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Feasibility of using 'lung density' values estimated from EIT images for clinical diagnosis of lung abnormalities in mechanically ventilated ICU patients

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Abstract

This paper reports on the results of a study which compares lung density values obtained from electrical impedance tomography (EIT), clinical diagnosis and CT values (HU) within a region of interest in the lung. The purpose was to assess the clinical use of lung density estimation using EIT data. In 11 patients supported by a mechanical ventilator, the consistency of regional lung density measurements as estimated by EIT was validated to assess the feasibility of its use in intensive care medicine. There were significant differences in regional lung densities recorded in the supine position between normal lungs and diseased lungs associated with pneumonia, atelectasis and pleural effusion (normal; $240 \pm 71.7\,\mathrm{kg\,m^{-3}}$, pneumonia; $306 \pm 38.6\,\mathrm{kg\,m^{-3}}$, atelectasis; $497 \pm 130\,\mathrm{kg\,m^{-3}}$, pleural effusion; $467 \pm 113\,\mathrm{kg\,m^{-3}}$: Steel–Dwass test, $p < 0.05$). In addition, in order to compare lung density with CT image pixels, the image resolution of CT images, which was originally 512×512 pixels, was changed to 16×16 pixels to match that of the EIT images. The results of CT and EIT images from five patients in an intensive care unit showed a correlation coefficient of 0.66 ± 0.13 between the CT values (HU) and the lung density values ($\mathrm{kg\,m^{-3}}$) obtained from EIT. These

results indicate that it may be possible to obtain a quantitative value for regional lung density using EIT.

Keywords: impedance, tomography, absolute lung resistivity, lung density, CT value

(Some figures may appear in colour only in the online journal)

1. Introduction

Mechanical ventilation is necessary in intensive care medicine. Although management of respiration with mechanical ventilation can improve the prognosis for acute phase patients, it has recently been found to produce ventilator_induced lung injuries (VILI) or ventilator-associated lung injuries (VALI) (Frank and Matthay 2003, Ricard *et al* 2003, Frank *et al* 2006). Additionally, acute respiratory distress syndrome (ARDS) is associated with non-homogeneous lesions in the lungs (Rouby *et al* 2003, Grasso *et al* 2009).

Generally, chest x-rays and computed tomography (CT) have been used for diagnosis of ARDS. However, information from a chest x-ray is limited. This makes it hard to reach a diagnosis, and hence the patient is often required to undergo a CT examination, which is a cumbersome procedure for a patient connected to a mechanical ventilator. Therefore, there is a need for local regional monitoring of lung lesions at the bedside, especially in an intensive care unit (ICU).

In some cases, electrical impedance tomography (EIT) has been used for the monitoring of lung lesions of patients (Victorino *et al* 2004, Arad *et al* 2009, Bikker *et al* 2009, Costa *et al* 2009, Zhao *et al* 2009, Adler *et al* 2012, Bläser *et al* 2014, Schaefer *et al* 2014, van der Burg *et al* 2014). Victorino *et al* verified the feasibility of management of a mechanical ventilator using EIT in animals and suggested that safe and protective lung treatment with EIT was possible. However, these EIT systems needed calibration to achieve quantitative and reproducible measurements.

Brown *et al* (2002) suggested a measurement method for calculating absolute lung resistivity and Nebuya *et al* (2011) measured lung density values from EIT data sets without calibration. However, the clinical feasibility of these methods for patients connected to a mechanical ventilator has not been investigated. We had earlier proposed the use of 'lung density' as an absolute measure of lung function using EIT data sets, but had not compared it with clinical results from patients with lung disease.

The current study assesses the feasibility of measuring lung density using two methods. The first method involves defining a region of interest (ROI) over four parts of the lung regions in an x-ray CT image and comparing the clinical diagnosis with the measured lung density ($kg\,m^{-3}$). Another approach carries out a comparison between CT values (HU) and lung density ($kg\,m^{-3}$), thus representing different physical properties of lung tissue, to assess the feasibility of using lung density values as a basis for clinical diagnosis of lung disease.

2. Methods

2.1. Determination of lung density using absolute lung resistivity

The assessment of lung density was suggested by Nebuya *et al* (2011). Absolute lung resistivity (AbR) was determined using the method devised by Brown *et al* (2002). In summary, this method returns the best estimate of the absolute value of lung tissue resistivity by comparing

the measured EIT data to computed data sets. Lung filling factor (FF) is the ratio of volume of air to condensed matter within the lung tissue.

