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Validation of remote dielectric sensing (ReDS™) technology for quantification of lung fluid status: Comparison to high resolution chest computed tomography in patients with and without acute heart failure☆

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ABSTRACT

Background: Pulmonary congestion is a common presentation of acute decompensated heart failure (ADHF). The ability to quantify increased pulmonary parenchymal water content in chest computed tomography (CCT) is well known. However, availability and radiation limitations make it unsuitable for serial assessment of lung fluid content. The ReDS™ technology allows quantification of lung fluid content.
Objective: The objective of this work was to validate the ability of the ReDS™ technology to quantify total lung fluid when compared with CCT in ADHF and non-ADHF patients.
Methods: Following CCT, ReDS measurements were obtained from consented subjects. ReDS measurements were then compared to the CCT using lung density analysis software. CCT results were converted from Hounsfield Units to percentage units, allowing comparison with the ReDS readings. The analyses, performed on 16 ADHF and 15 non-ADHF patients, were conducted by an independent observer blinded to ReDS outcomes.
Results: The fluid content averages and standard deviations for the non-ADHF group were 28.7 ± 5.9% and 27.3 ± 6.6% and for the ADHF patients 40.7 ± 8.8% and 39.8 ± 6.8% (CCT and ReDS respectively). Intraclass correlation was found to be 0.90, 95% CI [0.8–0.95]. Regression analysis yielded a slope of 0.94 (95% confidence interval [0.77–1.12]) and intercept 3.10 (95% confidence interval of [−3.02–9.21]). The absolute mean difference between the quantification of the two methods was 3.75 [%] with SD of 2.22 [%].
Conclusion: Current findings show high correlation between the ReDS noninvasive system and CCT in both ADHF and non-ADHF patients. Remote patient monitoring using ReDS™ based system may help in the management of patients with heart failure.

1. Introduction

Early detection of impending volume overload by sensing increases in pulmonary artery pressures in patients with heart failure facilitates intervention such as modification of pharmacological therapy or behavior (e.g., diet, mediation compliance) to avoid rehospitalizations. This was demonstrated in the COMPASS-HF [1] and CHAMPION [2] studies. However, these prior studies relied on invasive, permanently implanted pressure sensors. In addition, previous studies employing chest computed tomography (CCT) to quantify lung fluid content in heart failure patients spanning a wide range of symptoms (including patients

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in pulmonary edema) showed that symptoms (e.g., shortness of breath) occurred when lung fluid content increases above 50% of normal values [3–7]. A valid, noninvasive approach that provides equivalent information would provide many advantages.

We previously described the potential of a novel noninvasive electromagnetic energy-based technology [8] (Remote Dielectric Sensing, ReDS™) intended to quantify changes in lung fluid content. Briefly, ReDS™ technology (Sensible Medical Innovations Ltd., Kfar Neter, Israel) measures the dielectric properties of tissues. Low power electromagnetic signals are emitted across the thorax through the lung and the characteristics of the signals received after passing through the tissue are related to their dielectric properties which, in turn, are mostly determined by the lung's fluid content [8]. This contrasts with bio-impedance-based devices which apply low frequency currents to measure electrical resistance between body surface electrodes which is affected by many factors in addition to lung fluid content (e.g., electrode placement, body habitus, fat content, skin moisture) [9].

The purpose of the current study was to test the accuracy of the ReDS™ system by comparing its measurement of lung fluid content to that measured by chest computed tomography (CCT) which is currently the most accurate method for quantifying lung fluid content in vivo [10–12]. Patients with and without acute decompensated heart failure (ADHF) were recruited to ensure lung fluid contents spanning the range expected in clinical use.

2. Methods

2.1. Patients

A total of 36 patients were included from two different clinics. 19 patients recruited at Carmel Medical Center did not have any evidence of heart failure. 17 patients with ADHF were recruited at Rambam Medical Center. The ADHF patients underwent CCT as part of the study protocol during their ADHF-related hospitalization, with the presence of ADHF being the only inclusion criterion. The inclusion criterion for non-ADHF patients was that they had a clinical indication for CCT as an elective procedure. Exclusion criteria for the non-ADHF patients were clinically unstable patients, known pregnancy, recent cardiothoracic surgery, recent chest trauma or age < 18 years.

