Preliminary Results on Different Impedance Contrast Agents for Pulmonary Perfusion Imaging with Electrical Impedance Tomography

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Abstract.
Recent studies in animal models suggest that the use of small volume boluses of NaCl as an impedance contrast agent can significantly improve pulmonary perfusion imaging by Electrical Impedance Tomography (EIT). However, these studies used highly concentrated NaCl solution (20%) which may have adverse effects on the patients. In a pilot experiment, we address this problem by comparing a number of different Impedance Contrast Boluses (ICBs). Conductivity changes in the lungs of a sheep after the injection of four different ICBs were compared, including three NaCl-based ICBs and one glucose-based ICB. The following procedure was followed for each ICB. Firstly, ventilation was turned off to provide an apneic window of approximately 40 s to image the conductivity changes due to the ICB. Each ICB was then injected through a pig-tail catheter directly into the right atrium. EIT images were acquired throughout the apnea to capture the conductivity change. For each ICB, the experiment was repeated three times. The three NaCl-based ICB exhibited similar behaviour in which following the injection of each of these ICBs, the conductivity of each lung predictably increased. The effect of the ICB of 5% glucose solution was inconclusive. A small decrease in conductivity in the left lung was observed in two out of three cases and none was discernible in the right lung.

1. Introduction
Pulmonary perfusion is as important as lung ventilation as both elements are necessary to sufficiently describe the regional behaviour of lung tissues for applications such as the adjustment of ventilator settings [1]. However, the significantly smaller amplitude of the perfusion impedance change signal compared to the respiratory impedance change signal renders perfusion mapping very difficult.

Recently, Borges et al [2] proposed a novel method to determine regional blood flow based on impedance change. They used a bolus of hypertonic sodium chloride (20% NaCl) as an impedance contrast agent. An algorithm was then performed to follow the first–pass kinetics of this impedance contrast bolus to quantitatively measure the relative regional blood flow in the lungs and heart. The regional blood flow measured by EIT using this novel method, in both healthy and injured lung cases in six piglets, is highly correlated with that measured by SPECT.
The use of highly concentrated NaCl solution (20%), however, may have adverse effects on the patients, especially those who are critically ill with pre-existing cardiac or renal conditions. We address this problem by experimentally comparing a number of different Impedance Contrast Boluses (ICBs). The purpose was to find an alternative to the highly concentrated 20% NaCl solution for pulmonary perfusion/blood-flow imaging.

2. Method

2.1. Experimental procedure

The experiment was performed on a male Merino-cross, weighing 64 kg, using the KHU Mark 2.5 Impedance Imaging system [3] with 16 electrodes placed equidistant around the thorax of the animal in a transverse plane. The plane of electrodes was located at approximately the 6th intercostal space of the animal. The sheep was appropriately anaesthetised and mechanically ventilated. The animal was selected to lack any cardiac or respiratory problem. This experiment has been approved by the Westmead Hospital Animal Ethics Committee.

EIT data were acquired using the adjacent electrodes current injections (1 mA p-p, 50 kHz) and voltage measurements protocol at 33 fps. The experimented ICBs, in order of injection, included:

- ICB1: 60 ml of warm (37 °C) 3% NaCl solution,
- ICB2: 60 ml of cold (21 °C) 5% glucose solution,
- ICB3: 10 ml of warm (37, °C) 20% NaCl solution,
- ICB4: 60 ml of cold (21 °C) 3% NaCl solution,

The following procedure was followed for each ICB. Firstly, ventilation was turned off to provide an apneic window of approximately 40s to image the conductivity changes due to the ICB without the interference from the ventilation signal. Each ICB was then injected through a pig-tail catheter directly into the right atrium at no more than 10 seconds after the start of the apnea. The injection of each ICB took less than 5 seconds to complete. EIT images were acquired throughout the apnea to capture the conductivity change due to each ICB.

The experiment was repeated three times for each ICB, with 5 to 10 minutes between two consecutive injections. In order to prevent any residual effect, 60 ml of 5% glucose was injected into the ICB injection catheter before an ICB of a different type was injected, followed by 5 ml of the solution the successive ICB was based on. These injections were firstly, to erase the presence of the preceding ICB in the injection catheter and secondly, to dilute out any residual effect of the preceding ICB in the lungs.

2.2. Reconstruction algorithm and processing of reconstructed images

Standard time difference EIT was employed. The reference voltage measurement set was the computed mean of the first 1000 frames in each case. Notably, these were the frames in which the animal was mechanically ventilated. The GREIT reconstruction algorithm [4] was employed to reconstruct images based on an extruded sheep thorax FEM.

Two regions of interest (ROIs) were visually identified from the ventilation EIT images to represent the left and right lungs. The conductivity change within each ROI throughout the experiment was extracted and averaged to reflect the mean change. A Butterworth low-pass filter with the cut-off frequency of 0.3 Hz was used to reduce high frequency component of the signal, which included cardiac signal and noise.

