Electronic Spirometer Opportunity

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Dynamic Measurement Technologies

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EXECUTIVE SUMMARY

Patents (US, UK) for a novel electronic spirometer are available for licensing or assignment. Spirometers are devices for measuring lung performance to diagnose and monitor patients with respiratory diseases. The main diseases are asthma (300 million patients worldwide) and chronic obstructive pulmonary disease (COPD) which has an estimated 50 million patients in the US, Europe and Japan. All of these persons would benefit from regulatory monitoring of their condition with spirometers. The market for spirometers is estimated at $2 billion in 2010 for the US, Europe and Japan alone.

The technology described in the patent is for a spirometer that has high speed air flow measurement ability with a MEMs pressure sensor, a simple design with no moving parts, and a fully electronic design. This spirometer design has key advantages over existing spirometers that include high accuracy and potential for low cost production.

Dynamic MT is the holder of the patents and is based in Switzerland.

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THE PATENTS

Full details and copies of the patents are available on the websites of the US patent office http://www.uspto.gov and the UK patent office http://gb.espacenet.com

US patent # 7,063,669B2 "Portable Electronic Spirometer"

Filed:	July 15, 2002
Date of patent:	June 20, 2006
Renewed	December 20, 2009

Abstract

A spirometer having a housing with an elongated flow chamber open at one end, a pressure sensing end opposite the open end and an outlet passageway intercepting the flow chamber at an angle α and proximate the pressure sensing end. A differential pressure sensor is coupled to the pressure sensing end from a port at an angle β to an axis of the flow chamber. The angle α is substantially greater than 0° but substantially less than 180° while the angle β may range from 90° to 180°, such that a significantly increased measured air pressure results over that measured when α=180° and β=90°.

UK patent GB 2,388,665 "Portable Electronic Spirometer"

Filed	Feb 28, 2003
Published	Dec 21, 2005
Renewed	Feb 24, 2010

INTRODUCTION TO THE DEVICE AND ITS APPLICATION

New sensors based on MEMS technology exist today which, in combination with continued advances in microcontrollers, will make entirely new applications possible. Dynamic MT, based in Switzerland, combines these technologies to create entirely new electronic devices.

Dynamic MT has developed, patented and clinically tested a fully electronic spirometry device featuring a new mechanism involving no moving parts, high accuracy and low cost construction. This spirometer can be developed into a device suitable for diagnosis of respiratory diseases, as well as monitoring of asthma and COPD. A version could also be made that is ideal for clinical trials. A key feature of the device is electronic logging of patient data, which makes it ideal for home monitoring and clinical trials. An overview of the main respiratory diseases and current spirometry is given in the next section.

Patents have been granted in the US and the UK. Dynamic MT is seeking interested parties to license these patents for royalties or assignment for a one time payment.

BACKGROUND ON SPIROMETERS AND THEIR MARKET:

Spirometers are required for the diagnosis of asthma, chronic obstructive pulmonary disease (COPD), and other respiratory diseases. Asthma and COPD are by far the most common diseases requiring spirometers, but other important diseases include Cystic Fibrosis, Black lung, Silicosis, and Tuberculosis.

Asthma

Asthma is a disease of the bronchial tubes, or airways of the lungs, characterized by tightening of these airways. Common symptoms include shortness of breath, coughing, tightening in the chest, and wheezing. It is a chronic disease; people with asthma live with it every day and very often for their whole lives. People who have a family history of asthma have an increased risk of developing the disease however anyone can develop asthma at any time. Asthma is also more common in people who have allergies or who are exposed to tobacco smoke.

Asthma affects an estimated 34 million persons in the US[1] and 300 million worldwide[2]. When properly diagnosed, asthma can be treated well by several kinds of medicines. The world market for asthma medicines was estimated at $15 billion in 2006, and is estimated to grow to $17 billion by 2010[3]. Home monitoring of peak expiratory flow (PEF) by a spirometer is recommended by leading health agencies for asthmatics. Spirometers are also used by physicians to diagnose and monitor asthma.

