Image Registration for Quantitative Analysis of 3He MRI of the Mouse Lung

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INTRODUCTION: ^{3}He MRI is increasingly useful for regionally evaluating ventilation in mouse models of asthma before and after challenge with Methacholine (MCh) [1,2] Such changes can be effectively quantified by suitably normalizing the pre- and post-MCh images, and subtracting the two to generate a difference map depicting regional changes in ventilation[3]. However, difference mapping can in some instances be confounded by even sub-millimeter changes in the animal's position between the two images. This problem can be addressed by registering the two ^{3}He images to a common coordinate space without obscuring arising ventilation defects. Here we describe our approach to this problem, which now facilitates analyzing MCh-induced ventilation changes even in the presence of positional shifts.

METHODS: 3D ^{3}He images were acquired at a resolution of 156×156×1000μm^3 as previously described [2]. Image registration was performed using the Image Registration Toolkit developed by Rueckert *et al.* [4,5] Initial registration used a rigid transformation to bring the images into the same coordinate space. Rigid, rather than non-rigid registration was chosen because the latter could be confounded by ventilation defects that occur post-MCh. Registration used a normalized mutual information cost function and linear interpolation was used to estimate intensities at non-integral pixel locations. Registration was carried out at 3 resolutions. Lower resolution images provided an initial estimate used to register increasingly higher resolution images [4]. After registration based on mutual information, a second registration step based on landmarks was performed to improve visualization of airway constriction. Landmarks were chosen at the tip of the apical lobe, at the periphery of the lungs, and at the branching of the bronchii, similar to [6]. To estimate the effectiveness of registration steps, the mean relative RMS difference was calculated on a pixel-by-pixel basis for pre- and post-MCh images with and without registration according to $Diff_{RMS} = \sqrt{\sum(post - pre)^2 / 2\sum(pre^2)}$. Here, $Diff_{RMS}$=1 would correspond to complete mis-registration and $Diff_{RMS}$=0 represents complete registration. The registration method was tested in the three groups of mouse models imaged before and after MCh challenge (OVA/OVA N=6, OVA/OVA/DEX, N=4, OVA/PBS, N=4) [3].

RESULTS AND DISCUSSION: Figure 1 shows an animal with an extreme positional change (~5mm) in the pre- (A) and post-MCh (B) images and the associated error in difference mapping (C). This error in the difference map was dramatically reduced by registration (D). Applying the affine registration to the three study groups significantly reduced the RMS difference. The addition of landmark registration after the affine step did not reduce the RMS difference significantly (figure 2). However, landmark registration did improve the visual perception of airway narrowing (Figure 3).

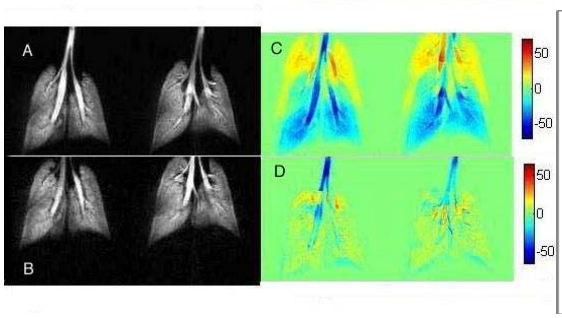

Figure 1

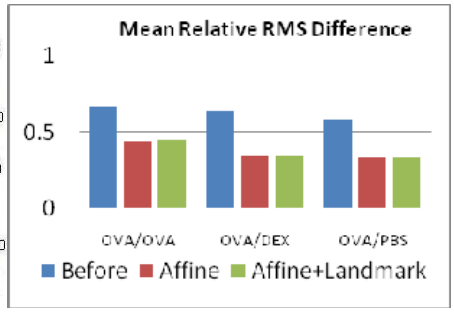

Figure 2

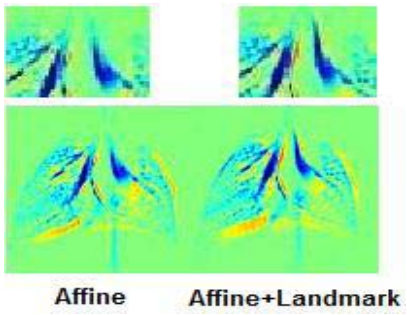

Figure 3

Using registration reduced the RMS difference in the OVA group by 33.7%, the DEX group by 45.5% and the PBS group by 42.43%. Note that in these groups the RMS difference is driven by both registration errors and actual induced ventilation defects and hence would not be expected to reach zero even when registration is perfect. Hence, we can only be certain that registration significantly reduced the error in the difference map and future studies are planned using deliberate positional shifts, but no MCh challenge, to fully characterize the robustness of the registration. The presence of ventilation defects also required us to avoid using non-rigid algorithms because their high-order polynomial fitting can cause defects to be treated as mis-registration and unintentionally removed. However, non-rigid algorithms will be essential for eventually permitting difference mapping between different mice, for example a control mouse and one with baseline ventilation defects. In that case, the use of land-mark based registration will be required.

CONCLUSIONS: The addition of affine registration to the technique of difference mapping creates a robust approach to analyzing ^{3}He MRI images of MCh challenge in mice and paves the way for better quantification and evaluation of different disease models and treatments.

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REFERENCES: [1] B Driehuys, He-3 MRI in Mouse Models of Asthma, Magnetic Resonance In Medicine 58: 893, 2007 **[2]** Thomas AC et al, NMR Biomed submitted. **[3]** N.N Mistry et al, Proceedings of ISMRM, 2008, Toronto, Canada. **[4]** C. Studholme, D.L.G.Hill, D.J. Hawkes, An Overlap Invariant Entropy Measure of 3D Medical Image Alignment, Pattern Recognition, Vol. 32(1), Jan 1999, pp 71-86. **[5]** D. Rueckert, L. I. Sonoda, C. Hayes, D. L. G. Hill, M. O. Leach, and D. J. Hawkes. Non- rigid registration using free-form deformations: Application to breast MR images. IEEE Transactions on Medical Imaging, 18(8):712-721, 1999. **[6]** Ireland et al, International Journal Of Radiation Oncology Biology Physics Volume: 68 Issue: 1 Pages: 273-281