Human Regional Pulmonary Gas Exchange with Xenon Polarization Transfer (XTC)

I. Muradian[1,2], J. Butler[3], M. Hrovat[4], G. Topulos[5], E. Hersman[2], E. Frederick[2,6], S. Covrig[1], I. Ruset[1], S. Ketel[1], W. Hersman[1], and S. Patz[2]

[1]Physics, University of New Hampshire, Durham, NH, United States, [2]Radiology, Brigham and Women's Hospital, Boston, MA, United States, [3]Physiology, Harvard School of Public Health, Boston, MA, United States, [4]Mirtech, Inc., Brockton, MA, United States, [5]Anesthesiology, Brigham and Women's Hospital, Boston, MA, United States, [6]Physics, University of Massachusetts – Lowell, Lowell, MA, United States

Introduction Single-breath XTC technique [1], an optimized version of XTC developed by Ruppert et.al. [2], is applied to human subjects. The potential of the method is tested in both normal subjects and asymptomatic smokers. The latter were chosen as a group people with possible early changes in the lungs, but whose PFT and spirometry tests were within a norm. High production rates of hyperpolarized xenon coupled with polarization levels comparable to those achieved with ^{3}He, made it possible to use XTC on human subjects. In addition they ensured high signal to noise ratios in the images and improved the accuracy of gas exchange measurements. In XTC, 3 GRE projection images (S_1, S_2, S_3) are acquired with multiple 180° spectrally selective pulses applied at -205ppm between S_1 and S_2 at +205ppm between S_2 and S_3. Then fractional gas transport $F(t_{exch}) = 1 - N\sqrt{\frac{S_3}{S_2}\frac{S_1}{S_2}}R_{RF}$ is calculated, where ratio (S_1/S_2) accounts for the signal decay due to T_1 and RF depletion, R_{RF} – for the difference in flip angles in 1st two images compared to the 3rd, and N is number of 180°'s.

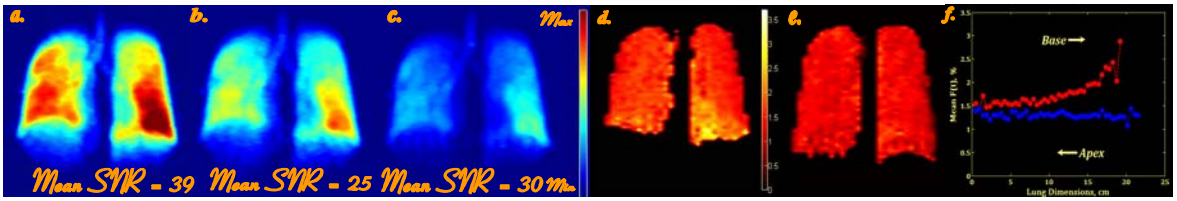

Fig.1 Coronal GRE projection images of the lungs and spatial distribution map of F(t). (***a***) was acquired before applying of the 180°s, (***b***) – after applying of the 180°s at -205ppm, and image (***c***) – after the ones at + 205ppm. The decay from ***a*** to ***b*** is due to T_1 and RF pulses, and from ***b*** to ***c*** - due to gas transport. F(t) maps at 47% TLC (***d***) and 63% TLC (***e***). The data is from a healthy non-smoker. <F(62ms)>=1.7% (47% TLC) and 1.3% (63% TLC). As expected, the mean F(t) decreases with lung volume increase, and S_A/V_{Gas} becomes more homogeneous; ***f*** - apex to base distribution of ***F(62.1ms)***: ***red*** - ~47% TLC (***a***); ***blue*** – ~63% TLC (***e***). Data strongly suggest that at lower lung volumes there is a "memory" of gravitational effects in the lungs, even though the data are collected on a supine subject. At higher lung volumes this effect is washed out, and the distribution is more homogeneous.

Methods All experiments were performed on a GE Signa Profile IV MRI magnet (0.2T) interfaced with a broadband Tecmag Apollo (Houston, TX) research console. A Mirtech, Inc (Brockton, MA) whole body transmit/receive coil (Q=300) was used for all studies. ^{129}Xe was hyperpolarized on site using a polarizer developed and built at the UNH [3]. All experiments were in compliance with local IRB and FDA IND approved protocols. Five healthy non-smokers and seven asymptomatic smokers participated in the study. For each subject, two lung volumes were chosen: ~45 and ~65% of TLC. Lower lung volume experiments were performed at least twice for the majority of the subjects to test repeatability. All but one subject underwent spirometry and PFT, to measure their lung volumes, DLCO and FEV1.

