EUROPEAN SYNCHROTRON RADIATION FACILITY

INSTALLATION EUROPEENNE DE RAYONNEMENT SYNCHROTRON

ESRF

Experiment Report Form

The double page inside this form is to be filled in by all users or groups of users who have had access to beam time for measurements at the ESRF.

Once completed, the report should be submitted electronically to the User Office using the **Electronic Report Submission Application:**

http://193.49.43.2:8080/smis/servlet/UserUtils?start

Reports supporting requests for additional beam time

Reports can now be submitted independently of new proposals – it is necessary simply to indicate the number of the report(s) supporting a new proposal on the proposal form.

The Review Committees reserve the right to reject new proposals from groups who have not reported on the use of beam time allocated previously.

Reports on experiments relating to long term projects

Proposers awarded beam time for a long term project are required to submit an interim report at the end of each year, irrespective of the number of shifts of beam time they have used.

Published papers

All users must give proper credit to ESRF staff members and proper mention to ESRF facilities which were essential for the results described in any ensuing publication. Further, they are obliged to send to the Joint ESRF/ ILL library the complete reference and the abstract of all papers appearing in print, and resulting from the use of the ESRF.

Should you wish to make more general comments on the experiment, please note them on the User Evaluation Form, and send both the Report and the Evaluation Form to the User Office.

Deadlines for submission of Experimental Reports

- 1st March for experiments carried out up until June of the previous year;
- 1st September for experiments carried out up until January of the same year.

Instructions for preparing your Report

- fill in a separate form for each project or series of measurements.
- type your report, in English.
- include the reference number of the proposal to which the report refers.
- make sure that the text, tables and figures fit into the space available.
- if your work is published or is in press, you may prefer to paste in the abstract, and add full reference details. If the abstract is in a language other than English, please include an English translation.

ESRF	**Experiment title:** Functional imaging of the effects of inhaled drugs and air pollution particles on regional ventilation in healthy and asthmatic animals	**Experiment number**: MD238
Beamline: ID17	**Date of experiment**: from: II/2006 to: II/2007	**Date of report**: 10.12.2007
Shifts: 15+15+17	**Local contact(s)**: Christian Nemoz	*Received at ESRF:*

Names and affiliations of applicants (* indicates experimentalists):

*** Anssi Sovijärvi** Helsinki University Central Hospital, Finland
*** Sam Bayat** University of Amiens, France
*** Kimmo Neitola** University of Helsinki, Finland
*** Liisa Porra**
*** Mikko Sipilä**
*** Satu Strengell**
*** Heikki Suhonen**
*** Pekka Suortti**
*** Jorge Manuel Costa** Geneva University Central Hospital, Switzerland
*** Walid Habre**
*** Tibor Janosi**
Zoltan Hantos University of Szeged, Hungary
*** Ferenc Petak**

Report:

This report is the first year report of Long Term Project for the period II/2006 to I/2008, where 90 shifts were granted for 2 years. The experiments were continuation of previous experiment series and the background and first results of the project are described in detail in earlier reports covering the period 2004-2006 (experiment series numbers MD76 and MD213).

Background and aim of the study:

Methacholine challenge (Mch) is routinely used as non-specific challenge to diagnose bronchial hyper-reactivity, although its effect in the lungs and main airways as compared to a specific allergen challenge are not precisely known. Tobacco smoke is an increasing health problem in the world, and more information about the acute effects of tobacco smoke in the lungs is needed. Traditional measurements of lung function such as spirometry can at best provide overall assessments and do not give any insight into the localization and heterogeneity of airway response. We have introduced a novel CT imaging technique that uses synchrotron radiation to quantitatively image inhaled stable xenon gas within the airways with a high spatial resolution (Bayat et al 2006). Using this method, regional lung volume, ventilation, and airway luminal diameters down to 2 mm can be measured. The spatial resolution of this technique is the best available for regional ventilation imaging in small animals, and the structure of the lungs can be studied simultaneously.

The aim of these studies was to use new asthma model using sensitized rabbits, and compare images obtained with synchrotron radiation with results on overall lung mechanics obtained with the forced oscillation technique (FOT) (Petak et al, 2006). This animal model was used to study first the effect of Mch in the lungs, and compare the results to the effects of allergen provocation, and the results were compared to the results from healthy animals. Secondly, the model was used to study the effect of acute tobacco smoke provocation in the lungs, and observe how previous smoke provocation affects the subsequent Mch provocation.

