Monitoring Lung Resistivity Changes in CHF Patients Using Bio-Impedance Technique

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ABSTRACT

The feasibility of a novel, designated system ("CardioInspect", Tel-Aviv University, Israel), implementing a hybrid approach of the bio-impedance technique, for monitoring lung resistivity in congestive heart failure (CHF) patients was assessed in a clinical study. In this preliminary study, 33 healthy volunteers and 34 CHF patients were measured with the system during tidal respiration, and the ability to monitor the respective lung resistivity values was assessed. Mean left and right lung resistivity values of (1205±163, 1200±165) [Ω·cm] for the control group and (888±193, 943±187) [Ω·cm] for the CHF group were found, indicating a significant (p<2·10-7) separation between the two groups. A long-term monitoring of two patients during medical treatment is also shown. This hybrid approach system is believed to improve the diagnostic capabilities of this illness, and help the physicians to better adjust the proper medication dosage on a frequent basis.

INTRODUCTION

Congestive heart failure (CHF) is a disease originating from an inadequacy of the heart to maintain blood circulation, resulting in congestion and oedema in the body tissues. Cardiogenic Pulmonary oedema (CPE) is a symptom of CHF, arising from the accumulation of excessive amount of watery fluids, transferred from the pulmonary capillaries to the pulmonary interstitium or into the alveoli. Monitoring the development of CPE is crucial, since it can rapidly deteriorate to cause acute respiratory distress, and may even prove fatal. Current non-invasive monitoring techniques include mainly X-ray CT and weighing, the former of which cannot be performed on a frequent basis due to the ionizing radiation involved, while the latter is far from being accurate. Therefore, it is beneficial to have an alternative method that is capable of monitoring CPE symptoms.

The bioelectrical impedance technique, in which information regarding the inner electrical properties of biological tissues is assessed by means of applying electrical current to the tissue and measuring the developing surface voltages, seems to be a suitable CPE monitoring modality. This technique has several advantages: it is a safe procedure, utilizing only very small amplitude AC currents, without the use of ionizing radiation or strong magnetic fields. Data can be collected continuously and over long-term periods, providing temporal information. The hardware is relatively easy to construct in a low cost and the system can be designed to be portable. A general scheme of a bio-impedance system consists of an electrode-array, attached to the body, through which the electrical current is injected in various combinations of source and sink and the voltage measurements are performed. Typically, the current frequency is set to O(10^4Hz) to minimize the effect of the dielectric properties of the tissues (the quasi-static approximation) on the one hand, yet to avoid safety limitations on the other hand. The measurements for each current injection combination are processed using sophisticated algorithms to produce an estimation of the internal resistivity that led to the observed surface voltages. CPE development causes changes in the electrical attributes of the lungs, since low conducting air inside the lungs is replaced by high conducting body fluids. As the lungs are relatively large organs and therefore their changes in resistivity are prominent enough, this suggests that the bio-impedance technique might be suitable for non-invasive CPE monitoring.

Over three decades ago it was first shown that the transthoracic electrical resistivity has a correlation to the amount of lung fluids[1]. A two-electrode configuration was used in this dog model study, which showed a clear influence of the amount of injected saline into one of the dog's lungs on the measured transthroracic impedance. Later clinical studies have employed the more conventional four-electrode configuration[2], where the transthoracic impedance along the long axis of the thorax is measured[3,4,5,6,7]. This methodology was found to be better immune to changes of tidal volume and chest movement errors. Still, these studies have shown inconsistent results, as not specifically measuring the lungs' impedance, but rather that of the whole thoracic volume. Such measurement can only supply global impedance information about the whole thoracic-volume impedance, and cannot separate between the various comprising compartments of the thorax, most importantly between the two lungs.

A relatively new development in the field of bio-impedance is electrical impedance tomography (EIT), in which the internal spatial distribution of impedivity is reconstructed from the multiple voltage measurements, yielding anatomical information. The feasibility of EIT to monitor pulmonary edema, using a large number of attached electrodes and complex reconstruction algorithms, was studied from the mid eighties[8,9,10,11,12,13]. Both animal and human studies have shown a clear correlation between reconstructed impedance changes and lung edema severity, in conditions such as unilateral lung damage or diuretics infusion treatment. These studies employed experimental EIT systems, which could be therefore implemented only in research laboratory applications, essentially lacking practical clinical use, due to the technical complexity in attaching a large number of electrodes to the body and knowing their precise positions. These limitations result in poor image reconstruction quality, making it difficult to provide satisfactory lung edema-severity diagnosis.