The respective protocols were approved by the IRB committees of Rambam Medical Center and Lady Davis Carmel Medical Center, Haifa, Israel. All the participating patients signed written informed consent prior to participation.

Each patient underwent ReDS and CCT measurements by a trained technical staff to quantify lung fluid content according to a standardized protocol. During the measurements, a spirometer (WaveFront™, Thor) was used for registration of breathing pattern to enable comparison between the two modalities at the same phase of respiration.

2.2. Chest CT measurements

The CCT test was performed according to routine practice by an experienced hospital technician. Patients were instructed to hold their breath as required by the standard CCT protocol. In order to record the air volume at the specific time when respiration was paused, the patient was asked to breathe through a spirometer (WaveFront™, Thor®) during scanning. This procedure allows for correction of lung air volume for appropriate comparison between the corresponding CCT and ReDS™ measurements.

After redacting patient identity, each CCT scan was saved to CD and analyzed subsequently by an independent blinded operator at a Siemens® workstation using lung analysis software (syngo.CT Pulmo 3D, Siemens®) which provides semi-automatic tools to analyze mean lung density (MLD). Mean lung density is defined as the average attenuation value of all voxels belonging to the lung and is measured in Hounsfield Units [HU].

MLD was then converted to fluid content (FC) in percentage units according to the equation: FC [%] = (MLD + 1000) / 10, which is based on the Hounsfield Units scale in which 0 HU is the value for water and −1000 HU is the value for air. The CCT FC values were then adjusted for the average lung volume obtained by spirometry to compensate for variations in lung air volumes during breath holds. The formula and other aspects of the protocols and analyses were previously validated and used by others [13–17]. This approach allows for comparison of ReDS and CCT readings in the same units of measure (i.e., percentage of lung volume consisting of water).

2.3. ReDS™

2.3.1. Technology

ReDS™ technology was originally developed by the military as a "see through wall" technology to identify survivors in rubble. The technology is based on a miniature radar system that employs low-power electromagnetic signals emitted into the body. The technology, implemented in a wearable vest, does not require contact with the skin and can be worn on top of clothing (Fig. 1).

Two sensors embedded in a wearable garment are attached to the body: one anteriorly on the chest and the other posteriorly on the patients' back. Each sensor is a small round device capable of transmitting and receiving the focused EM wave beam transferred through the pulmonary tissue. The analyzed signal reflects the dielectric properties of the section of the lung between the sensors. The dielectric coefficient of a material is represented by a frequency-dependent complex number describing its interaction with electromagnetic energy including the degrees of absorption, reflection and transmission of the energy. Since water has a very high dielectric coefficient, dielectric coefficients of tissues are determined predominantly by their fluid content [18,19]. For example, healthy fat tissue, which has low fluid content, is characterized by a relatively low dielectric coefficient, while healthy muscle tissue that is relatively rich in water is characterized by a higher dielectric coefficient. In addition, air has the lowest dielectric coefficient [18,19].

The dielectric coefficient of pulmonary tissue is determined by the dielectric coefficients of each of its components (e.g., blood, lung parenchyma, and air) and their relative concentrations. In the end, it is considered that the lung is primarily composed of air and water, components with widely different dielectric coefficients. Accordingly, the dielectric coefficient of the intact lung is very sensitive to the ratio between the volumes of air and water and thus, this number is a direct indicator of fluid concentration.

The healthy human lung (for an average 70 kg person) contains 450 to 500 ml of blood [20]. The extravascular compartment normally contains another 250 to 700 ml of fluid [21]. Since the normal total lung air volume at functional residual capacity is 1.8 to 2.2 l [22] with a tidal volume of 500 ml, it can be estimated that the intrathoracic fluid content ranges between 20 and 35% of the total volume. This range has been confirmed by lung density measurements performed by different quantitative imaging technologies (i.e. computed tomography, nuclear magnetic resonance imaging and positron emission tomography) [23–26].

2.4. Measurements

The ReDS™ measurements were performed by trained operators following the CT scan with patient lying in a hospital bed. Each patient's primary care physician was blinded to the ReDS™ data. The raw signals were stored on a computer and were analyzed using an algorithm that provided the pulmonary fluid content in units of percent (%). The operators and the observer who performed and analyzed the CT scans were also blinded to ReDS readings.

