we express the differences as absolute differences or as relative to the parameter value.

The first topic of this study is to investigate which type of scatter applies to the (absolute and percent) changes in inspiratory parameters (FIV1, Inspiratory Capacity (IC), Peak Inspiratory Flow (PIF) and Maximal Inspiratory Flow at 50% (MIF50)). Next, we determine the coefficient of repeatability (CR) for the given parameters.<sup>5,11</sup>

### Methods

A total of 79 (58 male) consecutive patients who met ATS-ERS<sup>12</sup> criteria for COPD were recruited from our outpatient clinic. Criteria for inclusion were a patient age  $\geq$ 40 years, a smoker or former smoker ( $\geq$ 10 pack years), stable disease and an ability to perform lung function tests. Excluded patients were those on oral corticosteroids or antibiotics in the month before inclusion, or those who had symptomatic heart failure, respiratory diseases other than COPD, a history of asthma, allergic rhinitis or active cancer disease (except basal cell carcinoma of the skin). The study was approved by the Hospital Medical Ethical Committee, and all patients gave informed consent.

Patients were asked not to use short-term bronchodilators for the six to eight hours prior to the study and long-term bronchodilators for at least 12 hours before the study. Tiotropium and theophylline b.i.d. were not allowed to be used for the 24 hours prior to the spirometric test. Before the tests, a 3.00-liter calibration syringe was used at three different emptying and filling speeds to check linearity, as recommended by ATS and ERS standards.<sup>9</sup> The ambient (room) temperature was measured before each test session so that BTPS corrections on the flows and volumes were adequately performed.

Lung function tests were performed five times on the first day (9, 10, 11, 14 and 15 hours) and once at nine hours within the following two weeks. Between the two days, the medication did not change. Also, on the second day the patients were requested

to discontinue bronchodilators as on day one.

For expiratory parameters, three adequate and acceptable flow volume curves were produced in accordance with conventional ATS/ERS criteria.<sup>9</sup> The largest forced vital capacity (FVC) and FEV1 were recorded. For the predicted FEV1 and FVC, the normal values of the European Respiratory Society were used.<sup>13</sup>

For inspiratory parameters, five adequate IC measurements and maximal forced inspirations after a slow and maximal expiration were obtained. Full inspiration was obtained when a plateau in the flow was reached or after at least an eight-second duration of the inspiration. Of these five maneuvers, we took the highest value obtained for the FIV1, IC, PIF and MIF50.<sup>10</sup> IC was measured by the method described by Hadcroft and Calverly<sup>14</sup> immediately before each forced inhalation.

If, during the inspiratory maneuvers, the vital capacity (VC) was reached before the FIV1, then FIV1=VC.

The flow-volume curves were measured with a V-MAX20 (Sensor Medics, ViaSys, Conshohocken, PA, USA).

In order to obtain proper inspiratory parameters after a slow expiration, we began the measurement during the slow expiration and stopped the procedure when the patient reached maximal inspiration; otherwise, the V-MAX20 software rejects the values obtained.

### Analysis

The five intra-day lung function parameter data were analyzed with the repeated measures ANOVA and Bonferroni's multiple comparison tests. The type of scatter (homoscedastic or heteroscedastic) was determined as follows. The differences between each test and retest value pair versus the average value were plotted as described by Bland and Altman.<sup>11</sup> Negative differences were transformed to positive values by taking the absolute values of the differences. We applied linear regression of these transformed differences on the average value of the parameter. When there is a pure homoscedastic scatter, the regression line will be close to horizontal and the slope will not significantly differ from zero. When there is a heteroscedastic scatter, the slope of the regression line will be significantly different from zero. For each parameter, scatter plots were made for both absolute differences and percentage differences

