Measurement of Lung Fluid Density Changes using Passive Leg Raising in Congestive Heart Failure

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Introduction: Heart failure leading to pulmonary oedema is characterised by an elevated left ventricular end diastolic pressure leading to an increased pressure in the left atrium and pulmonary vasculature. The resulting increased hydrostatic pressure at the pulmonary capillary bed causes fluid to leak into the interstitial spaces of the lung tissue (interstitial oedema) and subsequently the alveolar spaces (alveolar oedema)[1,2]. The aim of the present study was to use MRI as a model for the evaluation of the change in lung water concentrations during postural movement in heart failure patients and healthy controls. A measurable difference in the magnitude and rate of water transudation with postural changes between patients with heart failure and healthy controls may provide a model for the evaluation of pharmaceutical compounds such as TRPV4 inhibitors[3] for target validation and dose selection.

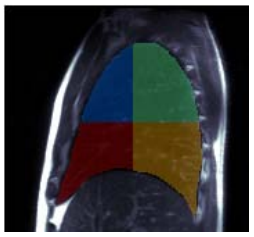

Fig. 1. Lungs are automatically divided into 4 quadrants, with high proton density and stronger PLR response in the two posterior regions.

Methods: Experiments were performed on a clinical 3T Siemens Verio scanner. 12 subjects with NYHA class I or II congestive heart failure (CHF) and 12 age and sex-matched healthy controls (HC) were evaluated. 600 free-breathing cardiac-gated HASTE volumes were acquired over approximately 30 minutes (effective TE=12ms, TR=1 RR interval, voxel size=2x2x6mm^3). Subjects were scanned from as soon as practicable after lying supine, before undergoing passive leg raising (PLR)[4] during scanning, where subjects had their legs raised to approximately 45° whilst lying supine in the scanner bore. PLR induces a reversible fluid shift leading to an increase in left-ventricular end-diastolic pressure (LVEDP). PLR was performed during scanning, resulting in a first acquisition of 150 HASTE volumes before leg raising (prePLR) and 200 HASTE volumes immediately after the onset of PLR (earlyPLR). Alternative sequences were used for 10 minutes, followed by a second continuous HASTE acquisition of 150 volumes (latePLR), and 100 volumes once their legs were returned level with the scan table (post-PLR). During PLR, CHF subjects were asked to subjectively rate their breathlessness on a scale of 0 (not breathless at all) to 10. Blood tests of NT-proBNP, a CHF assay, were also collected from CHF subjects. Automatic lung segmentation was performed via an active contour fit, which also subdivided the lung into 4 quadrants. Median signals were calculated for each quadrant.

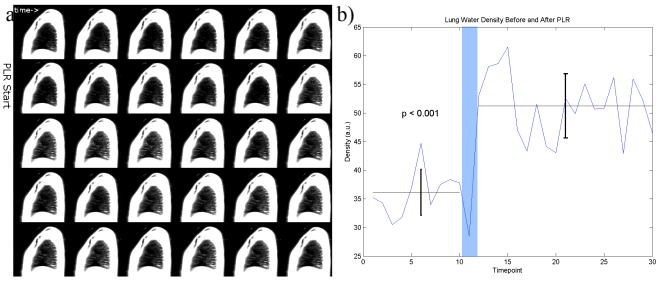

Fig. 2. Pilot PLR results to effect lung fluid changes. a) Raw sagittal HASTE images before PLR (top row), and as lung fluid density increases post PLR (rows 2 to 5). b) Median lung signal in the automatically segmented lung region.

Results: An example automated lung segmentation is seen in Fig 1. Static lung density followed the known gravity contours[5], best noted in Fig 3b, where the yellow ROI covering the posterior inferior quadrant shows the strongest signal, and the blue ROI covering the superior anterior the weakest signal. Good lung density response to PLR was noted in a pilot scan in a healthy volunteer (Fig 2.). Response to PLR was seen in all subjects in the cohort. The strongest responses were noted in the quadrants with the highest pre-PLR signal[6]. Unfortunately, a statistically insignificant difference (defined as $p>0.05$) in response between HCs and CHFs was found. Only two of 12 CHF subjects reported any dyspnea using the breathlessness scale in PLR, and only a single CHF subject entered the study with a high NT-proBNP level.

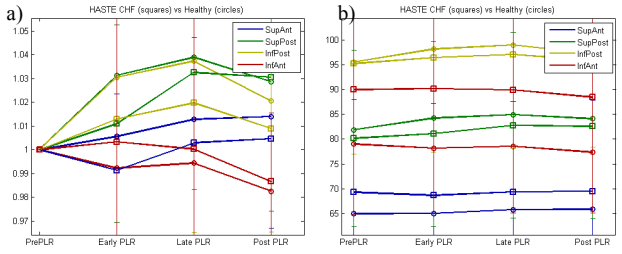

Fig. 3. PLR results in 12 CHF subjects and 12 HCs. a) Normalized signal to the pre-PLR lung density shows stronger responses in the posterior ROIs in both CHFs and HCs. b) Raw, unnormalized signals show higher lung fluid densities posteriorly, with an increased density in CHFs over HCs. *ROI colors match Fig 1.*

Discussion: Subjects enrolled in the CHF cohort had stable, well controlled heart failure, defined by no change in medication or admittance for acute decompensation in the previous 3 months. All patients were NYHA class I or II, and thus had no or only mild symptoms of CHF and were euvolaemic at time of scanning. There was no requirement for an echo to assess LV function and it is quite likely that most of these patients had mild to moderate LV dysfunction. CHF subjects exhibited neither dyspnea under PLR nor a high NT-proBNP level. Thus, it might be concluded that the lack of separation in PLR response between HCs and CHFs was due to a similar cardiovascular state, rather than a lack of sensitivity. In spite of the lack of separation between the CHF and HC groups, the HASTE acquisitions were able to map changes in lung fluid density induced by the fluid shift expected from PLR. It could be expected that a population of CHF subjects would show a greater change in lung fluid densities than healthy controls.

References. 1. Gheorghiade, et al. *Circulation* 2005;112:3958-68. 2. Picano, et al. *Heart failure reviews*;15:63-72. 3. Liedtke, et al. *AJP - Lung Physiol* 2004 287(2):L269-L271 4. Monnet, *Intensive Care Med* 2008 34:659–663. 5. Bankier, et al. *JMRI* 23:115–122 (2006) 6. Phillips ,et al. *AJ Appl Physiol* 1989;66:1197-208. 7. Chow, et al. *JCMR* 2009;11(1):41.