2.5. Statistical analyses

For descriptive statistics, continuous variables are presented as means ± standard deviation (SD) as well as minimum–maximum values. For categorical variables, the number and percent of non-missing values for each category within a parameter are calculated. For selected parameters, 95% confidence intervals of the mean are presented. T-test was used for comparing the fluid content [%] means of the two groups (ADHF and non-ADHF) based

Fig. 1. Wearable vest and console.

Table 1
Patients' characteristics.

Baseline characteristic			
Parameter	Mean ± SD [Min–Max]	ADHF	Non-ADHF
N	31	15	16
Age [year]	71.7 ± 11.2 [54–89]	73.8 ± 10.8 [56–89]	69.4 ± 11.6 [54–89]
Male n (%)	19 (61%)	10 (62.5%)	9 (60%)
Female n (%)	12 (39%)	6 (37.5%)	6 (40%)
Weight [kg]	77.3 ± 14.7 [57–113]	75.7 ± 15.7 [57–105]	78.9 ± 14.1 [60–113]
Height [meter]	1.68 ± 0.09 [1.55–1.86]	1.68 ± 0.08 [1.55–1.78]	1.69 ± 0.1 [1.55–1.86]
BMI [kg/m^2]	27.1 ± 4.8 [19.5–39.8]	26.7 ± 5.1 [19.6–39.8]	27.5 ± 4.7 [21.0–35.4]

on the values measured by both CCT and ReDS. Correlation values between ReDS and CCT in the ADHF group were calculated together with 95% confidence intervals and p-values. The correlation between the ReDS and CCT lung fluid content was calculated using intra-class correlation (ICC) type (1, 3) with 95% confidence intervals and p-values.

Bland–Altman analysis was used to compare the difference between the two lung fluid measurement methods (CT and ReDS).

Statistical significance is declared when the p value is found to be less than or equal to 0.05. All descriptive and inferential statistical analyses were performed using SAS statistical software, version 9.4.

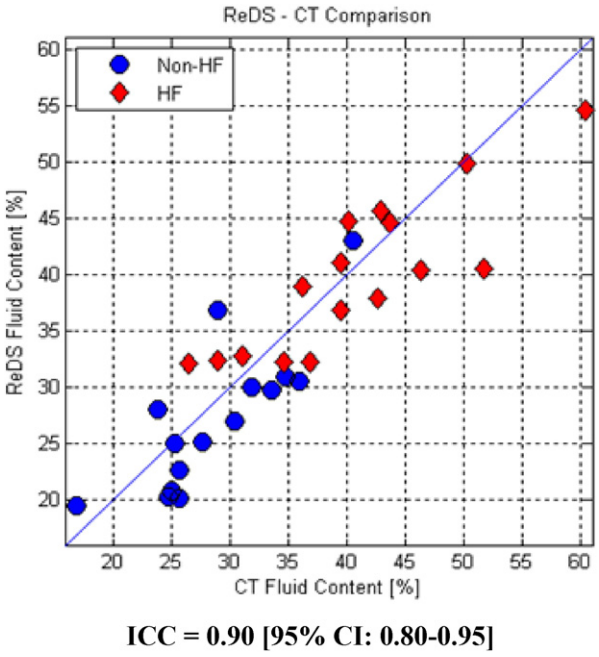


Fig. 3. ReDS™ vs. CT — comparison of lung fluid level quantification (N = 31).

3. Results

The final analysis included data from 31 of the 36 patients enrolled; low quality spirometry data acquisition prevented CCT and ReDS data comparison in 5 patients. Of the 31 patients in the final analysis, 16 patients were in the ADHF group and 15 patients were in the non-ADHF group. Patient characteristics are summarized in Table 1. The ADHF patients averaged 73.8 years of age weighing 75.7 kg with a BMI of 26.7; 62.5% were male. The characteristics of the non-ADHF group were similar with an average age of 69.4 years, a weight of 78.9 kg and a BMI of 27.5; 60.0% were male.