A function between AbR and FF was provided using a numerical lung model developed by Nopp *et al* (1997). If we know the density of the condensed matter of the lungs then we can relate FF to the overall density of lung tissue (Lung_density) as follows:

$$\text{Lung\_Density} = \frac{\text{Lung\_Weight}}{\text{Air\_Volume} + \text{Tissue\_Volume}} \tag{1}$$

$$\text{FF} = \frac{\text{Air\_Volume}}{\text{Tissue\_Volume}} \tag{2}$$

Substituting from equation (1) into equation (2)

$$\text{Lung\_Density} = \frac{\text{Lung\_Weight}}{\text{FF.Tissue\_Volume} + \text{Tissue\_Volume}} = \frac{\rho_t}{\text{FF} + 1} \tag{3}$$

and

$$\text{FF} = \frac{\rho_t}{\text{Lung\_Density}} - 1 \tag{4}$$

A value for $\rho_t = 1050\,\text{kg}\,\text{m}^{-3}$ is used (Boyd 1962). *AbR* was determined as a function of FF from the Nopp model (Nopp *et al* 1997).

2.2. Measurement of regional lung density and comparison with clinical diagnosis by a clinician

In the intensive care unit at Kitasato University Hospital, 11 male patients connected to a mechanical ventilator were selected for the measurements based on three factors which would not influence their main treatment. These factors were stable life condition, no excoriation at the area where measurement electrodes were to be placed and available bed rest.

EIT data was measured 207 times in total from the 11 male patients using a Sheffield Mk3.5 system (Maltron International Ltd.)(Wilson *et al* 2001). Eight Ag/AgCl ECG type electrodes were spaced equally around the thorax 5 cm above the level of the xiphoid process and data was collected in one minute epochs (1500 frames) of mechanical ventilation. Table 1 shows the patients' profiles.

EIT was reconstructed utilizing the Sheffield back projection method and a sensitivity matrix (Metherall *et al* 1996). Lung densities were estimated for four lung regions defined as right anterior, left anterior, right posterior and left posterior as shown in figure 1(*a*). The four regions of interest (ROIs) were fixed for all patients and postures.

The 548 measured lung regions were grouped into four clinical categories, namely normal lung (304) and three pulmonary diseases: pneumonia (33), atelectasis (136) and pleural effusion (75), following clinical diagnosis using both x-ray and CT images as shown in figure 1(*b*). The lung regions were defined as 'inner thoracic cavity' to include pleural effusion for clinical diagnosis.

The lung density for each lung region was estimated using 1 min of data that included 24 measurements made at frequencies between 2 and 768 kHz. The lung densities for the four clinical categories were compared statistically using the Steel–Dwass test ($p < 0.05$).

Table 1. Patients' profiles for Method 2.2 ($N = 11$).

Age (year)	60.8 ± 15.5
Weight (kg)	62.4 ± 8.0
Height (cm)	165 ± 4.0
BMI	23.0 ± 3.3
Gender (M: F)	11:0
RASS index	− 4.27 ± 1.0
Diagnosis	
Post CPA	2
Severe pancreatitis	2
Septic shock	4
Subarachnoid hemorrhage	1
Brain contusion	1
Severe pneumonia	1
	11

BMI: body mass index.
RASS: Richmond agitation and sedation scale.
CPA: cardio pulmonary arrest.