Chronic obstructive pulmonary disease (COPD)

Chronic bronchitis and emphysema are life threatening diseases that are in most cases caused by smoking. Up to 20% of all cigarette smokers will develop COPD[4]. COPD is a major cause of disability, and is the fourth leading cause of death in the United States. More than 12 million people are currently diagnosed with COPD in the US. An additional 12 million likely have the disease and don't even know it.[5] Together they form the fourth leading cause of death in the United States – about 150,000 of the 15 million sufferers in the US die from the disease each year. There are about 50 million COPD patients in the US, Europe, and Japan. Spirometers are needed for diagnosis and monitoring of COPD.

COPD is actually two conditions that are generally grouped together – chronic bronchitis and emphysema. Chronic bronchitis is an inflammation in the airways (bronchial tubes) that lead into the lungs. As a result, the airways produce more mucus than they would normally. Inflammation and extra mucus cause coughing.

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[1] American Lung Association. Epidemiology & Statistics Unit, Research and Program Services. Trends in Asthma Morbidity and Mortality, November 2007.

[2] World Health Organization. Global surveillance, prevention and control of chronic respiratory diseases: a comprehensive approach, 2007.

[3] *Source: ING. "Asthma & COPD - Clearing the air." 18 June 2007.*

[4] Heath JM (2000). Chronic obstructive pulmonary disease. In RE Rakel, ed., Saunders Manual of Medical Practice, 2nd ed., pp. 184–186. Philadelphia: W.B. Saunders.

[5] National Heart Lung and Blood Institute website

Long-term (chronic) mucus production and inflammation over many years can cause progressive and permanent damage. Inflammation, scarring, and the excess mucus make the airways smaller. It is more difficult to move air quickly through a small tube than a large tube. The extra effort of breathing through a smaller airway can make a person feel short of breath.

In emphysema, the elastic fibres that are an important part of the lung's structure are damaged by tobacco smoke and other lung irritants. This is especially harmful to the tiny air sacs (alveoli) at the end of the airways where oxygen moves into the blood. When air sacs are damaged, their walls break down and the sacs become larger. These large air sacs move less oxygen into the blood, which can leave the person feeling out of breath. When elastic fibres are destroyed, the smaller airways (bronchioles) tend to collapse when a person breathes out, trapping air in the lungs. This makes it more difficult to move fresh air into the lungs. As these diseases progress, the lungs capacity to process oxygen for the blood stream is reduced, and in many cases inhaled oxygen is required.

The key parameter to measure in diagnosis and monitoring of COPD is the amount of air a person can forcibly exhale in one second (FEV_1). A smaller FEV_1 result means the person has a hard time moving air into and out of his or her lungs. A signature of persons with obstructive flows is a lower than average FEV_1. To measure this quantity a spirometer must be used.

Spirometry

A spirometer is a device that monitors the flow of air in and out of a person's lungs. The device can be used for diagnosis and monitoring of pulmonary diseases, particularly Asthma and COPD. Spirometers are divided into two classes which have different specifications and purposes:

- Diagnostic devices (Fig. 1) to be used by physicians for diagnosis of the condition. They must be able to measure many different parameters of respiratory flow and have a higher degree of accuracy than monitoring devices.
- Monitoring devices (Fig. 2) which are used by patients to monitor their asthma daily. These must be cheap, portable, and easy to use by patients at home. Clinical trials devices must have similar properties but have different requirements for data transfer.

Figure 1: The Jaeger "Master Screen Body" is an example of a modern spirometer for diagnosis. It is expensive and is usually installed in hospital clinics and operated by respiratory specialists.

An overall summary of the uses for monitoring and diagnostic spirometers is given in

Table 1 on page 13. Monitoring spirometers measure a key parameter called peak respiratory flow or peak flow (PEF). Peak flow is greatly reduced during an asthma attack from e.g., 600 litres per min to 50 l/m. The state of the person's asthma should be monitored by measuring peak flow with a portable device. Doctors recommend that asthmatics monitor their asthma using portable peak flow devices on their own. This is also supported by the US government sponsored National Heart, Lung, and Blood Institute (NHLBI):

"The Panel recommends that patients, especially those with moderate-to-severe persistent asthma or a history of severe exacerbations, be given a written action plan based on signs and symptoms and/or peak expiratory flow. As in the 1991 report, daily peak flow monitoring is recommended for patients with moderate-to-severe persistent asthma. In addition, the Panel states that any patient who develops severe exacerbations may benefit from peak flow monitoring." [6]