As noted above, CCT was performed in all the ADHF patients as part of the study protocol. None of those patients had parenchymal pulmonary pathologies; one of these patients had COPD. For non-ADHF patients, CCT was performed as part of their routine medical work-up. In 12 patients, this was for evaluation of pulmonary diseases (such as cancer, pneumonia, atelectasis, suspected PE), of which 3 patients had COPD. For the remaining 3 patients, the CCT was for evaluation of diseases of the mediastinum or aorta. Fig. 2a shows the CT of an ADHF patient; his ReDS reading was 46%. In comparison, Fig. 2b shows the CT of an ambulatory non-heart failure patient; his ReDS reading was 23%.

The percent fluid content in the lungs ranged between 17% and 60% by CCT and between 19% and 55% by ReDS. With data from all patients pooled, lung fluid content averaged 34.9 ± 9.6% by CCT and 33.8 ± 9.2% by ReDS.

CCT and ReDS™ measurements of pulmonary fluid content were compared in each patient as summarized in Fig. 3. The intraclass correlation, which provides a mean to quantify the similarity between absolute values, was found to be 0.90 [95% CI: 0.80–0.95]. Regression analysis applied to these data yielded a slope of 0.94 (95% confidence interval [0.77, 1.12]) and intercept 3.15 (95% confidence interval of [−2.97, 9.27]).

The Bland and Altman analysis (Fig. 4) illustrates the agreement between the two modalities by plotting the difference between the ReDS™ and CT pulmonary fluid measurements as a function of the average of the two measurements for each patient. As the plot shows, the points are scattered roughly evenly across the entire 15–60% range of fluid content values, which indicates that ReDS and CCT have comparable accuracy at low and high values of lung fluid content. The absolute difference in measurements between the two methods (i.e., the sum of all |CT-ReDS™| values) was 3.75% with a standard deviation of 2.22%.

Both CCT and ReDS™ yielded higher values for pulmonary fluid contents in ADHF patients as compared to non-ADHF patients (Fig. 5, $p < 0.001$ for each comparison). The mean CT value for the ADHF group was 40.7% with 95% CL of [36.0%–45.4%] compared to 28.7% with 95% CI of [25.4%–32.0%] for the non-ADHF group. The ReDS values

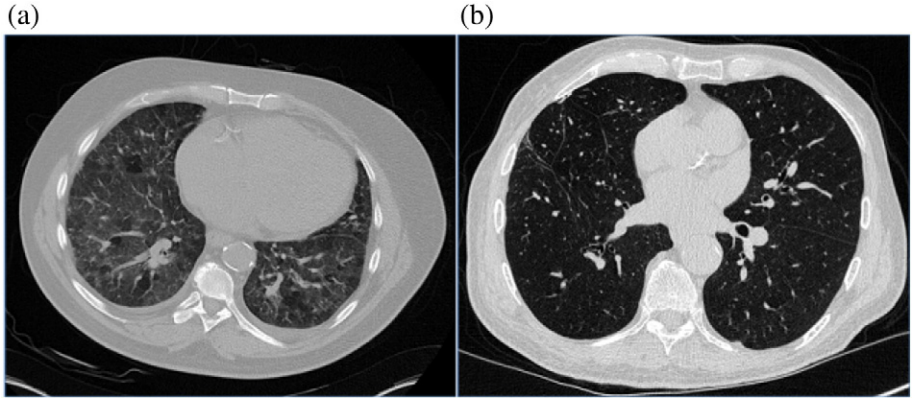


Fig. 2. (a) CT of ADHF patient with pulmonary edema (b) CT of ambulatory non-heart failure patient (dry lungs).