Relative conductivity change for each ROI in each case was calculated as:

\[ \frac{X_{\text{frames per second}}} {X_{\text{ref}}} \]
Figure 1. Relative conductivity change over time after the ventilator was turned off followed by injection of ICB1, ICB2, ICB3, ICB4 and without any ICB injection (Without ICB). Time $t = 0$ corresponds to the beginning of injection.

|       | Left Lung R | Right Lung R |
|-------|-------------|--------------|
| ICB1  | 1.08 ± 0.10 | 0.87 ± 0.09  |
| ICB3  | 1.23 ± 0.11 | 0.91 ± 0.11  |
| ICB4  | 1.04 ± 0.12 | 0.74 ± 0.12  |

Table 1. Mean and standard deviation of the maximum relative conductivity change (R) induced by the injection of three NaCl-based ICBs (ICB1, 3 and 4). The positive R values indicated an increase in conductivity.

$$R_{ICBx} = \frac{\sigma_{ICBx} - \bar{\sigma}_{Apnea}}{\bar{\sigma}_{Apnea}}$$

where $\bar{\sigma}_{Apnea}$ was the mean of the conductivities of each ROI from the beginning of apnea to the time at which ICB injection started or the first 10 s of apnea where there is no ICB injection.

3. Results

Figure 1 shows the relative conductivity change in the left and right lungs ROIs throughout the experiment with and without ICB injections. Observably, during apnea and without ICB injection, the conductivity of the two lungs were similar to each other and remained relatively flat throughout. Relative conductivity change after the introduction of contrast shows dependence on the type of ICB. The responses of the two lungs under the influence of the same ICB were similar but not identical, both in magnitude and phase.
4. Discussion and Conclusion

We report the conductivity changes due to four different ICBs in an ovine model. Our preliminary result shows conductivity contrast caused by injection of 10 ml of 20% NaCl (ICB 3) in the ovine model was much higher (up to 123% in the left lung) than the 10% previously reported in [2] in piglet models. We postulate that the discrepancy is due to the intrinsic differences in sizes of the blood volumes and tissue perfusion of each model.

The ICBs 1, 3 and 4 displayed similar dilution curves (based on the conductivity change), which were in agreement with the general shape that was previously reported [2; 5; 6].

The larger bolus size evidently compensated for the lower concentration of NaCl used in ICB 1 and 4 (3%) as the conductivity increases caused by these two ICBs were comparable to that caused by the ICB 1 (10 ml of 20% NaCl) (see Table 1). Furthermore, a warm (37°C) contrast bolus was marginally more effective than a cold (21°C) one as indicated by the slightly higher increase in conductivity caused by ICB1 compared with ICB2 (see Table 1). The closely matched results between ICB1 and ICB4 also indicated that the residual effect of previous ICBs, which we had encountered in the past experiments, were mitigated.

The glucose-based ICB effect on conductivity was unexpected based on previous reports that glucose should cause a decrease in conductivity [7]. In our in vivo experiment, the change caused by this ICB was inconclusive. In two out of three experiments, a small relative conductivity decrease was observed in the left lung (\(R = -0.14\) and \(R = -0.6\)). However, no such decrease were discernible in the right lung in all three cases. The small decrease observed were within experimental error (standard deviation for the NaCl-based ICBs were around 10%, see Table 1). Furthermore, even without any ICB injection, the conductivity of the two lungs fluctuate typically between −15% to +15% (see Figure 1), which was due to the movement of internal organs such as stomach, diaphragm and even the heart.

The results presently reported are in a preliminary stage, limited to one animal. We plan to repeat the experiments in more subjects to investigate the effect of each ICB in more detail.

In conclusion, the preliminary in vivo results demonstrate that 3% NaCl can produce comparable conductivity contrast to 20% NaCl for pulmonary perfusion blood flow indication. This is advantageous because 3% NaCl solution is readily available and routinely used in the ICU while highly concentrated 20% NaCl is rarely, if at all, used in clinical settings.

References

[1] Frerichs I, Pulletz S, Elke G, Reifferscheid F, Schadler D, Scholz J and Weiler N 2009 Respiration; international review of thoracic diseases 77 282–91
[2] Borges J B, Suarez-Sipmann F, Bohm S H, Tusman G, Melo A, Maripuu E, Sanstrom M, Park M, Costa E L V, Hedenstierna G and Amato M 2011 J Appl Physiol 112 225–236
[3] Oh T I, Wi H, Kim D Y, Yoo J P and Woo E J 2011 Physiological measurement 32 835–849
[4] Adler A, Arnold J H, Borsic A, Brown B H, Dixon P, Faes T J, Frerichs I, Gagnon H, Garber Y, Grychtol B, Hahn G, Lionheart W R B, Malik A, Patterson R P, Stocks J, Tizzard A, Weiler N and Wolf G K 2009 Physiological measurement 30 S35–S55
[5] Brown B H, Leathard A D, Sinton A, McArdle F J, Smith R W M and Barber D C 1992 Clin. Phys. Physio. Meas 13 175–179
[6] Frerichs I, Hinz J, Herrmann P, Weisser G, Hahn G, Quintel M and Hellige G 2002 IEEE transactions on medical imaging 21 646–52
[7] Hellige N C, Meyer B, Rodt T, Vogel-Claussen J, Hahn G and Hellige G 2012 Biomed Tech 57 (Suppl. 1) 525–528