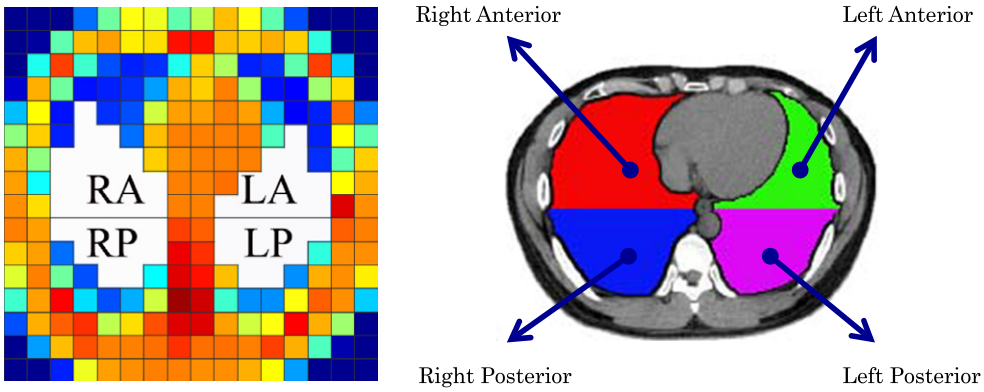

Figure 1. Definition of lung regions at the level of the EIT electrode plane. (*a*) A corresponding CT values image of the lungs with ROIs placed over the lung regions where lung densities were estimated from 16 × 16 pixels of EIT (white color). RA: right anterior, LA: left anterior, RP: right posterior, LP: left posterior. (*b*) Lung regions for clinical diagnosis of pulmonary diseases: normal, pneumonia, atelectasis and pleural effusion.

2.3. Evaluation of the correlation coefficient between CT and lung density values calculated pixel by pixel

Five patients who were connected to a ventilator, were studied by recording x-ray CT and EIT images within 24 h of each other. On one of the patients, both images were recorded three times on three consecutive days because the pathological situation had clearly changed. In total, seven x-ray CT and EIT images were analyzed. Table 2 shows the patients' profiles.

Table 2. Patients' profiles for Method 2.3 ($N = 5$).

Age (year)	59.6 ± 17.73
Weight (kg)	73.0 ± 9.5
Height (cm)	166 ± 4.7
BMI	26.5 ± 2.7
Gender (M: F)	5:0
X-ray CT recording	7
Diagnosis	
Post CPA	1
Lung Contusion	1
Pneumonectomy	1
Pneumonia	1
Abdominal Aortic Aneurysm	1
	5

BMI: body mass index.
CPA: cardio pulmonary arrest.

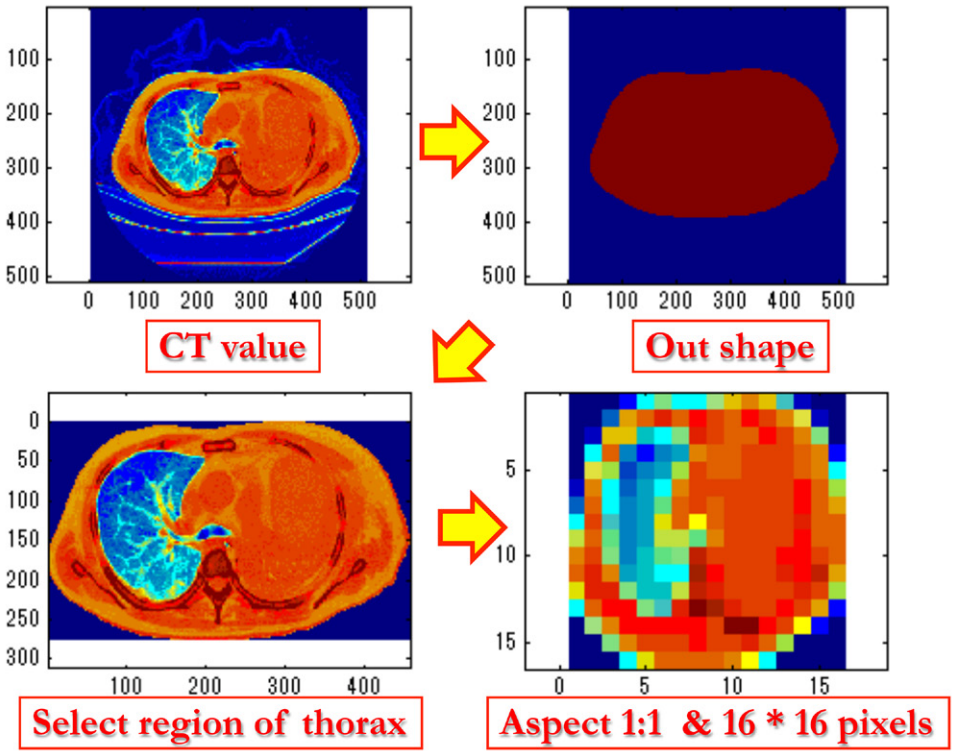

Figure 2. CT values from CT data compared with lung density estimated from EIT.

