

# **Abnormal ventilation assessed with Hyperpolarized $^3\text{He}$ MRI in young cystic fibrosis patients with normal lung function.** **Evaluation of immediate influence of a single chest physiotherapy session.**

E. Bannier<sup>1</sup>, K. Cieslar<sup>1</sup>, K. Mosbah<sup>1</sup>, F. Aubert<sup>2</sup>, F. Duboeuf<sup>1</sup>, Z. Salhi<sup>3</sup>, S. Gaillard<sup>1</sup>, Y. Berthezène<sup>1</sup>, P. Reix<sup>4</sup>, and Y. Crémillieux<sup>1</sup>

<sup>1</sup>Université de Lyon, CREATIS LRMN, Lyon, France, <sup>2</sup>Centre d'Investigation Clinique, Lyon, France, <sup>3</sup>Johannes Gutenberg Universität, Mainz, Germany, <sup>4</sup>Service de Pédiatrie, Hôpital Femme Mère Enfant, Lyon, France

**Introduction:** Cystic fibrosis is the lethal genetic pediatric disease with the highest incidence in the Caucasian population. An early and adapted treatment is essential to slow down disease progression. The purpose of this study is to assess the sensitivity of hyperpolarized (HP)  $^3\text{He}$  MRI for the detection of peripheral airway obstruction in cystic fibrosis patients with normal pulmonary function tests (PFT) and to observe the immediate effects of a single chest physical therapy (CPT) session.

**Methods:** 10 pediatric cystic fibrosis patients (5 females, mean age 10 years) with normal PFT (mean FEV<sub>1</sub>, 112%  $\pm$  14.5) were recruited for the study after approval from the local research ethics committee. PFT and ventilation imaging were repeated before and after 20 minutes CPT. 3D FLASH  $^3\text{He}$  imaging was performed on a 1.5T clinical Sonata MR scanner with the following sequence parameters: 400x400 mm<sup>2</sup> FOV, 64x128 image matrix, TR/TE=10/2.76 ms and 7° flip angle. For each acquisition a mixture of 200 ml of nitrogen and 300 ml of clinically certified highly polarized  $^3\text{He}$  was administered via a Tedlar bag. To cover the whole lung 16 to 24 7-mm slices were acquired under breath-hold and the acquisition lasted between 10 and 15 s.

Dual scoring was performed by two independent observers blinded to patient clinical data. The number of ventilation defects per slice (VDI) [1] were quantified prior to and after the CPT session. The ventilation fraction (VF) [2] was calculated using an in-house developed IDL software. Left and right lungs were contoured manually slice by slice on the native HP  $^3\text{He}$  images. An operator-defined threshold was then applied on the contoured ventilation images to extract the ventilated area. Lastly, the ventilation fraction, defined as the ratio of ventilated surface over total lung surface, was computed for each slice and the results prior to and after CPT were compared.

**Results:** All patients successfully and safely completed the protocol. Ventilation defects were found in all but one patient despite normal PFT (Figure 1). No correlation between FEV<sub>1</sub>, VDI and VF was found. After CPT, a redistribution of ventilation defects and a decrease in the number of small ventilation defects located at the lung periphery were observed, resulting in smoother lung contour. Individual results of quantification indicate that a single CPT session variably altered ventilation distribution showing either a decrease or an increase of the number of ventilation defects and the ventilated area but the average VDI and VF over all patients did not change significantly. Mean values obtained pre and post CPT and Spearman correlations between the changes are presented respectively in Table 1 and in Table 2.

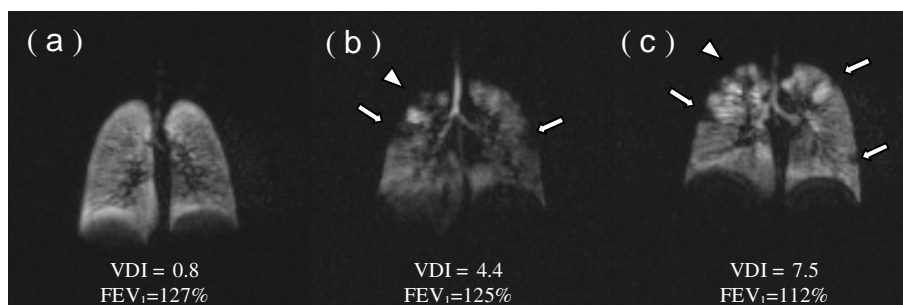


Figure 1: HP  $^3\text{He}$  images demonstrate peripheral wedge-shaped ventilation defects (white arrows) and hypointensity areas (arrowheads) in upper regions of the lung in three patients.

Marker	Pre CPT	Post CPT
FEV <sub>1</sub>	112.0 $\pm$ 14.5	107.4 $\pm$ 14.7
VDI	4.7 $\pm$ 2	4.7 $\pm$ 1.6
VF	78.1 $\pm$ 12.3	83.4 $\pm$ 12.2

Table 1: Mean values obtained pre and post CPT

Marker	Correlation
$\Delta\text{FEV}_1 / \Delta\text{VDI}$	0.719*
$\Delta\text{FEV}_1 / \Delta\text{VF}$	-0.110†
$\Delta\text{VDI} / \Delta\text{VF}$	-0.122†

Table 2: Spearman correlation between the variations measured with the different markers

\*: Correlation was significant ( $p < 0.05$ )

† Correlation was not significant

**Discussion and conclusion:** HP  $^3\text{He}$  MRI demonstrates potential in detecting local ventilation abnormalities in CF patients although PFT indicates normal lung function. Indeed, the mean VDI value in patients (4.7) found in this study is well above VDI (1.6) in healthy subjects reported in the literature [1]. Ventilation defects and changes induced by a sole CPT session can be visualized and quantified, opening up new perspectives in clinical trials and treatment efficiency measurements.

Therapeutic options for CF lung disease are developing rapidly and there is an ongoing need to improve the accuracy and validity of evaluation of clinical efficacy, especially in the younger population. Given the sensitivity of HP  $^3\text{He}$  MRI in depicting small ventilation defects in young asymptomatic CF patients, and the virtually unlimited number of examinations that can be performed using MRI, this technique could play a major role to study early treatment of mild disease.

## **References:**

[1] Mentore *et al.* *Acad Radiol* **12** (2005), [2] Woodhouse *et al.* *J Magn Reson Imaging* **21** (2005)