Both proposed approaches, i.e. the transthoracic impedance measurement and the EIT, have their characteristic drawbacks, as aforementioned. A hybrid approach, that provides local rather than global information, yet avoids the technical difficulties of EIT systems, might prove beneficial. In this work, the capability of such a hybrid approach bio-impedance system ("CardioInspect", Tel-Aviv University, Israel) for monitoring CHF patients was evaluated. The system provides local information regarding the electrical resistivity of the left and right lungs using degenerated EIT measuring scheme. It is a portable, user-friendly and clinically oriented system, specifically designed for the application of lung edema monitoring.

METHODS

System Description

A photograph of the "CardioInspect" experimental system, which was used in this work, is shown in figure 1. The system comprises of an 8-electrode belt, with an additional reference electrode attached on the waist for minimizing baseline drifts, an analogue unit responsible for current generation, current injection and voltage measurement, and an interface unit that contains a touch-screen, a printer, a digital control board. The system is powered from a rechargeable battery, which is also located within the interface unit, for complying with patient safety limitations.

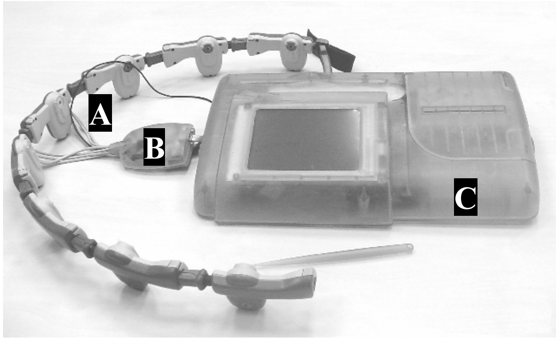


Figure 1 – A photograph of the experimental system.
A – Electrode belt
B – Analog unit
C – Interface unit, rechargeable battery, printer

An iterative parameter optimization scheme, based on the second-order Newton-Raphson method[14], is implemented in the system for estimating the left- and right-lung resistivity values in the thoracic geometry, shown in figure 2.

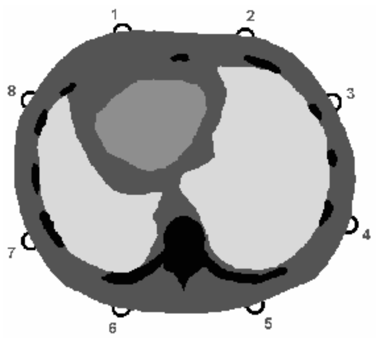


Figure 2 – A two-dimensional thorax model, employed in the Newton-Raphson optimization scheme. The locations of the eight electrodes are marked.

During the measurements procedure, the belt is worn around the patient's thorax while sitting, and the reference electrode is attached to his waist. The procedure is performed during tidal respiration to minimize lung resistivity changes due to breathing, and lasts approximately one minute.

Patient Characteristics

A preliminary study was conducted at the CHF clinic, the department of cardiology, Rabin medical center, and was approved by a local Helsinki ethics committee. The inclusion criteria for subject participation in the study were: (1) absence of a cardiac implantable device, and (2) a signed informed consent. The study was performed on two subject groups, the first of which was a control group consisting of 33 healthy subjects (50±16 years old, all male), while the second group comprised of 34 CHF patients (56±13 years old, all male), regularly monitored at the clinic, with various CHF severity degrees. An unpaired t-test was performed, showing that no significant difference between the two study groups' ages exists (p≅0.12).

RESULTS

Control group lung-resistivity reconstruction

The correlation between the mean lung resistivity reconstructed value and various anthropometric parameters (age, height, weight, body mass index (BMI) and body surface area (BSA)) of the control group was calculated using a two-sample paired t-test. Table 1 summarizes the results, from which it is clearly shown that there is no dependency of the reconstructed values on any of the tested properties, implying that any notable difference in the resistivity values between the control and CHF groups probably originates only from the pathological condition.