The Sheffield Mk3.5 EIT system was used in this study. To achieve a pixel by pixel comparison between CT values and lung densities, the shape of the thorax in the CT images was altered to become circular and the spatial resolution, which was originally 512 × 512 pixels, was changed into 16 × 16, similar to that of EIT (figure 2). The lung density at each

Table 3. Lung density measurements with respect to the patient's position and pulmonary disease in four areas of the lung (11 cases, 207 measurements, 548 lung areas).

		Supine			101
		Right lateral decubitus			48
		Left lateral decubitus			51
		Lung area			
Posture	RA	LA	RP	LP	
Normal	125	83	32	64	304
Pneumonia	13	4	12	4	33
Atelectasis	46	11	54	25	136
Pleural effusion	16	5	25	29	75
	200	103	123	122	548

RA: right anterior; LA: left anterior; RP: right posterior; LP: left posterior.

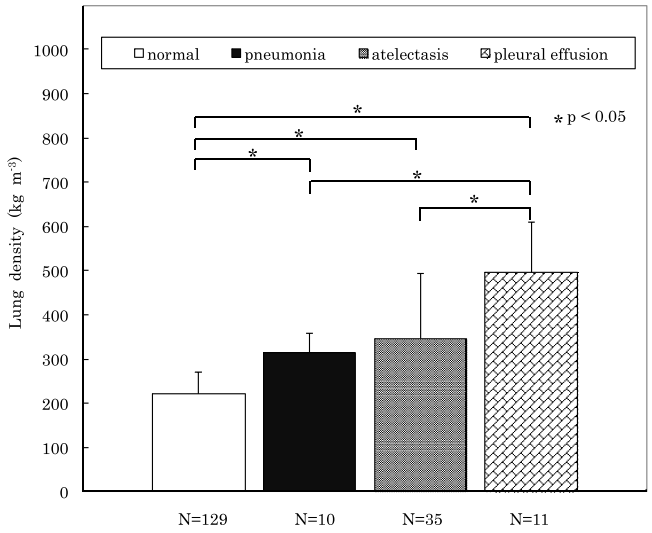

Figure 3. Relationship between pulmonary disease and lung density in the supine position. There were significant differences in the regional lung densities categorized for the four groups ($p < 0.05$) and the mean values of the regional lung densities in the three pulmonary diseases were higher than those for normal lungs.

pixel was estimated using one minute of data, at frequencies of less than 326 kHz. Regions of interest (ROI) over the lung area were chosen manually. Correlation coefficients were calculated between the CT values (HU) and the lung densities (kg m^{-3}) in all of the subjects.

The studies were approved by the ethics committee of the department of medicine of Kitasato University and informed consent was obtained from the patients' relatives.

3. Results

Table 3 gives statistics on the EIT measurements that were made in the clinically diagnosed groups. Approximately half of the EIT data was measured in the supine position and 40% of regional lung areas were diagnosed as normal.

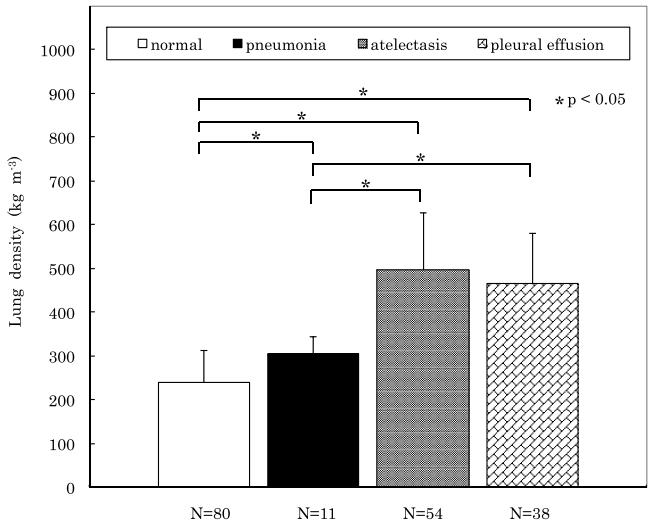

Figure 4. The relationship between pulmonary disease and lung density in the left lateral decubitus position. There were significant differences in the regional lung densities categorized for four groups ($p < 0.05$) but the mean value categorized for the pleural effusion group was decreased after a change of posture from a supine position to a left lateral decubitus.