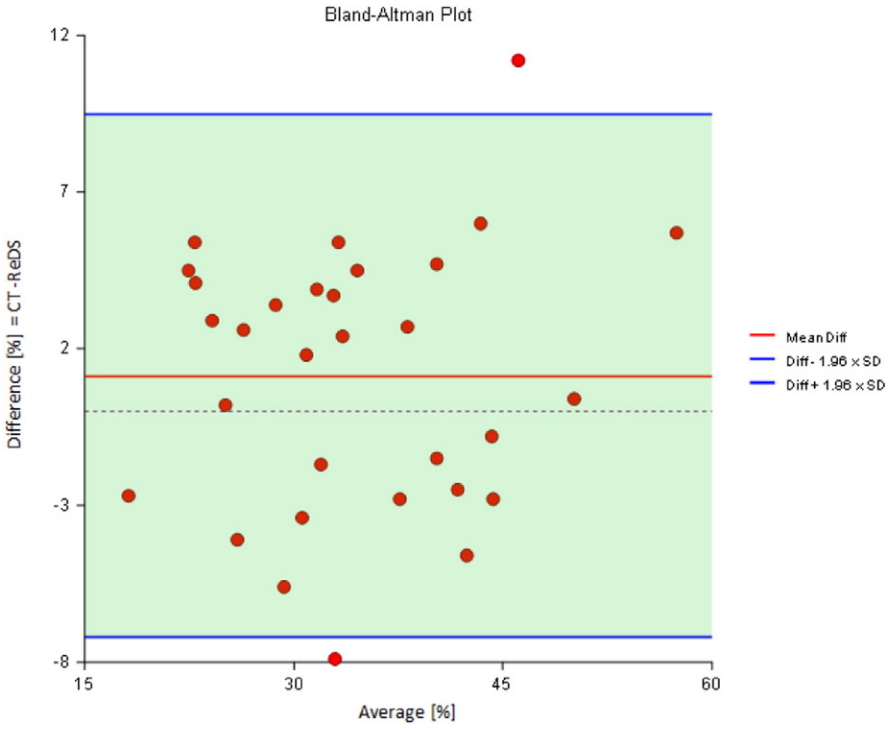
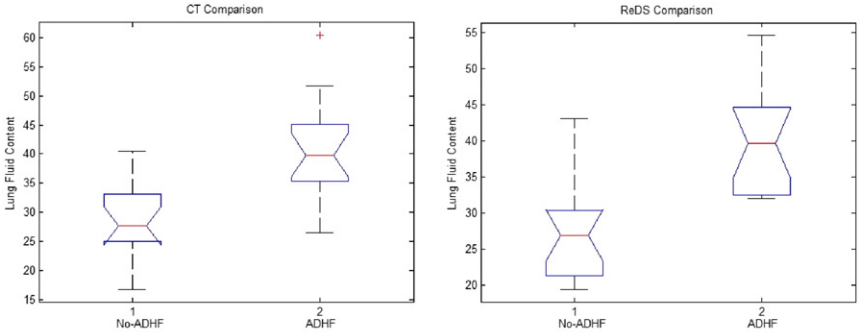


Fig. 4. Bland–Altman analysis comparing ReDS™ and CT pulmonary fluid quantifications.



CCT comparison between ADHF and Non-ADHF group*

Group	Mean	STD	95% CI
Non-ADHF	28.7	5.9	[25.4–32.0]
ADHF	40.7	8.8	[36.0–45.4]

*p-value = 0.0001

ReDS™ comparison between ADHF and Non-ADHF group**

Group	Mean	STD	95% CI
Non-ADHF	27.3	6.6	[23.6–31.0]
ADHF	39.8	6.8	[36.2–43.4]

**p-value < 0.0001

Fig. 5. Pulmonary fluid content: CCT and ReDS comparison between ADHF and non-ADHF group.

averaged 39.8% with 95% CL of [36.2%–43.4%] for the ADHF group compared to a mean value of 27.3% with 95% CL of [23.6%–31.0%] for the non-ADHF group.

4. Discussion

Dyspnea due to lung congestion is one of the leading manifestations of ADHF [27]. Early detection of systemic fluid overload and/or pulmonary congestion is the cornerstone for the prevention of acute HF decompensations, especially in high-risk patients. Accordingly, several strategies have been tested for early detection of meaningful increases in lung fluid content prior to full blown exacerbations requiring hospitalization. Remote telemonitoring using weight or detecting changes in bio-impedance, including internal implanted devices and wireless pressure sensors have been investigated with variable success [28–31]. The use of weight and symptoms as well as intrathoracic bio-impedance in randomized controlled studies had failed to reduce hospitalizations [32–34].