Source: Vitalograph.com

Figure 2: Example of a fully mechanical peak flow meter that is intended for home monitoring (Asmaplan+ by Vitalograph). The device is only capable of an approximate measurement of peak flow. Source: Vitalograph.com

Inexpensive devices for patents to monitor their condition are produced by numerous manufacturers. These mechanical devices usually contain a spring and slider or rotary vane that records peak flow. They have a low level of accuracy but are cheap to produce and typically cost from $15-30. Models are often sponsored by pharmaceutical firms and distributed through Doctor's offices or sold over the counter. These devices cannot be interfaced with a computer and their accuracy is limited. They are not capable of measuring FEV_1 which is relevant for COPD.

Typical difficulties with peak flow monitoring today are that the patient is not able to interpret the peak flow data or take any action as a result of it. Doctors are often unable to obtain reliable data from patients as the patients may often lack the discipline to log the numbers in a notebook in a systematic way. The current monitoring devices also create a difficulty for clinical trials as data can only be acquired from participants when they visit a clinic for lung function testing. An electronic device that can acquire data from a patient daily at home would be very

[6] National Asthma Education and Prevention Program Expert Panel Report 2: Guidelines for the Diagnosis and Management of Asthma, p. 4

beneficial. Any method that can be found that improves data acquisition and accurate transmission and interpretation of the data would be welcomed by the healthcare industry.

DESCRIPTION OF THE PATENTED INVENTION

Our patented spirometer measures airflow with a novel technique relying on the instantaneous measurements of air pressure in a channel. This technique was not used previously due to limitations in the ability to measure pressure electronically, and adequate microcontroller computation power at a low enough cost. Recent advances in MEMS and microcontroller technology of the last few years have now made this technique technically feasible.

Several prototypes have been built and extensively tested. One device has been tested in a clinical setting and the results were compared with a Jaeger "Master Screen Body" spirometer as shown in Figure 1. The two devices were operated simultaneously on each patient, and measurements of key flow were found to be comparable. This indicates the high accuracy and reliability of the new device.

Due to the design of the spirometer, an inexpensive model can be made that allows patients to monitor their asthma at home and store the results electronically for their physician. This device would be ideal for home monitoring of asthma and COPD and very useful for pharmaceutical firms in clinical trials of new respiratory medicines. Health insurers may also benefit by reduced health care costs since asthma patients will receiving improved care. Due to the advanced technology used and high accuracy, a version of the device can also be made into a diagnostic instrument. Three variants of this product are envisioned based on the same technology as follows:

1. Monitoring device for home use

The spirometer has one control to initiate the measurement process for simplicity of use. The device is battery powered, and compact. An internal clock records the time and date, and a flash memory records the full flow-time curves of the patient with a time-date stamp. A low power microcontroller can compute the peak flow and FEV_1 values which are displayed and recorded. A simple display indicates the peak flow for the patient, and gives advice to the patient on whether his medical condition is normal or if he/she should seek medical help. In the device construction, inexpensive electronics and mass production techniques will be used. A single handheld unit comprising both the measurement electronics and the flow chamber will be constructed from a biocompatible injection-moulded composite material.

As an optional extra, the device may be connected to a PC so that the device may be configured, calibrated electronically, and patient data may be transferred for display on a PC screen for analysis and printing. PC software would be provided allowing the concerned patient to monitor their own condition. To maximize simplicity for the patient and secure data privacy, data transfer can best be accomplished by bringing the device into the doctor's office for analysis. Software to allow the physician to manage the data of multiple patients will also be developed.

2. Clinical trials device

This device will have very similar properties to the monitoring device described above. A key difference would be that improved sensor electronics would be used to enhance accuracy. The data obtained from the device will need to be analysed in a different way than the home monitoring device. A partnership with a clinical trials firm will be concluded to ensure that the data is stored in a form that is compatible with standard analysis software.

3. Diagnostic device

A high end version of the device will be made for use by physicians in a clinical setting. This device will have a detachable, biocompatible flow head that can be disposed of after use. The flow head will be attached to state of the art MEMS sensors and a precision A/D converter. This will ensure levels of accuracy exceeding to the best spirometers currently available. A PC will be used to obtain the data directly from the device, the data will be analysed by the PC and displayed on the screen. The data may be archived for the doctor's records and printed.