In the first year total 3 of the experiments were performed and 47 shifts were used.

Beamline	Allocated Shifts	Start Date	Finish Date	Local Contact
ID17	15	07 December 2006	12 December 2006	Dr. Christian NEMOZ
ID17	15	05 February 2007	12 February 2007	Dr. Christian NEMOZ
ID17	17	11 July 2007	16 July 2007	Dr. Christian NEMOZ

Experiments MD238/1 and MD238/2:
First 2 experiments MD238/1 and 2 were conducted to study new asthma model with sensitized rabbits (Petak et al. 2006). Animals were sensitized to ovalbumine (OVA allergen) at ESRF. The imaging setup was modified because of new collaboration with groups from Geneva and Szeged using the FOT (Figure 1). In this study we aimed to evaluate regional differences of the effects of Mch and OVA challenges. Imaging was performed using K-edge Subtraction imaging (KES) (Bayat et al. 2006), 3 different Mch doses were used, and totally 28 animals were studied successfully. Experiment protocol consisted imaging at baseline, after 3 different Mch provocations, a recovery phase and an OVA provocation. An example of ventilation maps and changes in the main airways is presented in figure 2a and 2b. The results suggest that non-specific airway challenge with Mch has a predominant effect on the central airways, whereas a specific allergen challenge with OVA induces constriction in the central and peripheral airways equivalently. Correlation between images and information obtained from FOT is very good (figure 3a and 3b).

These results have been presented in following conferences:
L. Porra et al. Medical applications of Synchrotron Radiation conference, August 2007, Saskatoon, Canada.
S. Strengell et al. European Respiratory Society conference, September 2007, Stockholm, Sweden.
T. Janosi et al. European Respiratory Society conference, September 2007, Stockholm, Sweden.
S. Bayat et al. October 2007, Biomedical Engineering Society meeting, Los Angeles, USA.

Manuscript is under preparation and will be published later (Manuscript 2007).

Experiment MD238/3:
The third experiment concentrated on a new model to study the effects of acute tobacco exposure in rabbits. Experiment was performed with collaboration with the division of atmospheric physics at the University of Helsinki. Healthy and sensitized rabbits were exposed to tobacco smoke, and simultaneously the particle size distribution of smoke was measured. After the smoke exposure, the animals were provoked with Mch and OVA as in the previous study. Total of 11 animals were studied successfully with the experiment protocol. The results suggest that tobacco smoke causes unexpected dilatation in the airways in rabbit, and prevents later the constrictions caused by Mch infusion (Figure 4). Similar results have been reported earlier (Alving et al. 1993) in pigs. The analysis is not completed, and more experiments are required to finish this study.

First results will be presented at European Respiratory Society conference 2008, and manuscript will be prepared later.

References;
Alving K, Fornhem C, Lundberg JM. Pulmonary effects of endogenous and exogenous nitric oxide in the pig: relation to cigarette smoke inhalation. *Br J Pharmacol.* 1993 Oct;110(2):739-46.
Bayat S, Porra L, Suhonen H, Nemoz C, Suortti P, Sovijärvi AR. Differences in the time course of proximal and distal airway response to inhaled histamine studied by synchrotron radiation CT. *J Appl Physiol*. 2006 Jun;100(6):1964-73.
Peták F, Hantos Z, Adamicza A, Gálity H, Habre W. Development of bronchoconstriction after administration of muscle relaxants in rabbits with normal or hyperreactive airways. *Anesth Analg*. 2006 Jul;103(1):103-9.
Manusctript 2007. Functional imaging of regional airway and ventilation response to intravenous allergen and methacholine in a rabbit model of asthma studied by synchrotron radiation CT. In preparation.

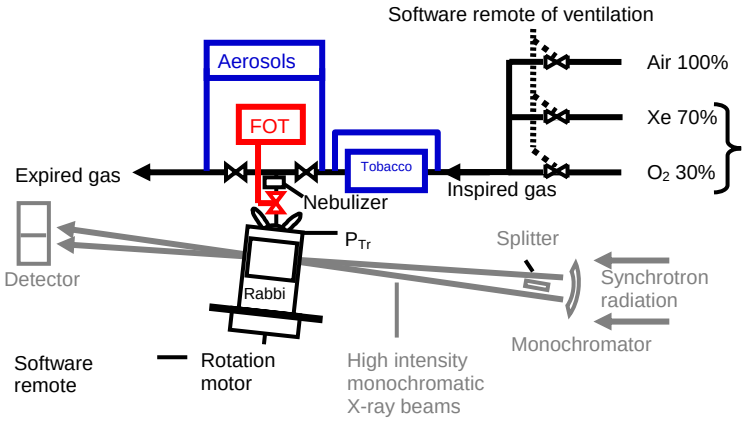

Figure 1: Imaging setup with new modifications; FOT measurement system used in all experiments is shown in red, and tobacco chamber and aerosol measurement system, used in MD238/III experiment is shown in blue.