Table 1. Characteristics of the COPD patient gro	up.
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Number of subjects	79	Range
Male (%)	58 (73)	
Height, m, mean (SD)	1.702 (0.1)	1.49-1.94
Weight, kg, mean (SD)	75.4 (15.9)	39.7-128
BMI, kg/m2, mean (SD)	25.7 (4.96)	18-47
Age, yrs, mean (SD)	65.4 (8.69)	44-83
Current smoker (%)	47 (59)	
FEV1, mean (SD)	1.48 (0.70)	0.37-2.65
Predicted FEV1, mean (SD)	2.83 (0.60)	1,26-4.23
FEV1, % predicted, (SD)	48.7 (12.6)	13.5-79.8
GOLD 1 number (%)	13 (17)	
GOLD 2 number (%)	24 (30)	
GOLD 3 number (%)	28 (35)	
GOLD 4 number (%)	14 (18)	

Legend Table 1: COPD= Chronic Obstructive Pulmonary Disease; BMI=Body Mass Index; FEV1=Forced Expiratory Flow in One second; GOLD= Global Initiative for Chronic Obstructive Lung Disease (stage 1,2,3 or 4).

Table 2. Mean and (SD) values of lung function parameters on five
occasions during the day

Parameter/ time	9	10	11	14	15
FEV1	1.48 (0.70)	1.48 (0.69)	1.48 (0.90)	1.48 (0.70)	1.41 (0.68)
FIV1	2.70 (0.85)	2.71 (0.87)	2.69 (0.87)	2.65 (0.84)	2.62 (0.81)
IC	2.13 (0.69)	2.15 (0.68)	2.17 (0.72)	2.18 (0.75)	2.14 (0.79)
MIF50	4.68 (1.63)	4.61 (1.61)	4.65 (1.62)	4.51 (1.55)	4.47 (1.18)
PIF	4.96 (1.67)	4.92 (1.66)	4.95 (1.67)	4.89 (1.61)	4.84 (1.65)

Legend Table 2: FEV1=Forced Expiratory Flow in one second; FIV1= Forced Inspiratory Flow in One second; IC-Inspiratory Capacity; MIF50= Maximal Inspiratory Flow at 50%; PIF= peak Inspiratory Flow.

Table 3. Linear regr	ession: standardi	zed slopes (r)	and P values; t	tests
whether the slope is	significantly dif	ferent from ze	ero. N=237	

Parameter	Standardized slope (r)	P value (significance from zero slope)
FEV1	0.37	<0.0001
%FEV1	0.10	0.1 (NS)
IC	0.27	< 0.0001
%IC	0.05	0.46 (NS)
FIV1	0.20	0.002
%FIV1	0.13	0.045
PIF	0.20	0.002
%PIF	0.24	0.0002
MIF50	0.22	0.0009
%MIF50	0.14	0.0267

Legend Table 3.: FEV1=Forced Expiratory Flow in one second; FIV1= Forced Inspiratory Flow in One second; IC-Inspiratory Capacity; MIF50= Maximal Inspiratory Flow at 50%; PIF= peak Inspiratory Flow. See also Figures 2 and 3 and the text for further explanation.

Table 4. Coefficients of repeatability (CR) retested after one hour (n=237),after five hours(n=79) and after 3-10 days (n-76) (in % from initialvalue/absolute value)

Parameter	Retest after one hour	Retest after five hours	Retest another day
FEV1	11.8	13.7	17.9
IC	18.9	21.3	22.7
FIV1	13.5	17.9	18.0
PIF	17.9	17.8/ 0.90	17.9/ 0.85
MIF50	20.4	21.0	19.2

Legend Table 4.: FEV1=Forced Expiratory Flow in one second; FIV1= Forced Inspiratory Flow in One second; IC-Inspiratory Capacity; MIF50= Maximal Inspiratory Flow at 50%; PIF= peak Inspiratory Flow.

from the average value. With linear regression, we tested for the significances of the slopes. Instead of slopes, we present standardized slopes, ie, correlation coefficients, as these can be compared across parameters and methods. The coefficient of repeatability (CR), as established within one hour, intra-day and inter-day, was determined by the method described by Bland and Altman.11 The CR was determined as 1.64 times the standard deviation of the differences, represented as absolute values or as percentages of the average values. We performed a one-tailed test instead of a two-tailed test, as the interventions we were interested in were expected to improve a parameter; hence, we took 1.64 times SD instead of 1.96 X SD. This use of a one-tailed test is analogous to the way in which lower limits of normals are calculated.13 CR was used instead of the more common coefficient of variation (CV) because CV does not take into account the type of scatter that can be visualized by the scatter plots of Bland and Altman.11

### Results

Seventy-nine patients were included for day one (intra-day

measurements), and 76 were measured again within the following two weeks. For two patients, we were unable to get an appointment within the two weeks, and in one there was an exacerbation. The baseline patient characteristics are summarized in Table 1.

