Abstract— Bioengineering of the respiratory system is the main focus of the activities of two labs (Lares, Laboratorio di Analisi della Respirazione and TechRes, Technological Respiratory Lab) at the TBMLab of the Politecnico di Milano. The main mission of these two integrated labs is to create innovation in the field of respiratory medicine, throughout the development of new methods for analysis, functional evaluation and treatment of the respiratory diseases and to generate new knowledge in the physiology and pathophysiology of the respiratory system. Among the numerous methods and techniques developed up to now by Lares and Techres, in particular Opto-Electronic Plethysmography (OEP) and Forced Oscillations Technique (FOT) led to important results regarding physiology and pathophysiology of the respiratory system, functional assessment for the evaluation and optimization of rehabilitative, pharmacological and mechanical ventilation treatment.

I. INTRODUCTION

In the world, hundreds of millions of people struggle each year for life and breath due to lung diseases, including chronic obstructive pulmonary disease (COPD), asthma, lung cancer, pneumonia, tuberculosis, and more than 10 million die. Chronic respiratory diseases cause approximately 7% of all deaths worldwide and represent 4% of the global burden of disease. In addition to diminished and ruined lives, the cost of lung disease is huge in terms of lost productivity and increased health care expenses. The research in the field of respiratory medicine is therefore essential.

The research activities in the field of the Bioengineering of the Respiratory system started in the early '90s, when the group of the Lares (Laboratorio di Analisi della Respirazione) of the Dipartimento di Bioingegneria began to developed new methods based on 3-D motion analysis systems to analyze thoraco-abdominal kinematics during breathing. In the following years, an increasingly body of research was developed. The mission of the two labs (Lares, Laboratorio di Analisi della Respirazione) and TechRes (Technological Respiratory Lab) that nowadays work in synergy at the TBMLab of the Dipartimento di Bioingegneria, is to create innovative approaches, methods, techniques, with the final aims to better understand the physiology and pathophysiology of the respiratory system, to develop new tools for the functional assessment of its different aspects and to evaluate and optimize the rehabilitative, pharmacological and mechanical ventilation treatment.

II. OPTO-ELECTRONIC PLETHYSMOGRAPHY

Opto-Electronic Plethysmography (OEP) is a new noninvasive new method for the analysis of the respiratory system that was designed, developed and validated in the Lares lab and is currently being transferred into clinical use. OEP, starting from the 3-D coordinates of reflective markers positioned on a subject’s trunk and acquired by an opto-electronic system for motion analysis, allows a breath-by-breath and within-breath accurate measurement of the volume variations of the entire chest wall and its different compartments (rib cage and abdomen, right and left parts) [Ferrigno et al 1994, Cala et al, 1996, Aliverti et al, 2001]. Different experimental protocols and computing methods allow to obtain the volume variations under different conditions and validation studies have shown that such a method provides also a very accurate and noninvasive measurement of lung volume variations during breathing without a mouthpiece, noseclip or other connections to the patient. This is particularly useful in numerous situations, e.g. when breathing through a mouthpiece and flowmeter or from a spirometer is extremely difficult, like in children or uncooperative adults, during sleep, phonation or mechanical ventilation. Measurements performed by spirometers or pneumotachographs, moreover, are impractical and inaccurate for prolonged measurement, limit subject's mobility, introduce additional dead space, and make the subject aware that his breathing is being measured.

Fig. 1. OEP: principle of measurement
A. OEP: physiological studies

With OEP, different geometrical models of the chest wall and its different compartments can be defined. Since the first studies, developed in collaboration with P.T. Macklem of the McGill University, the chest wall was modeled as being composed of three different compartments: pulmonary rib cage, abdominal rib cage and abdomen. In addition, basing on proper biomechanical models and combined measurements of volumes and pressure, respiratory mechanics can be accurately described in terms of forces, work and power developed by the different respiratory muscles and rib cage distortion. A first set of studies was addressed to study human respiratory muscle action and control during exercise [Aliverti et al, 1997, Kenyon et al, 1997]. Successively, we determined the effects of expiratory flow-limitation (EFL), a typical condition of COPD, on pump function in exercise. Therefore, we studied healthy subjects exercising with a Starling resistor placed in the expiratory line and showed the negative effects on the cardiovascular system of the excessive use of expiratory muscles in these conditions [Aliverti et al, 2002, 2005, 2008]. To better understand cardio-pulmonary interactions, a new method, called double body Plethysmography (DBP) was successively developed by combining OEP with whole body plethysmography (WBP). DBP allows to measure blood shifts from the thorax to the extremities (Vbs) as the difference between changes in trunk and body volume. Using this new technique we recently found that the diaphragm assisted by simultaneous contractions of abdominal muscles with appropriate pressure and duration can produce a circulatory output as great as resting cardiac output at rest, as well as ventilation and therefore the abdominal circulatory pump can act as an auxiliary heart. These findings have important potentials for cardio-pulmonary resuscitation [Aliverti et al, 2009, 2010].

