Gadolinium enhanced SPI to assess lung ventilation

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Introduction

The Single Point Imaging sequence (SPI) has been shown to be a very sensitive method for imaging lung tissue in-vivo [1]. Due to the use of pure phase-encoding, SPI images, unlike conventional spin warp sequences, are free from geometric distortions caused by susceptibility variations. In addition, extremely short detection times are possible since no gradient switching is required between excitation and data acquisition. However, the technique is inherently slow, so in order to keep acquisition times reasonably short, low flip angles are employed to allow for short repetition times.

The amount of signal available from lung parenchyma can be significantly increased by the administration of aerosolised contrast agents which shorten T_1. Initial studies using aerosolised Gd-DTPA demonstrated the feasibility of imaging pulmonary ventilation [2]. More recent studies have investigated using modified contrast agents in order to further increase signal enhancement [3]. Other studies demonstrated the application of mechanical ventilation in order to administer agents to larger animals [4]. Proton enhanced lung MRI studies have up to now only employed the use of T_1-weighted spin echo or sometimes gradient echo sequences. However, these sequences are not able to resolve much of the available signal from lung parenchyma due to rapid T_2^* decay, which becomes even shorter with the application of paramagnetic contrast agents. The application of gadolinium enhancement in combination with Single Point Imaging tackles this problem and so looks to be a promising method for assessing lung ventilation.

Methods

Animals and administration: All experiments complied with the UK Animals (Scientific Procedures) Act, 1986 and local ethical guidelines. Healthy male Wistar rats (220-240g) were given a pre-medication of midazolam and subsequently anaesthetised with isoflurane. Animals were intubated prior to mechanical ventilation using a 16 GA. catheter. The ventilator was set to provide a tidal volume of 2.5-3.0mls at a rate of 60 bpm. Throughout the study; temperature, respiration and ECG were monitored and maintained to ensure physiological homeostasis. The contrast agent (Gd-DTPA-BMA or Omniscan) was diluted 1:1 in physiological saline and aerosolised using an Aeroneb Pro nebuliser system producing particles of 1-2 microns. The contrast agent was administered with the animal in situ inside the magnet bore in order to allow for baseline images to be acquired.

MRI: Imaging was performed on a 7T Bruker Biospec system using a 60 mm birdcage coil to acquire volume images of the entire thorax. The previously reported SPI protocol [1] was used to image rat lung before and after Gd-enhancement, along with an optimised RARE sequences for comparison. The SPI protocol used [128x128x32] matrix, FOV 8x6x5cm, FA = 3°, TR = 1 ms, detection time (t_p) = 200µs and Nex = 1. The RARE sequence used a [128x128] matrix, TR = 765ms, TE = 3.7ms, Nex = 8 and also employed a reordered phase encode start, to shorten the effective echo time to 7.4 ms. The standard FLASH sequence (FA/TR/TE = 30°/148ms/3.3ms) was used to check for oedema. Another SPI protocol with matrix [64x64x16], TA=1min was used to collect images every 2 minutes in order to assess the increase in enhancement over the course of contrast dosing.

Results and discussion

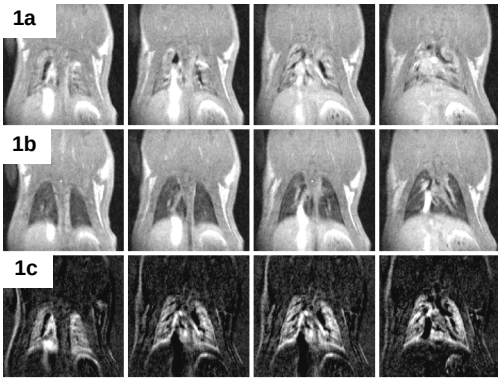


Figure 1 – Consecutive, coronal, SPI images taken a) after and b) prior to administering aerosolised contrast agent for 10 minutes. The difference images c) clearly identify the enhanced 'ventilated' areas of lung.

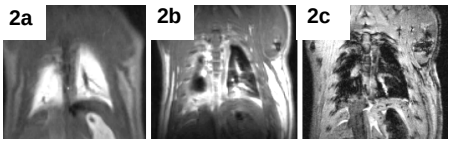
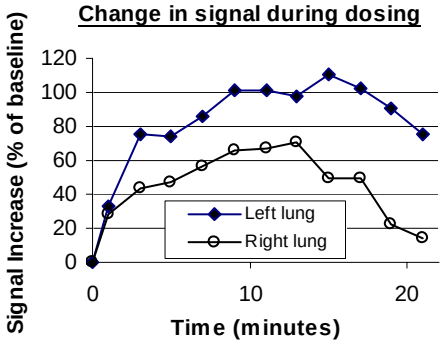


Figure 2 - Comparison of a) SPI (t_p=150µs) b) RARE (optimised) and c) standard FLASH sequences, images taken are of rat lung after administration of the aerosol contrast agent for 20 minutes (images acquired post-mortem).



Graph 1 - Change in signal intensity over 20 minutes of aerosolised contrast agent delivery measured using the 64x64 matrix SPI images.

The gadolinium enhanced SPI images (figure 1a) were acquired after 10 minutes of aerosolised contrast agent administered via mechanical ventilation. Baseline images (figure 1b) were obtained prior to contrast dosing, which allow for subtraction images (figure 1c) to be produced. The coverage of the nebulised contrast agent throughout the lung is reliably consistent with the dosing regime adopted. The particle size produced by the nebuliser system was chosen to allow the aerosol droplets to penetrate to the lung periphery. The change in signal intensity, over baseline SPI images, was found to increase by up to 100% within 10 minutes (see graph 1). The signal intensity has also been shown to decrease if dosing continues for longer than ~10 minutes, whilst using SPI with a detection time t_p=200µs. The signal can be recovered by decreasing the detection time further. The problem of administering too much contrast into the lung is more problematic for conventional imaging sequences. Figure 2 shows a comparison between a) SPI, b) RARE (optimised) and c) FLASH sequences taken of rat lung dosed for 20 minutes and subsequently imaged post-mortem. It is clear that even the optimised RARE image (figure 2b) exhibits significant areas void of signal as a consequence of too much contrast agent. This loss of signal is likely due to a detrimental drop in T_2, whereas in the SPI images there is significant enhancement throughout the lung region.

Conclusion

Gd-enhanced SPI has been shown to provide reliable images of ventilated lung parenchyma with higher levels of signal than can be achieved with conventional spin warp sequences, especially when obtained at high field. SPI appears to be far more robust to the problems of over-deposited contrast agent, which can lead to areas void of signal. Further work is under way to apply the Gd-SPI technique to assess ventilation in animal models of pulmonary obstructive disease.

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References

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