Hyperpolarised ^{3}He diffusion: detection of age and smoking induced changes in alveolar volume

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Problem

A technique capable of measuring alveolar dimensions *in vivo* would be invaluable for the study of lung physiology, lung disease and for the development of therapeutic agents. This study aims to investigate whether hyperpolarized ^{3}He diffusion measured using MRI could be used to measure alveolar volume changes due to aging and tobacco smoke inhalation.

Method

Twenty nine volunteers with normal lung function (FEV1/FVC > 70%) were recruited. These comprised 12 non-smokers (9M, 3F), 12 passive smokers (11M, 1F) and 5 smokers (4M, 1F). Spirometric lung function tests were carried out to standard criteria[1] on all volunteers using an electronic spirometer (Jaeger Flowscreen, Viasys Healthcare, UK).

Hyperpolarised ^{3}He was produced using metastable optical pumping[2] and delivered to the volunteer in a Tedlar gas sample bag. The volunteer lay supine in the scanner and was asked to inhale a 300 ml bolus of helium gas (3% ^{3}He) at the end of a normal exhalation, then immediately to take an extra small intake of air (100-150ml) to flush the helium into the lung periphery. The ^{3}He Apparent Diffusion Coefficient (ADC) was measured during a breath-hold, with the volunteer's lungs in the tidal volume range. Diffusion measurements were made using a 0.15T MR scanner. A modified RARE sequence (TE=14 ms, Tacq=896ms) was used to produce a series of 64 echoes with incrementally decreasing amplitude due to diffusion. A global ADC value for the lungs was calculated by fitting to the exponentially decaying echo train. Measurements were made on one individual to determine assess how ADC varied with lung volume. These results were used to convert ADC values into alveolar volumes normalized to non-smokers.

Results

In non-smokers ADC increased with age (Figure 1). The calculated alveolar volumes for non-smokers were converted into alveolar surface areas per unit volume (AWUV) which closely matched the histological data of Gillooly and Lamb[3]. Age normalized ADC (NADC) values and hence alveolar volumes for the majority of active and passive smokers were significantly higher than for non-smokers (Table 1 and Figure 2). For non-smokers normalized alveolar volumes were almost independent of lung volume (FVC) as shown in Figure 2.

Conclusion

Hyperpolarised ^{3}He diffusion can be used as a probe of alveolar volume. The measurement is sensitive and repeatable (COV 4%) and can detect age related changes and the effects of smoking. The technique opens up the possibility longitudinal studies into the effects of disease, therapy, alveolar development and senescence, in living people.

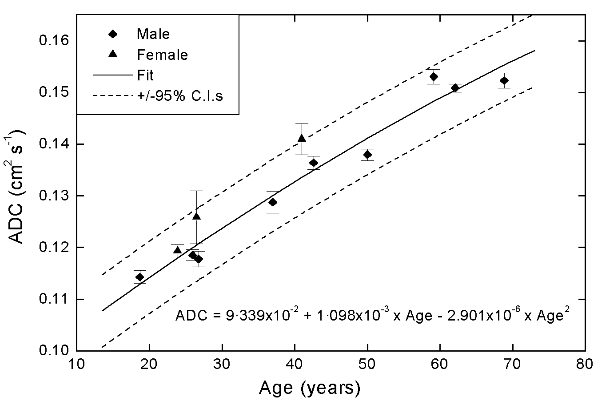

Figure 1: Plot of apparent diffusion coefficient (ADC) against age for asymptomatic non-smokers

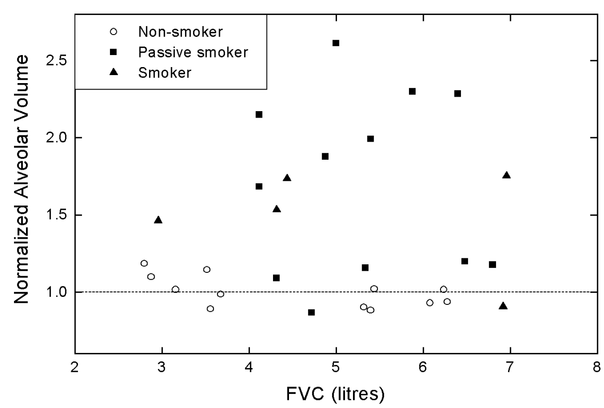

Figure 2: Plot of alveolar volume against FVC

	n	ADC ($cm^2 s^{-1}$)	NADC ($cm^2 s^{-1}$)
Non-smokers	12	0.136 (0.015)	0.113 (0•003)
Passive smokers	12	0.157 (0.024)*	0.134 (0•017)*
Active smokers	5	0.154 (0.015)+	0.127 (0•010)+

Table 1: ADC and NADC of ^{3}He for non-smokers, active and passive smokers. Values are Mean (SD).
* = ($p < 0.01$) $^+$ = ($p < 0.025$)

References

1. American Thoracic Society. *Am J Respir Crit Care Med* (1995); **152**:1107-1136.
2. Owers-Bradley et al. *J Magn Reson Imaging* (2003);**17**:142-6.
3. Gillooly M and Lamb D. *Thorax* (1993); **48**:491-5