An Adaptive K-means Approach for Assessment of Ventilation Defects in Asthma and Cystic Fibrosis Using Hyperpolarized Helium-3 MRI

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Target audience: Clinicians and researchers interested in the quantitative evaluation of ventilation defects in obstructive lung disease.

Purpose: To evaluate whether automated methods for ventilation defect identification can be improved by adding B_1 inhomogeneity corrections and excluding pulmonary vasculature by automated segmentation.

Methods: *Subjects*: A total of 91 subjects (83 with asthma and 8 with cystic fibrosis (CF)) underwent spirometry and hyperpolarized ^{3}He MRI at 1.5T (Signa HDx, GE Healthcare, Milwaukee WI). ^{3}He images were acquired using a fast 2D gradient echo sequence with the following scan parameters: TR/TE = 6.5/2.9ms, flip angle = 7º, FOV = 40×40 cm, matrix = 128×128, slice thickness = 1 cm, 16-25 axial slices. The percent predicted forced expiratory volume in 1 second (%FEV1) and FEV1/forced vital capacity (FVC) were recorded from spirometry.[2] *Image analysis*: Ventilation defects were identified independently using three methods: manual segmentation, a semi-automated method recently proposed by Kirby *et al*[1] which uses K-means clustering (hereafter the "Kirby method"), and an extension of the Kirby method which includes adaptive defect calling with the removal of vasculature and correction for B_1 inhomogeneity (hereafter "adaptive K-means"). The adaptive K-means method is illustrated in **Fig. 1**. The histogram of the corrected ^{3}He image was sorted into 10 bins. Highly defected lungs tend to have binary (black-white) signal intensities, whereas less defected lungs tend to have more subtle signal heterogeneity requiring refined sub-classification. Therefore, if the count in the first bin (low intensity) exceeded 10% of all lung voxels, the first cluster was defined as the defect population. Otherwise, the first cluster was further classified into 4 sub-clusters with the first 2 sub-clusters having the lowest signal intensity labeled as defects. Finally, the segmented vasculature was removed to obtain the defect mask. The percent ventilation defect (%VD) was calculated as %VD=100% × defect volume/total lung volume. *Statistical analysis*: Bland-Altman plots were used to examine the agreement between the two K-means-based methods and manual segmentation. A linear mixed-effects model was used to compare %VD measured by the K-means-based methods against the manual segmentation. The Spearman correlation was computed between spirometric measures and 3 sets of %VD measurements.

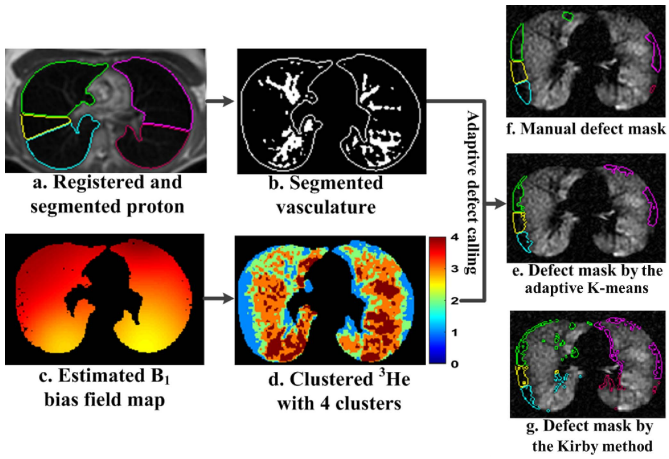

Fig. 1 The adaptive K-means defect segmentation workflow. The proton image (**a**) was registered to the ^{3}He image by a rigid registration and the total lung cavity was segmented using a region-growing method. The pulmonary vasculature (**b**) was segmented by standardizing transformation[3] and K-means clustering. The ^{3}He image was corrected using B_1 bias field estimation[4] (**c**) and classified into 4 clusters (**d**) by K-means. The defect mask (**e**) was determined adaptively based on the percentage of low-intensity signal. Segmented defects in the same asthma subject are also shown for manual segmentation (**f**) and the Kirby method (**g**). The lobar segmentation (color-code) was done on CT and is not necessary for the method if whole lung data are desired.

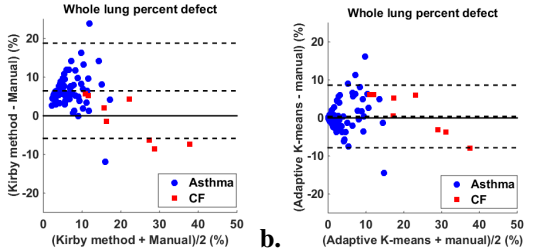

Fig. 2 Bland-Altman plots showing a 6.5% bias in the Kirby method compared to the manually segmented %VD (**a**), whereas the bias was not statistically significant for the adaptive K-means method (**b**).

Results and Discussion: The two K-means-based defect quantification techniques both took less than 3min vs 27min per study for manual segmentation. Compared to the manual measurements, %VD by the Kirby method was significantly higher (p<0.0001) with a bias of 6.5% (**Fig. 2a**), whereas the adaptive K-means method yielded a statistically insignificant bias, 0.4% with p=0.45 (**Fig. 2b**). The %VD determined by both manual segmentation and the adaptive K-means method showed significant negative correlation with %FEV1 and %FEV1/FVC (**Table 1**). The %VD measured by the Kirby method, however, was not correlated with either of the 2 spirometric measures. Interestingly, all three methods measured similar %VD in CF subjects (>20%, **Table 1**), a group with more persistent focal obstruction compared to asthma, suggesting the greater contrast between defect and ventilated signals could be accurately separated by the simpler intensity-based K-means classifier. By comparison, asthma subjects had much lower %VD and were more affected by the presence of voids from blood vessels and variations in ^{3}He contrast due to B_1 inhomogeneity, which may challenge a simple K-means classifier to differentiate vessels and signal shading from true ventilation defects.

Table 1 Percent ventilation defect (%VD) measurements and Spearman correlation between %VD and spirometric measures among 3 defect segmentation methods

Methods	Mean %VD (std dev)		Correlation ρ (p-value)	
	Asthma (n=83)	CF (n=8)	%VD vs. %FEV1	%VD vs. %FEV1/FVC
Manual	3.2 (3.8)	21.7 (12.1)	**-0.43 (<0.0001)**	**-0.41 (0.0001)**
Kirby method	10.4 (5.7)	20.9 (7.1)	-0.15 (0.18)	-0.15 (0.18)
Adaptive K-means	3.5 (4.5)	22.9 (7.2)	**-0.30 (.0048)**	**-0.29 (0.0084)**

p<0.05 was considered as significantly correlated.

Conclusion: The adaptive K-means approach significantly improved the performance of K-means clustering in identifying ventilation defects and reducing bias. This results in improved agreement with manual segmentation and better correlation with spirometric measures than the K-means classification method introduced by Kirby with comparable processing time and a time savings of ~10 times over manual methods.

References: 1. Kirby M et al. *Acad Radiol*. 2012 . 2. Hankinson JL et al. *AM J Respir Crit Care Med.* 1999. 3. Nyul LG et al. *Magn Reson Med.* 1999. 4. Tustison NJ et al. *IEEE Trans Med Imaging.* 2010.