The intra-day mean and SD values did not differ significantly (repeated measures ANOVA) on different occasions that day (see Table 2). Therefore, we took three value pairs per parameter for each patient with a one-hour difference (9–10, 10–11 and 14–15 hours) for determination of the type of scatter and the one-hour coefficient of repeatability.

The scatter of differences in IC values versus average IC value on two occasions in-between one hour is shown in Figure 2, panel A. The scatter becomes wider when the average IC increases. Panel B presents the same data, except that negative difference values are made positive and a linear regression line is added to the figure. The regression line is not flat (P<0.0001), as it would be if the scatter was independent of the IC (Table 3). On the other hand, when the difference in IC is expressed as a percentage of the average IC (Figure 2, panel C), an evenly distributed scatter can be seen along the whole range of the average IC. The slope of the linear regression line is now nearly flat (Figure 2, panel D) and is not significantly different from zero (Table 3). The other parameters were investigated in the same way as the IC, and the results of the linear regression are presented in Table 3. To visualize the (more homoscedastic) spread, the scatter plots of the FIV1, IC, MIF50 and PIF expressed as percentage differences can be seen in Figure 3.

We did not find a flat regression line for either presentation of the parameters (as differences in liters or as percentage differences of the average value); however, for all but the PIF, we found a more flat regression line corresponding to a lower (r) value when the percentage difference of the average value was used (less significant difference from zero, as can be seen in Table 3).

The coefficients of repeatability for IC, FIV1, MIF50 and PIF are graphically presented as Bland–Altman plots in Figure 4, panels A–D. The spread around no difference (solid line) can be seen, and the coefficient of repeatability is presented as the dotted lines  $\pm 1.64 \times$  standard deviation. We can also see the relatively even spread around the solid line, which is an indication of a more homoscedastic spread. In patients with COPD, we found that the one-hour random variabilities expressed as the coefficients of repeatability (CR) for the lung function parameters are: IC: 19%, FIV1: 14%, PIF: 18% and MEF50: 21% (Table 4). In the same way as the one-hour coefficients of repeatability, the intra-day coefficients of repeatability and the in-between day coefficients of repeatability are investigated. The intra-day random variabilities expressed as the coefficients of repeatability (CR) for the lung function parameters are: IC, 21%; FIV1, 18%; PIF, 18% or 0.90 l/; and MEF50, 21% (Table 4). The inter-day random variabilities expressed as the coefficients of repeatability (CR) for the lung function parameters are: IC: 23%, FIV1: 14%, PIF: 18% and MEF50: 21% (Table 4).

### Discussion

This study has shown that within the same subject, differences in lung function parameters (IC, FIV1, MIF50 and PIF) before and after one hour can more appropriately be described when taken as the percentages of the initial values than as differences in the absolute values because of the more homoscedastic



**Figure 1: Theoretical types of scatter.** Bland and Altman plots with theoretical types of scatter. The vertical axis shows the test (T) retest (R) difference (T-R); the horizontal axis shows the average (T+R/2). Each point corresponds with one test-retest pair. Left panel: dataset with a random scatter not dependent on the parameter value. Right panel: same dataset, but now the percent change from the average parameter value is shown; the scatter is highly dependent on the parameter value. In the left panel, the scatter can be described with just one value, e.g., the coefficient of repeatability (CR). In the right panel, the scatter cannot be precisely described with one value because the scatter on the low and high parameter values will not precisely reflect a fixed CR. Thus, for describing random variation, a homoscedastic scatter is preferred.