Table 1 – Dependency of reconstructed lung resistivity values on various anthropometric properties for the control group

Parameter	R	p-value
Age	0.26	0.18
Height	0.13	0.50
Weight	0.08	0.68
BMI	0.04	0.84
BSA	0.10	0.61

Group separation

The reconstruction results for the lung resistivity values of the two study groups are shown on a scatter plot in figure 3. In this graph, the right-lung versus the left-lung reconstructed resistivity values are plotted for all subjects. An apparent separation between the two groups is observed, where the lower lung resistivity values belong to the CHF patients, indicating larger fluid volumes in their lungs. The mean left and right lung resistivity for the control group is (1205±163, 1200±165) [Ω·cm] and for the CHF group (888±193, 943±187) [Ω·cm]. An unpaired two-sample t-test proved this separation to be significant for both lungs (with $p<2\cdot10^{-7}$). It can be noticed that while the mean resistivity value for the left lung and the right lung is balanced for the control group, the right-lung resistivity value is larger by 55 Ω·cm than the left value for the CHF group, though not significantly (p=0.23).

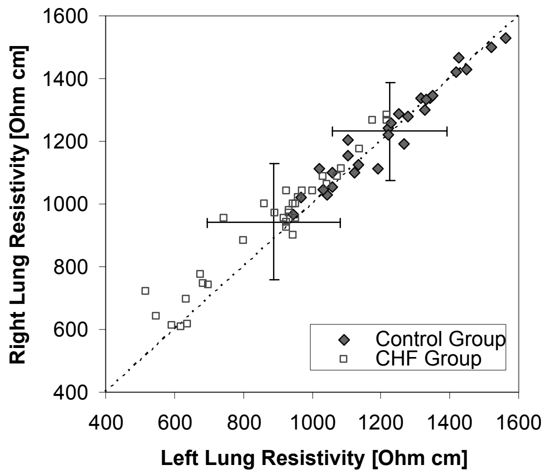
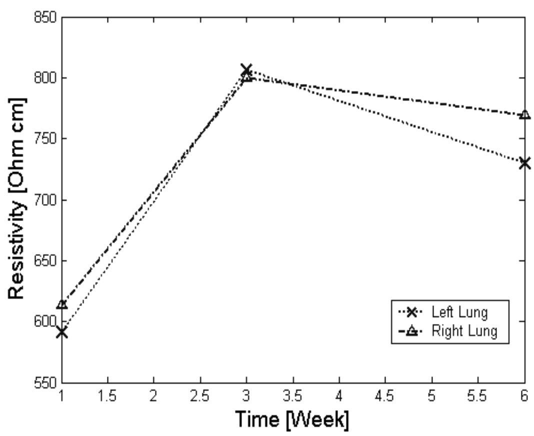


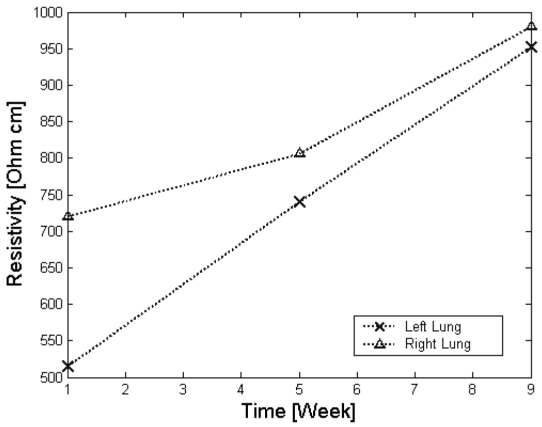
Figure 3. A scatter plot of right vs. left-lung resistivity reconstruction values for control (diamonds) and CHF (squares) groups.

Monitoring

The system capability for long-term monitoring of edema severity was tested on two CHF patients (aged 53 and 67 years old for subjects 1 and 2, respectively). These patients were measured three times in a period of a few weeks while in medication treatment. The left and right-lung resistivity reconstruction values for the two patients are given in figures 4a and 4b as a function of measurement time. A general increase in both lung resistivity values was measured for the two subjects, indicating an improvement in the edema severity level. This improvement was found to be in correlation with an expert physician diagnostics, and with the decrease of weight for the two patients (from 72 to 64 kg and from 63 to 60 kg for subjects 1 and 2, respectively).



a – Subject 1



b – Subject 2

Figure 4. Left (crosses) and right (diamonds) lung resistivity reconstructions as a function of measurement number (in weeks)

DISCUSSION

In this work, the performance of a portable stand-alone hybrid bio-impedance system was evaluated for monitoring lung edema in CHF patients. The system was clinically studied on control and CHF groups and preliminary results were presented.