COMPETITIVE ADVANTAGE

This new spirometry technique is superior to existing spirometry techniques (pneumotach, ultrasound, hot wire anemometer) for the following reasons.

Low cost, robust design

- The device will have a lower cost to build than existing electronic flow meters due to the lack of moving parts and a solid state design.

Ease of sterilization and maintenance

- Flow detection mechanism has no moving parts, fine screens, meshes or delicate sensors to trap contaminants

High accuracy

- Fully electronic flow sensing with no mechanical parts to introduce errors
- Fully automatic correction of altitude, temperature, and barometric pressure effects

More parameters can be measured than similarly priced devices

- A complete flow versus time profile is measured, allowing any analysis to be performed by the on-board microcontroller
- Short time scale for measurement allows unprecedented flow resolution

Data transfer and storage capabilities

- Data transfer from the device to other computers and the internet for analysis will encourage use by patients and physicians. No need for users to record time, date, and measurement values with a pen and paper

TESTIMONIAL FROM A RESPIRATORY SPECIALIST

"I have reviewed and examined a new spirometer produced by Dynamic MT AG. This spirometer has a novel design with no moving parts that has some clear advantages over existing spirometers. The spirometer is easy to sterilize, purely electronic, and should be relatively inexpensive to produce. It should be possible to produce a version of the device for diagnosis of respiratory diseases in a clinical pulmonary function laboratory but also for home monitoring of respiratory diseases. Home monitoring of asthma is recommended by the medical community, and a reliable low cost electronic device would be very desirable. An accurate and fully electronic peak flow meter would be superior to current mechanical home monitoring devices.

The device measures PEF, FEV1, FVC and other flow parameters as well as stores the entire flow time curve. A printed report can also be produced which contains predictive values and the most relevant patient information. Accuracy in the measurement of PEF is superior to mechanical peak flow meters that are currently available at low cost.

The accuracy of the device was tested with a 2 liter calibration syringe and was found to be very accurate in measuring flow volumes. The spirometer was also tested on patients in my office in parallel with a high precision diagnostic spirometer (E. Jaeger Würzburg) as a reference system- the accuracy was comparable to the Jaeger.

The results could be well integrated in the diagnosis and therapeutic management of respiratory diseases. Compared to other spirometers, the Dynamic MT spirometer provides a much higher frequency measurement of the patient's flow as a function of time.

Overall, it is likely that the Dynamic MT spirometer could be developed into an excellent instrument for home monitoring and diagnosis. The Dynamic MT spirometer could be developed into several highly competitive products that would be very desirable for respiratory specialists, general practitioners, and respiratory patients."

- Dr. med M. Heitz, Respiratory Specialist, Zurich, Switzerland.

POTENTIAL CUSTOMERS FOR SPIROMETERS

An overview of the value proposition of an electronic spirometer is described below for several potential customer groups. A comprehensive list of indications requiring spirometers is presented in the table on page. 13.

Physicians: The device could also be used to enable doctors to monitor patient asthma and COPD more accurately and conveniently. Unlike currently available mechanical devices, the new device records the flow parameters with a date and time stamp electronically, and has a high degree of accuracy. Currently doctors must rely on patients recording this information by pen and paper making it far less reliable. Improved home monitoring will result in healthier patients and provide more information to assist in disease management.

Firms engaged in respiratory R&D: Speed is a key factor in the cost of clinical trials. It is estimated that using electronic means to record clinical data should reduce the time to market for drugs in Phase III trials, resulting in a NPV improvement of $180-$230 USD million per drug[7]. Asthma patients participating in clinical trials could automatically enter their data online with the new device, thus reducing cost and time associated with clinical trials.

Payors: Regular use of an electronic spirometer by high risk asthmatics should reduce the cost of treating asthma in hospital visits. A recent study indicated that patients who use home monitoring have 97% less visits to emergency rooms[8]. Payors could be approached to discuss the ways that an electronic home monitoring spirometer may be able to reduce health care costs.