**Figure 2: Types of scatter of the Inspiratory Capacity (IC).** Panel A: Bland–Altman plot showing the absolute difference of Inspiratory Capacity (IC) versus the average; it shows a heteroscedastic scatter of the IC. Panel B: Absolute difference of IC versus average IC plus linear regression; this panel shows a slope in the regression line. Panel C: Difference IC now presented as the percentage of the average value; this panel shows a homoscedastic scatter. Panel D: Percentage difference of IC versus average IC plus linear regression; this panel shows a flat slope of the regression line, not significantly different from zero. The dashed lines in panel B and D represent the confidence interval of the regression line.

scatter. All measured parameters showed a scatter that was significantly dependent on the average parameter value and thus is heteroscedastic if we present the differences in liters or L/sec. On the other hand, if we represent the difference as the percentage of the average value (which is nearby the initial value), we found no significant dependence on the parameter value for IC and less dependence on the values for the FIV1 and MIF50.

Several studies have addressed the variability of lung function parameters, especially on forced expiration,<sup>15-19</sup> but used the variation coefficient instead of the method described by Bland and Altman.<sup>11</sup> Therefore, the type of spread was not investigated. In the ATS-ERS statement, the method of Bland and Altman is

described as the preferred method for investigating the random variation, and this method makes the type of spread visible.<sup>5,11</sup>

The only exception is the PIF, which displays a slightly steeper slope when expressed as the percentage difference.

The one-hour repeatability is by far the most important random variability because most interventions we are interested in, such as bronchodilator response, can be measured within one hour. Subjects must at least exceed this random variation before it can be decided that an improvement of an intervention can be attributed to that intervention. We did not find any CR for inspiratory parameters in the literature.



**Figure 3: Linear regression of transformed Bland-Altman pots.** Left panels show the scatter (absolute differences and regression lines for FIV1, MIF50 and PIF). Right panels show the percentage differences for the same parameters. The dashed lines represent the confidence intervals of the regression lines. All slopes of the regression lines are significantly deviated from flat (zero); however, apart from the PIF, the percentage differences show regression lines that are more flat (closer to a zero slope). FIV1= Forced Inspiratory Flow in One second; MIF50= Maximal Inspiratory Flow at 50%; PIF= peak Inspiratory Flow.

We decided to pool our patients' data (with one-hour differences measured at three time-points a day per patient) to obtain more data points and, thus, more reliable results. This pooling was possible because we found no significant differences between the group means and spreads and no significant differences of the parameters between the measurements between 9 a.m. and 2 p.m. This result is in contrast with Calverley et al.<sup>20</sup> and van Noord et al.,<sup>21</sup> who found significantly lower values at 3 and 6 a.m.; however, we did not measure at these hours.

We chose the CR instead of the more popular variation coefficient because it more precisely reflects the repeatability and provides a graphical representation of the type of scatter, as stated by Bland and Altman<sup>11</sup> and the recommendations of the ERS-ATS committee.<sup>5</sup> The CR for the PIF is less than that for the MIF50 which may be because the MIF50 is situated near the PIF in maximal inspiratory flow volume curves but is seldom exactly aligned; thus, the MIF50 demonstrated more spread.

Whether PIF improvement is therefore more sensitive to bronchodilators than PIF is not answered by this study.

The intra-day coefficients of repeatability are important to know when we are performing interventions that take more than one hour, ie, medications such as theophylline, tiotroprium or other interventions that take more time to retest.