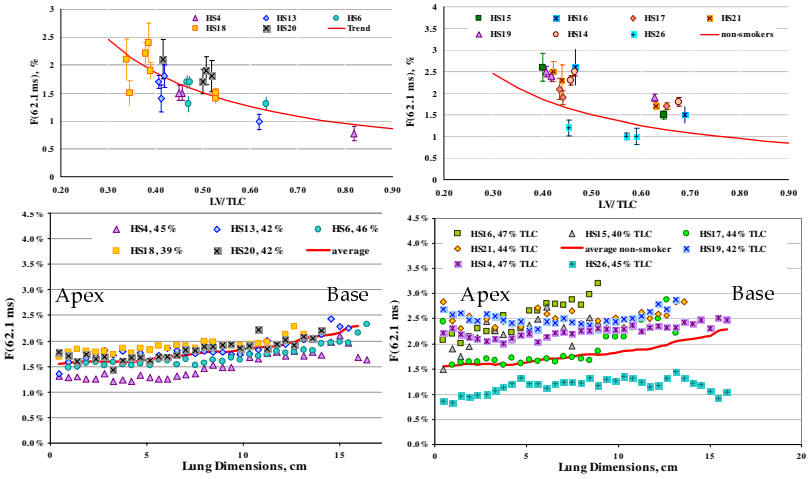

Figure 2. <F(t)> vs. LV/TLC; and apex-base distribution of F(t). ***a:*** <F(t)> from all healthy non-smokers is in good agreement within the error. ***b:*** data from the smokers – <F(t)> is higher for most of them. Red line in both graphs is a trend-line, corresponding to the non-smokers. Apex-base distribution of fractional gas transport for non-smokers (***c***) and asymptomatic smokers (***d***). Data from healthy non-smokers are in great agreement, except the one from HS4, who shows a steeper gradient. This discrepancy might be due to age differences in the subjects (55 vs. 25-35). As for the smokers, there is no common trend. The red line in both graphs represents the average apex-base trend from non-smokers.

Results XTC is a powerful technique capable of delivering information on regional lung characteristics. Fig.1 shows sample images from XTC-MRI (a-c), F(t) maps at 45 and 65% TLC (d-e) and their apex-base distribution (f). In a model of pulmonary parenchyma where alveoli are characterized as roughly spherical, with a uniformly distributed characteristic linear dimension r, the lung's gas volume (V_{Gas}) ~r^3 while the surface area (S_A) ~r^2. This implies the surface area density per gas volume, S_A/V_{Gas}~1/r, and hence decreases with lung volume. With XTC we observed such behavior - <F(t)> decreased with the increase of the lung volume for all subjects (fig.1(d-e), fig.2(a-b)). Fig.7(c–d) shows apex-to-base plots at lower lung volumes. As evident from fig.7(c), there is a common trend in the apex-base distribution for the non-smokers. The smokers' data do not show a common behavior (fig.7(d)). Fig.8 compares XTC MRI to DLCO (a) and FEV1 (b). Here we plot DLCO (a), FEV1 (b), <F(t)> (c) and its heterogeneity $\sigma_{F,Phys.}$ (d) vs. smoking history. In fig.8(c), at 0 pack years we have <F(t)> averaged over all non-smokers.

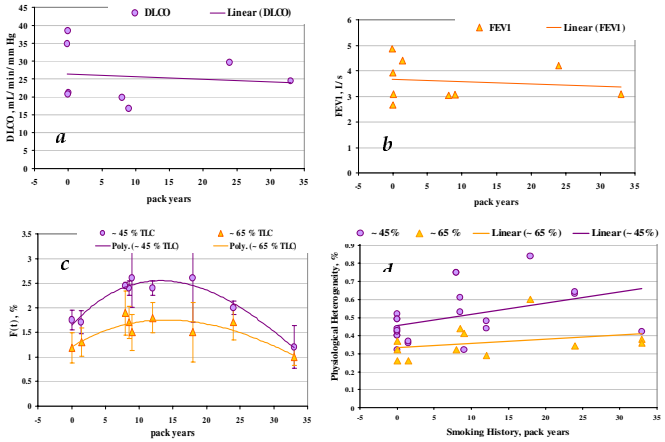

Figure 3. Comparison of XTC with PFT (DLCO) and spirometry (FEV1). ***a:*** DLCO vs. smoking history; ***b:*** FEV1 vs. smoking history; ***c:*** <F(t)> vs. smoking history; ***d:*** Phys. heterogeneity vs. smoking history.

Discussion Despite the limited statistics a noticeable trend appears in the non-smokers' apex-base distribution, which is not the case with the smokers' data. One possible reason could be that early changes in the lungs do not necessarily follow an identical path in all subjects. Moreover, the dependences of <F(t)> and $\sigma_{F,Phys.}$ on the smoking history are in marked contrast to the failure of DLCO and FEV_1 to detect any changes in normal or asymptomatic smokers. This is strong evidence that XTC is more sensitive to early changes in the lungs compared with these commonly used tests. However, a larger study population in both groups will be necessary to confirm these preliminary results.

Acknowledgements This work was supported by NIH RO1 HL073632

References [1] Patz et.al.,14thAnnual ISMRM, Seattle,p.192(2006). [2]Ruppert etal.,MRM 51:676-687(2004); [3]Ruset et.al,Phys.Rev.Lett.96,053002(2006).