B. OEP: analysis of chest wall mechanics in different diseases and conditions

In collaboration with numerous national and international research and clinical centers several hundreds of patients have been studied following different experimental protocols by OEP, specifically developed for different applications and experimental or clinical situations. In patients with COPD, we found that, despite the common knowledge, several patterns of end-expiratory volume regulation occur during exercise [Aliverti et al, 2004, 2005b, 2009b] and these different behaviors constitute an important factor determining the level of exercise intolerance. At least three separate mechanisms of exercise limitation in COPD, including dynamic hyperinflation leading to an inability to increase tidal volume, skeletal muscle dysfunction resulting from prolonged deconditioning and systemic disease, inadequate energy supplies to meet locomotor and respiratory muscle demands [Aliverti et al, 2008b].

III. MULTIMODAL IMAGING ANALYSIS OF THE DIAPHRAGM, AIRWAYS AND LUNG

In a first set of studies, ultrasounds have been combined with OEP to measure axial motion of the right-sided area of apposition of the diaphragm. Simultaneous measurements by OEP showed that accurate measurements of abdominal volume variations allow to estimate diaphragm fiber length [Aliverti et al, 2003]. Free-hand US scanning combined with OEP and optical tracking of the probe allowed to obtain 3D reconstruction of diaphragm shape and geometry in different postures [Patruno et al, 2005, Quaranta et al, 2008]. Computer Tomography and 3He MR imaging methods can identify specific regions of hyperinflation and/or trapped gas, as our preliminary data demonstrate [Salito et al, 2009].
A set of new algorithms for airway segmentation, branch recognition and labeling, 2D and 3D image registration, and parenchymal tissue analysis based on the calculation of Specific Gas Volume (SVg) have been developed to determine heterogeneity of trapped gas in emphysema and potential target regions for endoscopic interventions like bronchopulmonary conduits (“stents”) between conducting airways and emphysematous lung parenchyma.

IV. FORCED OSCILLATION TECHNIQUE

The Forced Oscillation Technique (FOT) is a non-invasive tool for the assessment of the mechanical properties of the respiratory system introduced for the first time by Dubois in 1956 [Dubois et al, 1956]. Briefly, FOT consists in stimulating the respiratory system by a pressure oscillation and in analysing its mechanical response in terms of impedance (Zrs). Zrs is the spectral relationship between pressure (P) and airflow (V') and it is composed of a real part, called resistance (Rrs), and an imaginary part, called reactance (Xrs), which provides information about the compliance and inertance properties of the system. FOT can be implemented in various ways depending on the sites of measurement and of application of forced oscillations. Most commonly both the application of the forced oscillations and the measurement of flow and pressure are performed at the airways opening, providing the respiratory system input impedance (Zin). Figure 4, is a schematic representation of the measuring principle and of the measurement set-up for the assessment of Zin.

The stimulating signal can be either single-frequency or composite, different frequencies revealing different mechanical properties.

The contribution of TechRes Lab in this field is the development of new data processing algorithms and indexes that opened the way to different promising clinical applications. In fact part of the research activity of TechRes Lab is focused on developing new approaches based on FOT for the diagnosis and clinical management of respiratory disorders.

One of the first relevant results was a new non-invasive method to automatically detect Expiratory Flow Limitation (EFL) [Dellacà et al, 2004]. The possibility to automatically identify the presence of EFL can be used to customize either the administration of drugs [Dellacà et al, 2009] and mechanical ventilation settings in COPD patients [Dellacà et al, 2006].

The most attractive features of FOT are: 1) it does not require the cooperation of the patient so it can be performed in non-cooperative patients and in unsupervised environments, 2) if the frequency of the stimulus is high enough compared to the breathing rate the measurement is not affected by the spontaneous activity of the respiratory muscles.

Given these peculiar characteristics of FOT we found it particularly suitable for the remote monitoring of chronic diseases and for the assessment of lung function of mechanically ventilated patients.

Nowadays home monitoring is becoming a valid alternative to traditional health care solutions for the management and control of various types of illnesses. This is noticeably true also for the main respiratory pathologies (asthma, COPD, Obstructive Sleep Apnea Syndrome), which require frequent, eventually daily, evaluations of lung function. So far, only spirometry has been used for the self assessment of respiratory diseases at home, but spirometry is intrinsically not accurate when performed without supervision of trained personnel. Moreover, it cannot be properly carried out in non collaborative subjects (elders, children, persons with other disabilities, etc).

The TechRes Lab is combining the concept of telemedicine to the measurement of innovative respiratory derived from FOT with the aim of:
- analyzing the temporal fluctuations that characterize respiratory pathologies and understanding the mechanisms underlying such abnormal variability;
- evaluating the effects of medications;
- developing innovative clinical tools for a better management of respiratory diseases and for the early detection of acute events (exacerbations).

The aim of assessing respiratory mechanics during
mechanical ventilation is to optimize the ventilatory strategy by tailoring the ventilatory parameters on the single patient and adjusting them as the patho-physiological conditions change. So far our studies have been addressed the optimization of positive end-expiratory pressure (PEEP). The rationale of a PEEP optimization strategy is to provide to the patient the lowest level of pressure that is able to achieve adequate lung volume recruitment in RDS and airway patency abolishing airway obstruction and EFL. Further increases of PEEP would hyper-inflate the lung, overdistend the parenchyma and impair hemodynamics without any beneficial effect on the respiratory function. This approach fits to the management of COPD patients and of infant and adult respiratory distress syndrome (RDS).

Fig. 6. FOT applied to mechanically ventilated infants.

V. REFERENCES