We selected the 9-to-14-hour difference because all parameters as group means did not change during this interval. There was a small but significant decrease in some parameters (FEV1 and MIF50) on the 9-to-15-hour interval; therefore, we took the 9-to-14 as our difference. We think that this decrease in some parameter values may be due to the fact that patients at the end become tired of repeating this procedure five times a day, during which time they were not allowed to take any bronchodilator drugs, or that there may be some circadian effect.<sup>20,21</sup> The higher intraday CR value, than the one hour CR value, could be expected because of the greater time interval. Improvements of interventions taking more than one day can be considered as beyond random variation when the inter-day coefficients of repeatability are taken into account. Between the two days, patients did not change their medication and no exacerbations occurred. A weak point of these CR is that we were unable to see all patients on an exact inter-day interval of one week because we were dependent on when our patients were able to visit our outpatient department again. As the smallest interval was three days, and the greatest interval was eight days, the analyses were all conducted within two weeks. In general, the longer the interval between the two measurements (from one hour to several days), the greater the CR obtained. This result may be caused by the longer time period for weather to influence the patients or other effects of irritants in the environment. Similar to the one-hour and intra-day random variation, we were unable to find the inter-day random variation on inspiratory parameters in the literature.

The subjects in this study include the investigation of only patients with COPD, so it does not extend to normal patients or those with asthma or restrictive disease. The random variation in these groups may be different.

The type of scatter was only examined after one hour, and it may be different when other intervals are taken into account. The wash-out time for Tiotropium was 24 hours, although some



**Figure 4: Coefficient of repeatability.** Panels A–D show Bland–Altman plots of the percentage difference versus the average of the IC, FIV1, MIF50 and PIF. The coefficient of repeatability (CR) corresponds with the dotted lines; in panel A, e.g., the coefficient of repeatability takes the value = 18.9%, which is 1.64xSD. IC- Inspiratory Capacity; FIV1= Forced Inspiratory Flow in One second; MIF50= Maximal Inspiratory Flow at 50% ; PIF= peak Inspiratory Flow; SD=standard deviation.

investigators used 48 hours for this drug. We think this 24 hours time period had limited influence on the test-retest results. We used all data including the outliers to construct the Bland and Altman plots; in small samples, this can influence the linear regression of the transformed Bland and Altman plots when the outliers are in the lower or upper zones of the average parameter value.

### Conclusions

Differences in lung function parameters (IC, FIV1, MIF50 and PIF) are described with less dependence on the parameter values when taken as percentages from the initial values than as absolute difference values.

The random variation expressed as coefficients of repeatability for several time intervals are presented.

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Postoperative Hypoxemia...continued from page 44 OSA nor suffering from an episode of hypoxemia is associated with increased risk of adverse outcomes, it may be reasonable to discharge patients with a diagnosis of OSA home after regional anesthesia for ambulatory orthopedic surgery.

Our data provide support for current consensus based clinical guidelines for OSA patients undergoing ambulatory anesthesia.<sup>5</sup> Peripheral and minor procedures, use of regional anesthesia, and limited requirement for strong postoperative opioids are all considered to decrease risk per these guidelines.<sup>5</sup> Our procedure types (ambulatory orthopedic), predominant use of regional anesthesia (95% of procedures), and modest requirement for postoperative intravenous opioids (0-36% of patients) likely decreased the inherent risk for complications in these patients to the point that hypoxemia from OSA was no longer a significant negative event.

Our surgical population underwent exclusively elective ambulatory orthopedic procedures such as knee and shoulder arthroscopy which are frequently performed and growing in volume. The latest data set (2009) from the National Survey of Ambulatory Surgery from the National Center for Health Statistics reported that greater than 39 million ambulatory surgical procedures are performed annually in the United States and that musculoskeletal procedures such as orthopedics are the 2nd most commonly performed type of procedures.<sup>12</sup> Ambulatory surgery is increasingly popular worldwide, thus our findings should have widespread clinical applicability.

There are several limitations to our study. The data collection was retrospective and has typical limitations in that data may have been missed or miscoded. The diagnosis of OSA was based on ICD9 codes, thus severity of OSA could not be ascertained. Few patients underwent general anesthesia, thus results can not be extrapolated to such patients.

### Conclusions

Episodes of postoperative hypoxemia in OSA patients undergoing ambulatory surgery with regional anesthesia were not associated with increased adverse outcomes or unplanned hospital admission. Our OSA patients had similar rates of unplanned hospital admission as previously reported in normal patients. Thus, this study provides original data that support current clinical OSA guidelines recommending that such patients do not require overnight monitored observation.

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