# Abnormalities of Lung Structure in Children with Bronchopulmonary Dysplasia as Assessed by Diffusion Hyperpolarized Helium-3 MRI

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**Introduction:** Bronchopulmonary dysplasia (BPD) is a chronic lung disease that begins when an infant is born prematurely, and its lungs are forced to function as a gas exchange organ during a stage of lung development when alveoli are just beginning to form[1]. Inflammation and injury to the lung at this time are thought to affect subsequent lung development and result in alveoli that are abnormally large in size and reduced in number[2]. However, our understanding of the morphological alterations of lung structure in children with BPD is limited due to the difficulty of obtaining lung tissue from the living child and the small number of studies investigating lung autopsy specimens[3]. Diffusion hyperpolarized helium-3 (HP $^3$He) MRI has detected alterations in the lungs of animals and patients with emphysema[4-7]. The purpose of this study was to determine whether diffusion HP $^3$He MR detects abnormalities in lungs of children with BPD.

**Methods and Materials:** 45 subjects, including 32 healthy subjects with a history of uncomplicated term birth and 13 with a history of preterm birth complicated by subsequent BPD, underwent diffusion HP $^3$He MR at 1.5 T (Sonata, Siemens) and spirometry. Coronal images covering the entire lung were acquired with two b values, 0 and 1.6 s/cm$^2$, using a GRE sequence that included bipolar diffusion sensitization gradients (TR/TE 11/6.7 ms, FA 7$^o$, matrix 80 x 128) during a breath hold following the inhalation of a mixture of HP $^3$He and nitrogen. The breath hold duration varied depending on the number of slices required to cover the lung but was typically ~6s. Apparent diffusion coefficient (ADC) maps were calculated assuming mono-exponential signal loss due to diffusion[7], and the mean ADC from the whole lung was calculated for each subject. The percent of the lung volume with an ADC greater than 0.2 cm$^2$/s was calculated for each subject. The mean ADC increases with age during childhood due to the enlargement of the alveoli with lung growth [8], so the mean ADC of all subjects was corrected for age using the linear regression coefficients of the mean ADC vs age curve from the healthy subjects. The ADC maps were graded by a radiologist as either homogeneous or heterogeneous.

**Results:** The healthy subjects ranged in age from 4.5 to 19.9 years (mean 10.2 years) and the children with BPD ranged in age from 5.9 to 14.5 years (mean 9.7 years). The group average of the mean ADC was greater for the subjects with BPD (0.198 cm$^2$/s) than for the healthy subjects (0.157 cm$^2$/s), p=0.0001, Figure 1. After correcting for age, the group average of the mean ADC remained elevated for the subjects with BPD (0.223 cm$^2$/s) relative to the healthy subjects (0.181 cm$^2$/s), p<<0.0001. The group average of the percent of the lung volume with an ADC greater than 0.2 cm$^2$/s, an ADC metric which is more sensitive to focal areas of ADC elevation, was 35% for subjects with BPD and 11% for healthy subjects, p=0.001. All of the ADC maps of the healthy subjects were graded as homogeneous, whereas, 5 of 13 (38%) subjects with a history of BPD had heterogeneous ADC maps, Figure 2. All of the children with BPD had an abnormal FEV1 %predicted (less than 80%), and there was a moderate correlation between age-corrected mean ADC and FEV1 %predicted, R=-0.51. The ventilated lung volume from the MR images was slightly but not significantly lower for the subjects with BPD than the healthy subjects, mean 2.3 L and 2.7 L respectively, p=0.32.

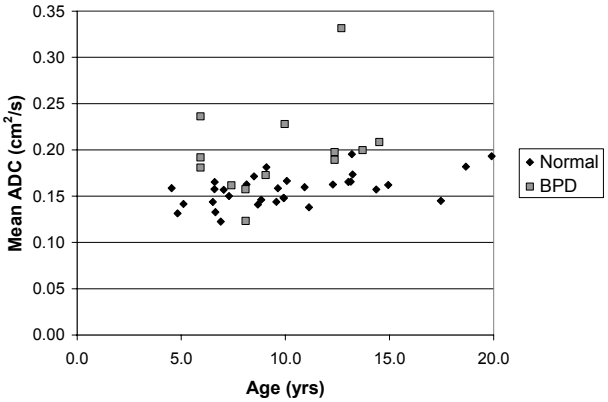


**Figure 1:** Mean ADC vs age (not corrected for age).

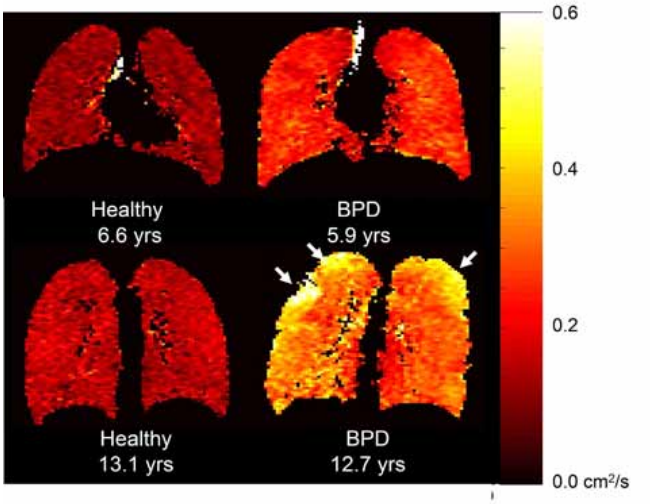


**Figure 2:** Coronal ADC maps in two healthy children have homogeneously low ADC values although the older child has slightly higher ADC values. Coronal ADC maps in two children with BPD demonstrate diffusely elevated ADC values. The 12 year old also has an heterogeneous pattern with focal areas of marked ADC elevation.

**Conclusions:** Children with a history of preterm birth and BPD had elevated ADC values and the same or slightly lower lung volumes as compared with age matched healthy control subjects. These findings are consistent with the limited histological data demonstrating that children with BPD have enlarged alveoli that are reduced in number. Currently, there are no non-invasive methods for assessing alterations in lung structural development so it is difficult to monitor the effectiveness of treatment in children with BPD. Diffusion HP $^3$He MR has the potential to provide this much needed information.

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**References**

1. Hislop AA,et al. *Early Hum Dev* 1987;**15**(3)**:**147-64.
2. Coalson JJ. *Semin Neonatol* 2003;**8**(1)**:**73-81.
3. Jobe AH. An unk *Am J Respir Crit Care Med* 2002;**166**(12 Pt 1)**:**1529-30.
4. Chen XJ, , et al. *Proc Natl Acad Sci* 2000;**97**(21)**:**11478-81.
5. Peces-Barba G, et al. Eur Respir J 2003;22(1):14-19.
6. Saam BT, et al. *MRM* 2000;**44**(2)**:**174-9.
7. Salerno M, et al *Radiology* 2002;**222**(1)**:**252-60.
8. Altes T, et al. IISMRM 2004