However, it was demonstrated in the CHAMPION study [3] that use of invasive pulmonary artery pressure monitoring successfully reduced the rate of hospitalizations by 33% over a mean follow-up time of 15 months. Most recently, during the open access phase of the study, there was a 48% reduction in the rate of readmissions over an additional mean 13 months follow-up period among the control group patients compared to their hospitalization rate during the randomized phase during which therapy was not guided by pulmonary artery pressure readings [35].

The ReDS™ system, which sends a focused electromagnetic beam through the chest cavity enabling direct measurement of the lung fluid content, is portable, non-invasive and easy to use and requires minimal patient collaboration. In our previous studies, we showed in an animal model that both chest CT and ReDS™ technology were sensitive in detecting changes in lung fluid content and demonstrated a high interclass and Pearson correlation coefficients of 0.95 [8] (and unpublished data). Moreover, we showed the fast response of ReDS™ to induced changes in pulmonary fluid volume status. In the clinical studies, we also demonstrated a strong correlation between ReDS™ measurements and fluid status during diuresis measured throughout the hospital admission of the ADHF patients [8]. The results of the present study provide direct validation of the accuracy of ReDS when compared to CCT, the current gold standard for measuring lung fluid content. This contrasts with bio-impedance-based measurements which are affected by many factors other than lung fluid content. Accordingly, ReDS may provide information that is clinically comparable to hemodynamic measurements, but is noninvasive.

5. Limitations

The present study focused on validating ReDS to measure lung fluid content. Direct comparison of ReDS to pulmonary pressures has not yet been performed. Nevertheless, initial results indicate that detection of changes in lung fluid content by ReDS measurements can be used to guide medical therapy and reduce HF hospitalizations in patients at high risk for readmission (ReDS-HF) [36,37]. Further validation of this finding is being obtained in a prospective, randomized study (SMILE™, NCT02448342).

6. Summary and conclusions

In summary, we have demonstrated that fluid content quantified by the ReDS™ system is highly correlated to CCT in quantifying pulmonary fluid content over a wide range of fluid content levels spanning the applicable clinical range. The ReDS™ system offers a reliable, non-invasive and portable technology for detection of even mild lung fluid content changes at the pre-symptomatic state, and may potentially assist monitoring patients with fluid management problems (including HF) during hospital admission and/or in ambulatory settings. Initial experience with ReDS™ guided-remote patient monitoring has been presented recently [36,37]. A larger randomized study is currently recruiting patients and will test the hypothesis that ReDS-based lung fluid status monitoring reduces the rate of heart failure readmissions (SMILE™, NCT02448342).

Clinical perspective

The ReDS™ technology described in this paper provides an absolute measure of lung fluid content that makes the measure immediately actionable. A reliable, non-invasive and portable technology for detection of lung fluid content changes at the pre-symptomatic state, can assist monitoring patients with different fluid management problems such as trauma, heart failure, and renal failure. Monitoring and management by ReDS technology is applicable either during admission and/or in the ambulatory setting, and may potentially help reduce readmissions of these patients, a significant clinical challenge especially in the heart failure patients' population.

Conflict of interest

The two studies described were sponsored by Sensible Medical Innovations Ltd. (SMI). Dr. Azzam, Dr. Gaspar, Dr. Faranesh-Abboud and Dr. Nizar have nothing to declare. Dr. Abraham is an SMI consultant. Dr. Amir was an SMI consultant at the time of study enrollment. Dr. Burkhoff is a consultant to SMI. Dr. Abbo is an SMI employee.