The system overcomes much of the major limitations of currently utilized monitoring methods and provides a safe, relatively cheap and compact application. With relatively minor modifications this system can be adapted to home environment use, with a possibility to perform as a tele-homecare device, by transmitting patient's measured data to a medical call center for expert's analysis. These features suggest that the currently burdensome necessity of many CHF outpatients to be regularly monitored at the hospital may be avoided in the near future, which besides the improvement of life quality will save considerable hospitalization costs.

The first attempts to monitor pulmonary edema using electrical impedance technique were done in the early seventies[15,16]. In these works a small number of electrodes, usually two or four, were attached to the body, and the measured surface voltages were related, using simplified electrical models of the body, to the amount of fluids inserted into the lungs. A current representative of this approach, also termed impedance cardiography, is the commercially available BioZ system ("Cardiodynamics"), see e.g. Greenberg *et al.* 2000[17], that extracts hemodynamic thoracic fluid content measures using transthoracic impedance measurements. However, this impedance technique approach can only yield estimation to the general thorax conductivity, without separation to the different thorax compartments, while the general thorax conductivity might be influenced heavily by other non-edema-related factors such as surrounding fat layers. In that sense, EIT, which usually utilizes a larger number of attached electrodes, is preferred because it can provide conductivity estimation to specific parts of the thorax. In this view, some of the principles of EIT were implemented in this study and the distinct resistivity value of each of the lungs was assessed using optimization of parameters. Additionally, the system employed in this study performs noninvasive measurements, making it suitable for patients who do not carry an implantable device. Such a device is an integral part of other intra-thoracic impedance monitoring systems[18], e.g. Insync Sentry ("Medtronic"), where electrical current is injected between a right ventricle lead and the implanted pacemaker, and the developing voltage over the left lung is measured. Not only is this kind of measurement invasive, that it can only give estimation for the left lung fluid content.

A significant separation of means between the two groups' typical lung resistivity values was found, showing the capability of the system to classify the patients. This separation probably results from the pathology condition of the CHF group, as no dependence was found between the lung resistivity of the control group and their anthropometric parameters. Furthermore, additional external factors e.g. smoking or pulmonary disease at baseline did not bias the observed results, as no such conditions were dominant in the study group.

It should be noted that in this stage of the study, all CHF patients, although inner-classified into various illness degrees, were considered a unified group. Moreover, the exact condition of the CHF patients on the trial date, regarding the degree of lung fluid accumulation, was not referred to in the performances analysis. These two factors prohibit the possibility of specificity/sensitivity analysis or the drawing of a receiver operating characteristic (ROC) curve at this stage. Nevertheless, these assumptions surely tend to lower the sensitivity of the system, and should be addressed in a later study. It was found that while the left and right-lung reconstructed resistivity values were balanced for the control group, the right lung seems to be associated with a higher resistivity than the left lung for the CHF group, possibly implying on a unilateral pulmonary edema. Although this imbalance was found to be not significant ($p=0.23$), it is still an interesting finding, the physiological origins of which should be further studied. Pathological conditions such as enlarged cardiac volume or unilateral pleural effusion are possible origins for the left-right lung resistivity asymmetry; however, these conditions were scarce among the CHF study group, thus such a correlation could not be tracked.

The systems' capability for long-term monitoring edema severity was generally demonstrated on two CHF patients. The results, which showed a gradual decrease in the reconstructed lungs' resistivity, were correlated with both weight decrease and physician's diagnosis, suggesting the present system as an alternative system for CHF monitoring over long periods. Due to the limited scope of this monitoring phase, no conclusive comments are intended to be established at this point, although the preliminary outcome is encouraging and coherent with the expected theoretical trends. Further comprehensive clinical trials should be obviously conducted, which should include larger statistical populations for both study groups and patient classification according to the severity of edema. These studies should also employ long-term hemodynamic correlations to the fluid accumulation levels during the diuresis treatment and to the patient symptoms, to investigate the possibility of early edema deterioration detection.

While the present study was aimed for the specific medical application of CPE monitoring, no doubt that it also applicable to monitoring other pulmonary function disorders that are characterized by substantial lung resistivity change, such as pneumonia, lung ventilation, or cystic fibrosis.

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