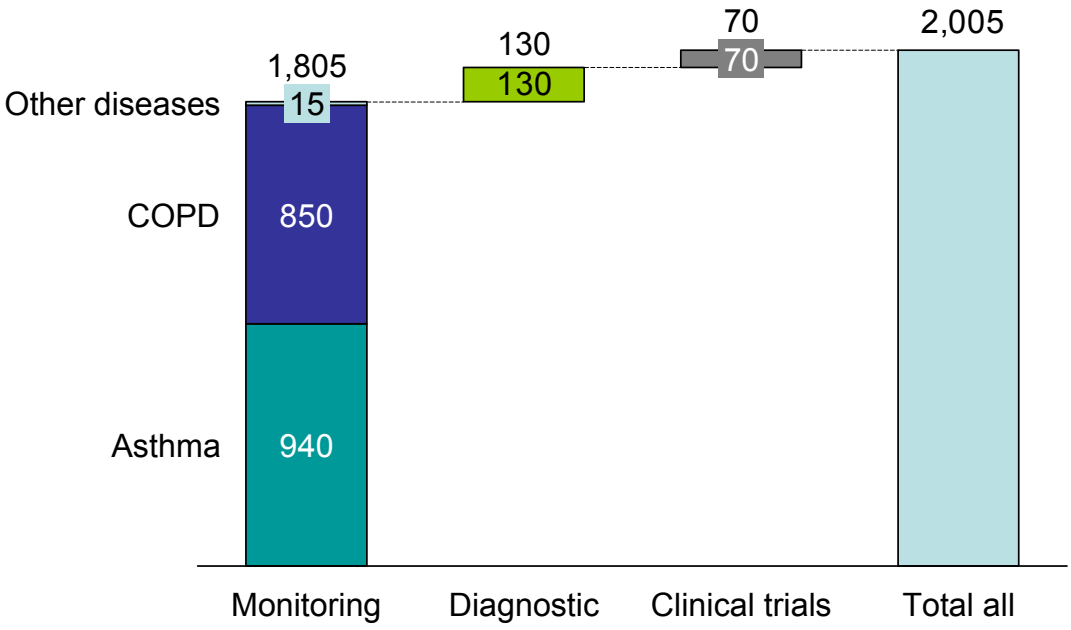
Patients: A well designed spirometer should improve a person's management of asthma and COPD as well as prevent unnecessary hospitalizations and improve their quality of life. The spirometer for asthmatics is analogous to blood glucose monitors for diabetics which are widely available at drugstores and other retail outlets worldwide.

[7] McKinsey analysis
[8] Doherty GB, Ross RN, Ross PE., *Disease Management and Health Outcomes 3*: 89-98 Feb 1998

MARKET SIZE FOR SPIROMETRY

Dynamic MT estimates that the overall global spirometry market is $2.0 billion USD per year, and breaks down by application and disease as described in Fig. 3. Further details on these estimates and the assumptions made are available for discussion.

Figure 3: Estimated Spirometry Market Size for US, Europe and Japan, USD millions



COMPETITION

To our knowledge there are only a few firms that make low cost electronic flow meters for home monitoring, and one example is the "PiKo1" by Ferraris or the MicroLife digital by MicroDirect. These devices typically use a mechanical means to measure the air flow which is then converted to an electrical signal. This limits their accuracy since the mechanical parts have momentum and friction, and reduces the number of parameters measured to only peak flow (PEF) and possibly forced volumes FEV_1 and FEV_6. These devices are unable to measure the entire flow-time curve accurately which makes many other forms of analysis possible. In addition the mechanical parts are hard to sterilize which limits the usefulness of the device. Prices range typically from $50-$100 for these devices.

The vast majority of monitoring spirometers are currently mechanical devices similar to that shown in Fig. 2 that only measure peak flow and are priced between $20-$50. We believe the spirometer described here could be cost competitive with these devices and is greatly superior.

Other electro/mechanical spirometers, priced in the range from $300-$1,000, are produced by the several companies. They tend to use rotating vanes to measure airflows, or pressure differences across a flow barrier such as a screen or mesh. These are priced so high that they are beyond the home monitoring market, but are targeted more at physicians who wish to have a handheld or portable device for their practice.

There are numerous companies that market diagnostic spirometers; no clear leader is in sight. The more influential players appear to be Jaeger-Toennies, Vitalograph, and Clement Clarke. Diagnostic spirometers tend to be priced from 1,000$ to 10,000$ and are typically sold through medical distributors. Sales volumes and entry barriers are low, but margins are typically high.