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References

[1] R.C. Bourge, W.T. Abraham, P.B. Adamson, et al., Randomized controlled trial of an implantable continuous hemodynamic monitor in patients with advanced heart failure, J. Am. Coll. Cardiol. 51 (11) (2008) 1073–1079.
[2] W.T. Abraham, P.B. Adamson, R.C. Bourge, et al., Wireless pulmonary artery haemodynamic monitoring in chronic heart failure: a randomised controlled trial, Lancet 377 (9766) (2011) 658–666.
[3] J.J. Marini, T.W.E., Acute Lung Injury, 1998 187.
[4] F.S. Bongard, M. Matthay, R.C. Mackersie, L.F. Lewis, Morphologic and physiologic correlates of increased extravascular lung water, Surgery 96 (2) (1984) 395–403.
[5] D.A. Warrell, T.M. Cox, J.D. Firth, E.J. Benz Jr., Oxford Textbook of Medicine, vol. 1Oxford University Press, 2003 1132.
[6] Q. Hamid, J. Shannon, J. Martin, Physiologic Basis of Respiratory Disease, BC Decker Inc., 2005 207.
[7] E.E. Bittar, Pulmonary Biology in Health and Disease, Springer-Verlag, 2002 244.
[8] O. Amir, D. Rappaport, B. Zafrir, W.T. Abraham, A novel approach to monitoring pulmonary congestion in heart failure: initial animal and clinical experiences using remote dielectric sensing technology, Congest. Heart Fail. 19 (3) (2013) 149–155.
[9] W.H.W. Tang, W. Tong, Measuring impedance in congestive heart failure: current options and clinical applications, Am. Heart J. 157 (3) (2009) 402–411.
[10] L. Gattinoni, A. Pesenti, M. Bombino, et al., Relationships between lung computed tomographic density, gas exchange, and PEEP in acute respiratory failure, Anesthesiology 69 (1988) 824–832.
[11] L.M. Malbouisson, J.C. Muller, J.M. Constantin, et al., the CT Scan ARDS Study Group, Computed tomography assessment of positive end-expiratory pressure-induced alveolar recruitment in patients with acute respiratory distress syndrome, Am. Respir. Crit. Care Med. 163 (2001) 1444–1450.
[12] N. Patroniti, G. Bellani, E. Maggioni, A. Manfio, B. Marcora, A. Pesenti, Measurement of pulmonary edema in patients with acute respiratory distress syndrome, Crit. Care Med. 33 (11) (2005 Nov) 2547–2554.
[13] R.J. Maunder, W.P. Shuman, J.W. McHugh, S.I. Marglin, J. Butler, Preservation of normal lung regions in the adult respiratory distress syndrome. Analysis by computed tomography, JAMA 255 (1986) 2463–2465.
[14] B.A. Simon, Non-invasive imaging of regional lung function using X-ray computed tomography, J. Clin. Monit. Comput. 16 (2000) 433–442.

