

## FUNCTIONAL LUNG MRI FOR NON-INVASIVE MONITORING OF REGIONAL EFFECTS OF INHALED HYPERTONIC SALINE IN CHILDREN WITH CYSTIC FIBROSIS

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**Target audience:** MDs and PhDs interested in lung MRI

**Purpose:** Quantification of regional effects of inhaled hypertonic saline (7% NaCl) by functional lung MRI in children with cystic fibrosis (CF).

**Methods:** Lung MRI was performed in CF patients (n=5, 3 female, 2 male, age 12-15 years) before and after a single treatment of inhalation of hypertonic saline, using the following protocols at 1.5T.  $T_1$  relaxation measurement with a series of inversion recovery SnapShot fast low-angle shot: TE 0.8ms, TR 3.0ms, flip angle 8°, 32 inversion times within a timeframe of 200ms - 6400ms, acquisition matrix 128 x 64, field of view 50cm x 50cm, slice thickness 15 mm, gap 7.5mm. Coronal slices covering both lungs were acquired. Images were obtained after breathing room air and again at the same slice position while breathing oxygen (O<sub>2</sub>). Oxygen was administered using a full covering air cushion face mask with a filter, a 2.6 liter reservoir and a flow rate of 15 l oxygen/min. Images acquired breathing 100% O<sub>2</sub> were registered on the room air images using a phase-sensitive, non-rigid registration. Afterwards  $T_1$  maps were calculated using non-linear image registration and a self-developed MATLAB script (MATLAB 2012a, Mathworks, Natick, Massachusetts, USA). Lungs were segmented on the room air  $T_1$  maps and then transferred onto the corresponding co-registered oxygen  $T_1$  maps. As a functional parameter, the difference between  $T_1$  times breathing room air and 100 % O<sub>2</sub> ( $T_1$  ratio =  $T_1$  21% O<sub>2</sub> -  $T_1$  100% O<sub>2</sub>) was calculated. Pulmonary perfusion with a  $T_1$ -weighted 4D contrast-enhanced 1<sup>st</sup>-pass perfusion sequence: slice orientation: coronal, TE/TR 0.71/2.13 msec, flip angle 25 degrees, FOV 50 cm, slice thickness 6 mm, acquisition matrix 97x192, with parallel imaging acceleration (GRAPPA) factor 2. Pulmonary blood flow (PBF) maps were calculated using model independent deconvolution, for the whole lung and split for upper and lower lung segments. Expecting positive therapy effects, a single-sided paired t-test was used for statistical analysis.

**Results:** A single treatment of inhalation of hypertonic saline resulted in a marked increase of pulmonary blood flow (Figure 2) and of oxygenation (displayed by ratio of  $T_1$  values breathing room air or 100% O<sub>2</sub>). Results are summarized in Tables 1-3.

**Table 1:** Pulmonary blood flow [ml/100 ml/min] and  $T_1$  ratio [%] in the whole lung

| Patient | PBF pre | PBF post | $T_1$ ratio pre | $T_1$ ratio post |
|---------|---------|----------|-----------------|------------------|
| 1       | 64.46   | 71.75    | 8.9             | 9.5              |
| 2       | 75.01   | 89.98    | 3.4             | 13.5             |
| 3       | 114.48  | 132.65   | -               | -                |
| 4       | 148.07  | 191.65   | 7.6             | 14.7             |
| 5       | 128.73  | 135.24   | 9.0             | 15.5             |

**Table 2:** Pulmonary blood flow [ml/100 ml/min]

|                | Pre treatment | Post treatment | Mean difference | p-value | Confidence interval |
|----------------|---------------|----------------|-----------------|---------|---------------------|
| Whole lung     | 106.2         | 124.3          | 18.1            | 0.0275* | -0.62-36.83         |
| Upper segments | 107.7         | 124.7          | 17.0            | 0.0062* | 6.08-28.00          |
| Lower segments | 99.7          | 122.7          | 23.0            | 0.0250* | -0.003-46.07        |

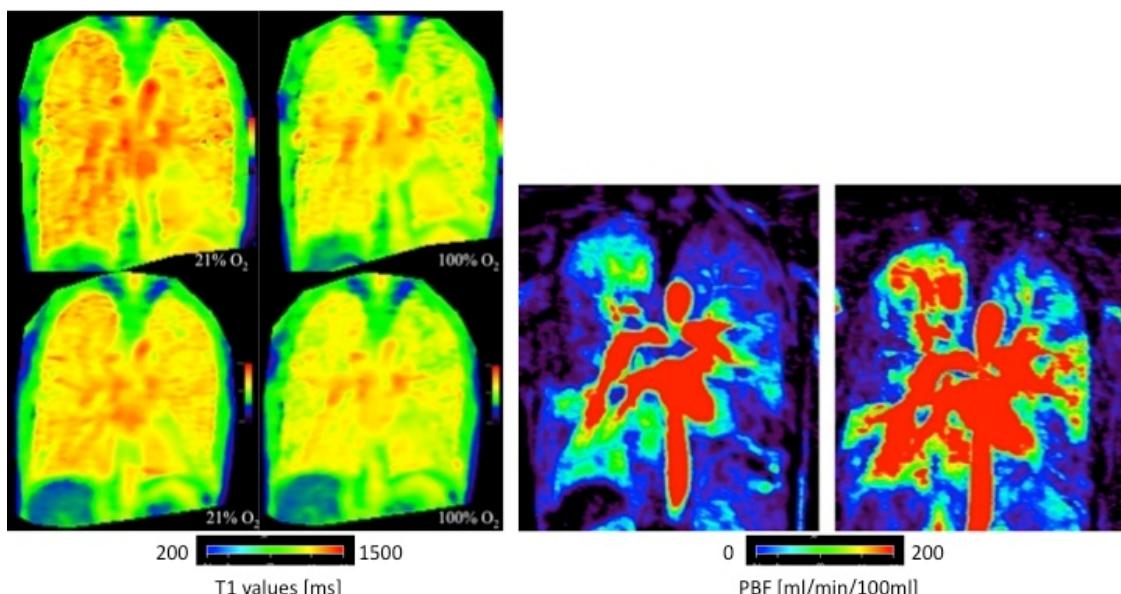
\* = Statistically significant

**Table 3:**  $T_1$  ratio [%] breathing room air and 100% O<sub>2</sub> before and after saline inhalation

|                | Pre treatment | Post treatment | Mean difference | p-value | Confidence interval |
|----------------|---------------|----------------|-----------------|---------|---------------------|
| Whole lung     | 7.2%          | 13.3%          | 6.1%            | 0.0270* | -0.19-12.31         |
| Upper segments | 7.4%          | 12.5%          | 5.1%            | 0.0348* | -0.76-10.96         |
| Lower segments | 7.0%          | 14.0%          | 7.0%            | 0.0233* | 0.19-13.86          |

\* = Statistically significant

**Conclusion:** This study shows for the first time a significant increase in pulmonary blood flow and oxygenation after a single treatment with inhalation of hypertonic saline (7% NaCl) in patients with cystic fibrosis, assessed by functional lung MRI, making it a promising, non-invasive, radiation-free tool for visualization and quantification of regional effects in the treatment of patients with cystic fibrosis.



**Figure 1:**  $T_1$  maps of a patient with cystic fibrosis before (upper row) and after (lower row) single treatment of inhalation of hypertonic saline.

**Figure 2:** Regional perfusion deficits in a patient with cystic fibrosis before (left) and after (right) inhalation of hypertonic saline, showing a marked increase in pulmonary blood flow after saline inhalation.