INVENTORS

David Brawner, Ph.D.

Dr. Brawner is a physicist trained in British Columbia, Canada and Princeton University, USA where he received his Ph.D. in experimental solid state physics. In 1992 he came to Switzerland where he worked as a researcher at the ETH "Laboratorium für Festkörperphysik". During this period he had experience designing and building electronic research equipment, measuring physical properties, and programming computers for data analysis.

In 1997 Dr. Brawner joined McKinsey, became a project manager and specialized in technology projects. He had experience with transportation, insurance, pharma, chemicals, and e-business clients. He was also very active in recruiting for McKinsey. In addition he also worked to develop R&D and eHealth strategies for a leading pharmaceutical firm. Based on this experience in healthcare, he was inspired to consider how he could use his physics background to develop medical devices.

Dr. Brawner has worked as an independent management consultant since 2002 assisting government and multinational clients in the healthcare and pharmaceutical industries. Dr. Brawner is president of Dynamic MT.

Dr. Christopher Hegarty

Dr. Christopher Hegarty is an electrical engineer and physicist trained at the University of Queensland in Australia and the University of California at Berkeley, where he received his Ph.D.

From 1993 – 1997 he was director of research at ESEC SA where he led the development of new semiconductor automation products and software systems, including the “ESEC Autoline” which won the Innovation Award for Canton Zug in 1995. During his time at ESEC he gained extensive experience in leading large R&D efforts for both complex mechanical/electronic systems and software products.

In 1997 Dr. Hegarty joined McKinsey and rose to the level of associate principal before leaving to co-found Dynamic MT AG. At McKinsey he specialized in high-technology and IT projects. His main industries of expertise were electronics, energy, healthcare, IT architecture and financial services. He was a leader in McKinsey's global semiconductor and IT architecture practices. From 2003 - 2007 Dr. Hegarty was Vice President and General Manager of the Microcontroller business unit at Infineon Technologies in Munich, Germany

Dr. Hegarty's extensive hands-on experience in semiconductor physics, electronic design and software engineering provide an excellent background for him to design the devices described in this report. Dr. Hegarty has worked professionally in four continents (Australia, North America, Europe and Asia) and has a wide network of colleagues in the electronics, semiconductor and academic world. He is currently the CEO of MAPPER Lithography in the Netherlands.

TABLE 1: Additional indications of Spirometry[9]

Diagnostic devices

To evaluate symptoms, signs, or abnormal laboratory tests

- Symptoms: dyspnea, wheezing, orthopnea, cough, phlegm production, chest pain
- Signs: diminished breath sounds, over-inflation, expiratory slowing, cyanosis, chest deformity, unexplained crackles
- Abnormal laboratory tests: hypoxemia, hypercapnia, polycythemia, abnormal chest radiographs

To measure the effect of disease on pulmonary function

To screen individuals at risk of having pulmonary diseases

- Smokers
- Individuals in occupations with exposures to injurious substances
- Some routine physical examinations

To assess preoperative risk

To assess prognosis (lung transplant, etc.)

To assess health status before enrolment in strenuous physical activity programs

Monitoring devices

To assess therapeutic interventions

- Bronchodilator therapy
- Steroid treatment for asthma, interstitial lung disease, etc.
- Management of congestive heart failure
- Other (antibiotics in cystic fibrosis, etc.)

To describe the course of diseases affecting lung function

- Pulmonary diseases, Obstructive airways diseases, Interstitial lung disease, Cardiac diseases,
  Congestive heart failure, Neuromuscular diseases, Cuillain-Barre Syndrome

To monitor persons in occupations with exposure to injurious agents

To monitor for adverse reactions to drugs with known pulmonary toxicity

Disability / Impairment Evaluations

To assess patients as part of a rehabilitation program

- Medical
- Industrial
- Vocational

To assess risks as part of an insurance evaluation

To assess individuals for legal reasons

- Social Security or other government compensation programs
- Personal injury lawsuits
- Others

Public Health

- Epidemiologic surveys
- Comparison of health status of populations living in different environments
- Validation of subjective complaints in occupational / environmental settings

Derivation of reference equations

[9] Adapted from: Crapo, R.O. 1994. Pulmonary-function testing. New England Journal of Medicine **331**: 25-30.