[15] N. Morooka, S. Watanabe, Y. Masuda, Y. Inagaki, Estimation of pulmonary water distribution and pulmonary congestion by computed tomography, Jpn. Heart J. 23 (1982) 697–709.
[16] S. Kato, T. Nakamoto, M. Iizuka, Early diagnosis and estimation of pulmonary congestion and edema in patients with left-sided heart diseases from histogram of pulmonary CT number, Chest 109 (1996) 1439–1445.
[17] E.M. Snyder, K.C. Beck, S.T. Turner, E.A. Hoffman, M.J. Joyner, B.D. Johnson, Genetic variation of the beta2-adrenergic receptor is associated with differences in lung fluid accumulation in humans, J. Appl. Physiol. (1985) 102 (2007) 2172–2178.
[18] C. Gabriel, S. Gabriel, E. Corthout, The dielectric properties of biological tissues: I. Literature survey, Phys. Med. Biol. 41 (1996) 2231–2249.
[19] S. Gabriel, R.W. Lau, C. Gabriel, The dielectric properties of biological tissues: II. Measurements in the frequency range 10 Hz to 20 GHz, Phys. Med. Biol. 41 (1996) 2251–2269.
[20] T.K. Agasti, Textbook of Anesthesia for Postgraduates 1st Edition, first ed. Jaypee Brothers Medical Pub, October 31, 2010 34.
[21] C.J. Wallin, L.G. Leksell, Estimation of extravascular lung water in humans with use of $2H_2O$: effect of blood flow and central blood volume, J. Appl. Physiol. (1985) 76 (5) (May 1994) 1868–1875.
[22] P.H. Quarijer, G.J. Tammeling, J.E. Cotes, O.F. Pedersen, R. Peslin, J.-C. Yernault, Lung volumes and forced ventilatory flows, report working party standarization of lung function tests. European community for steel and coal official statement of the European Respiratory Society, Eur. Respir. J. 6 (Suppl. 16) (1993) 5–40.
[23] U.J. Schoepf, J.E. Aldrich, Multidetector-Row CT of the Thorax, Springer Verlag, 2004 126.
[24] J. Branislav, Advances in Radiation Oncology in Lung Cancer, Springer, 2005.
[25] J. Kalef-Ezra, A. Karantanas, P. Tsekeris, CT measurement of lung density, Acta Radiol. 40 (1999) 333–337.
[26] C.G. Rhodes, P. Wollmer, F. Fazio, T. Jones, Quantitative measurement of regional extravascular lung density using positron emission and transmission tomography, J. Comput. Assist. Tomogr. 5 (6) (1981 Dec) 783–791.
[27] J.A. Ezekowitz, A.F. Hernandez, C.M. O'Connor, et al., Assessment of dyspnea in acute decompensated heart failure: insights from ASCEND-HF (acute study of clinical effectiveness of nesiritide in decompensated heart failure) on the contributions of peak expiratory flow, J. Am. Coll. Cardiol. 59 (2012) 1441–1448.
[28] G. Giamouzis, D. Mastrogiannis, K. Koutrakis, et al., Telemonitoring in chronic heart failure: a systematic review, Cardiol. Res. Pract. 2012 (2012) 410820.
[29] E.K. Heist, J.M. Herre, P.F. Binkley, et al., Analysis of different device-based intrathoracic impedance vectors for detection of heart failure events (from the detect fluid early from intrathoracic impedance monitoring study), Am. J. Cardiol. 114 (2014) 1249–1256.
[30] M.T. Ledwidge, R. O'Hanlon, L. Lalor, et al., Can individualized weight monitoring using the HeartPhone algorithm improve sensitivity for clinical deterioration of heart failure? Eur. J. Heart Fail. 15 (2013) 447–455.
[31] M.K. Shochat, A. Shotan, D.S. Blondheim, M. Kazatsker, I. Dahan, A. Asif, Y. Rozenman, I. Kleiner, J.M. Weinstein, A. Frimerman, L. Vasilenko, S.R. Meisel, Non-invasive lung IMPEDANCE-guided preemptive treatment in chronic heart failure patients: a randomized controlled trial (IMPEDANCE-HF trial), J. Card. Fail. (April 4 2016).
[32] S.I. Chaudhry, J.A. Mattera, J.P. Curtis, J.A. Spertus, J. Herrin, Z. Lin, C.O. Phillips, B.V. Hodshon, L.S. Cooper, H.M. Krumholz, Telemonitoring in patients with heart failure, N. Engl. J. Med. 363 (2010) 2301–2309.
[33] F. Koehler, S. Winkler, M. Schieber, et al., Telemedical interventional monitoring in heart failure (TIM-HF), a randomized, controlled intervention trial investigating the impact of telemedicine on mortality in ambulatory patients with heart failure: study design, Eur. J. Heart Fail. 12 (12) (2010) 1354–1362.
[34] D.J. van Veldhuisen, F. Braunschweig, V. Conraads, I. Ford, M.R. Cowie, G. Jondeau, J. Kautzner, R.M. Aguilera, M. Lunati, C.M. Yu, B. Gerritse, M. Borggrefe, DOT-HF Investigators, Intrathoracic impedance monitoring, audible patient alerts, and outcome in patients with heart failure, Circulation 124 (16) (2011) 1719–1726.
[35] W.T. Abraham, L.W. Stevenson, R.C. Bourge, J.A. Lindenfeld, J.G. Bauman, P.B. Adamson, for the CHAMPION Trial Study Group, Sustained efficacy of pulmonary artery pressure to guide adjustment of chronic heart failure therapy: complete follow-up results from the CHAMPION randomised trial, Lancet 6736 (15) (2015) 1–9.
[36] W.T. Abraham, O. Amir, J.M. Weinstein, A. Abbo, G.T. Ben, Evaluation of ReDS-guided patient management in ambulatory heart failure patients at-risk for rehospitalization, Eur. J. Heart Fail. 17 (2015) 78–79.
[37] W.T. Abraham, O. Amir, J.M. Weinstein, A. Abbo, T. Ben-Gal, Remote dielectric sensing (ReDS)-guided patient management of ambulatory heart failure patients reduces rehospitalization rates, J. Card. Fail. 21 (8) (2015) S77.