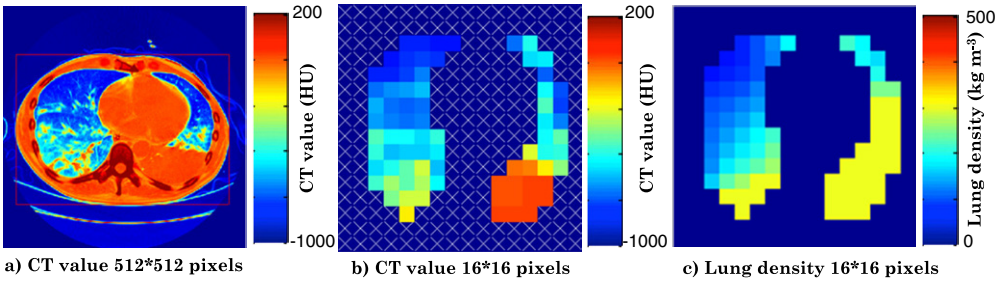

Figure 5. A comparison of CT values (HU) and lung density ($kg\,m^{-3}$) in a patient.

Figure 3 shows the relationship between pulmonary disease and the measurements of lung density in the supine position. There were significant differences in regional lung density between the four groups; regional lung densities in the three pulmonary disease groups were higher than for those in the normal lung group (normal: $221 \pm 49.4\,kg\,m^{-3}$, pneumonia: $314 \pm 44.1\,kg\,m^{-3}$, atelectasis: $346 \pm 148\,kg\,m^{-3}$, pleural effusion: $495 \pm 114\,kg\,m^{-3}$).

In addition, when the posture of the patients was changed from supine to the lateral decubitus position (figure 4), there was a significant difference in the regional lung densities between pneumonia and atelectasis but no significant difference between atelectasis and pleural effusion (normal: $240 \pm 71.7\,kg\,m^{-3}$, pneumonia: $306 \pm 38.6\,kg\,m^{-3}$, atelectasis: $497 \pm 130\,kg\,m^{-3}$, pleural effusion: $467 \pm 113\,kg\,m^{-3}$).

Figure 5 shows the result of a comparison between CT and lung density values in one patient. The pixel by pixel comparisons are in reasonable agreement around the regions of both lung collapse and consolidation. The data from all five patients is plotted in figure 6.

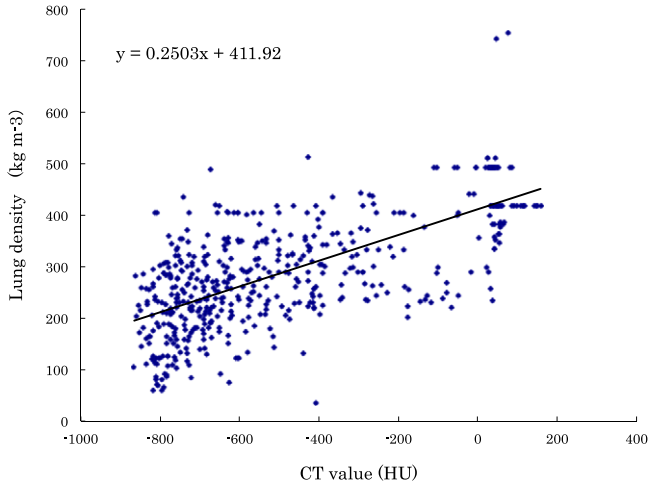

Figure 6. The relationship between CT values (HU) and lung density ($kg\,m^{-3}$) in five patients.

Correlation coefficients were determined for individual patients and the averaged correlation coefficient in five patients was 0.66 ± 0.13 between CT value and lung density.

4. Discussion

In this study, the use of EIT to determine regional lung density for the evaluation of lung disease was assessed. Equation (1) shows that a decrease in air content of the lungs is associated with an increase in lung density. Pneumonia is described as an inflammation of the parenchyma of the lungs and accumulation of abnormal alveolar filling with pus and fluid. Atelectasis is alveolar collapse. Both these disease conditions would decrease the air content when compared with a normal lung. The third condition of pleural effusion causes excess fluid to accumulate in the pleura. As the density of this fluid will be considerably higher than that of the lungs in the other two diseases, regional lung density was expected to show the highest value.

The results given in figure 3 show statistical differences between the regional lung densities in the case of normal lungs and those affected by pulmonary diseases. The regional lung density in the pleural effusion group showed the highest value. However, there were no significant differences between pneumonia and atelectasis in the supine position. The reason for this is believed to arise from the difficulty of discriminating between pneumonia and atelectasis. In some of the cases used in this study, both diseases were present in the same region. To achieve higher discrimination, smaller regions should be used for lung density measurement and clinical diagnosis based on the chest x-ray and CT. However, there were statistically significant differences between the lung regions of pneumonia and atelectasis when the posture was changed from supine to the left lateral position. This may result from the fact that atelectasis can easily change the degree of alveolar collapse, depending on body posture. However, alveolar filling with pus and fluid in pneumonia is not dependent on posture. These factors may explain why the lung density differences are affected by postural change.

In the cases of pleural effusion, regional lung density did change when the patient's posture was altered from supine to the left lateral decubitus position. The cause of these significant changes in regional lung density associated with pleural effusion was considered to be the movement of pulmonary edema with changes in posture.

Errors will have arisen from the use of fixed regions of interest (ROIs) to estimate lung densities. The same ROIs were used in all patients and postures. Changes in the areas of dependent and nondependent lungs will occur when body posture is changed. In future similar studies of lung density, ROIs should be changed for every patient and as a function of posture. This was not possible with the relatively small number of pixels used in the current study.

The correlation coefficients comparing CT values and regional lung densities calculated from the EIT measurements were significant. However, the alteration of the thorax shape into a circular shape and the manual placement of the ROIs will necessarily have introduced errors as a result of the associated poor registration results in the two imaging modalities. Deformation of the CT images to make them circular was carried out in order to match the circular EIT images. The EIT images using linear back projection do not take into account boundary shape. Ideally, it would be better to construct a finite element model of the thorax, created from CT slices for each patient, and to estimate the lung density by solving the inverse problem for the true body shape, but this is not easy and is likely to introduce additional errors in the calculation of absolute lung resistivity. Grychtol *et al* (2010) suggested how to define ROIs of lung automatically. This methodology could be applied in subsequent studies of this kind.

The method of measuring lung density requires measurements to be made over a wide frequency range. In this study, the number of high frequency measurements used was reduced from 24 to 18 to avoid measurement errors at higher frequencies. Making accurate impedance measurements at high frequency is known to be difficult. We also observed noise at higher frequencies in the data collected in the ICU. Therefore, development of a more accurate measurement device at high frequency will be necessary to get more accurate results for the estimation of lung density.

A further problem in the study arose because CT and EIT measurements were often not made on the same day, because of limitations in ensuring the presence of clinical staff who could help to obtain measurements in the ICU. Lung disease can change within periods as short as 30 min, so in our study this will have reduced the correlation between the CT and EIT measurements of lung density. However, none of the patients showed significant changes in the chest x-ray images, PaO_2, SaO_2 or $PaCO_2$ within 24 h. Therefore, it was assumed that there would not be large changes in CT and lung density values. If possible, future studies should reduce the interval between the CT and EIT measurements.

ROIs were defined pixel by pixel manually to cover the lung area. In five patients, there was no area of pleural effusion existing outside of visceral pleura. Strictly speaking, lung density should not include pleural effusion. Therefore, a modified definition of lung density will be needed to give a clear objective definition of the ROIs.

Although in principle both parameters, CT values and lung density, may not be the same, because they are derived from x-ray absorbance and electrical resistivity respectively, the results of this study suggest that lung density might be a useful index for the evaluation of lung disease. However, the method needs to be refined, taking into account the problems that have been described. Further experiments are also required to verify the findings with reference to a larger number of patients.

These results indicate that it is possible to obtain a quantitative value for regional lung density using the EIT technique with no risk of exposure to harmful radiation as in x-ray and CT.

Whilst CT has the advantage of providing much better anatomical diagnosis, EIT may be a useful technique for daily monitoring of the lung function of patients in an intensive care unit.

5. Conclusion

In this study, the use of EIT to estimate lung density has been assessed using two methods. One result showed good agreement between EIT and the clinical diagnosis of pneumonia, atelectasis or lung water. A second result indicated that there were good correlations between lung density ($kg\,m^{-3}$) and CT values (HU). These results appear to show that lung density measurement is a potential method for the evaluation of lung disease.

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