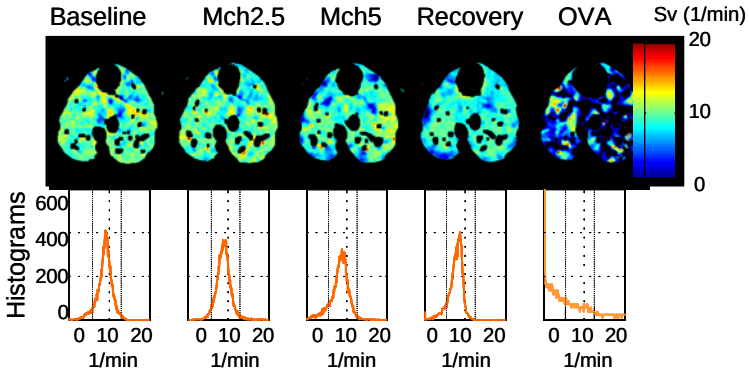

Figure 2a: Ventilation maps and their histograms before and after Mch provocation with 2 different doses at recovery phase and after OVA allergen injection.

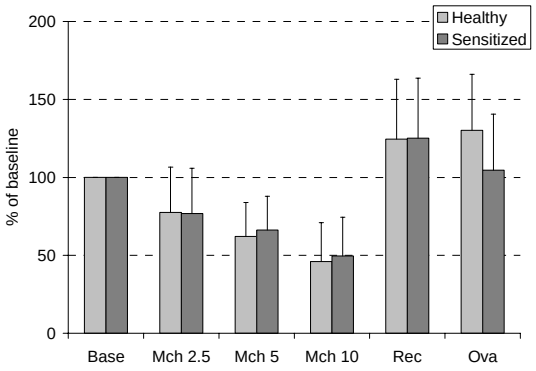

Figure 2b: Airway cross-sectional areas decrease after Mch with a good dose response. At recovery phase airways are dilatated, and OVA affects only in sensitized rabbits.

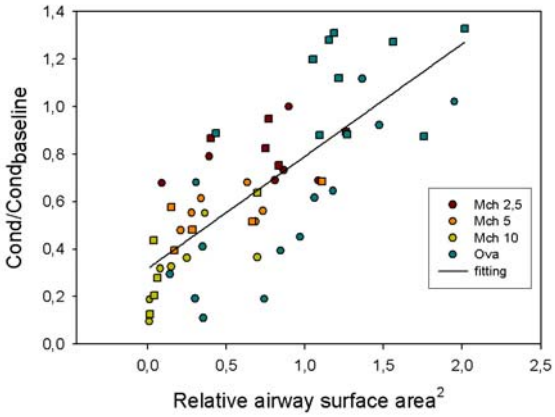

Figure 3a. Correlation between image and FOT data conductance vs. airway surface area. R=0.57. □ notes healthy animals and o notes sensitized animals.

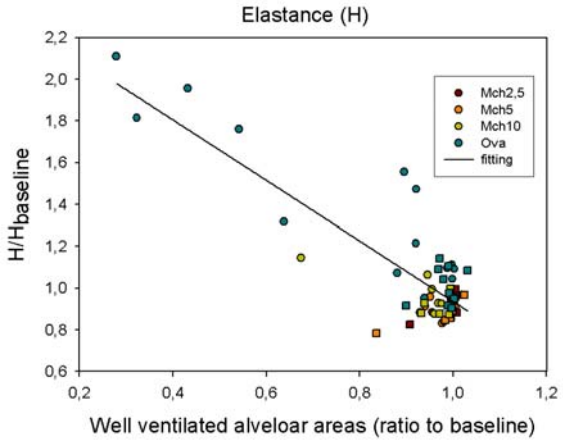

Figure 3b. Correlation between well ventilated lung areas vs. elastance (H). R=0.72. □ notes healthy animals and o notes sensitized animals.

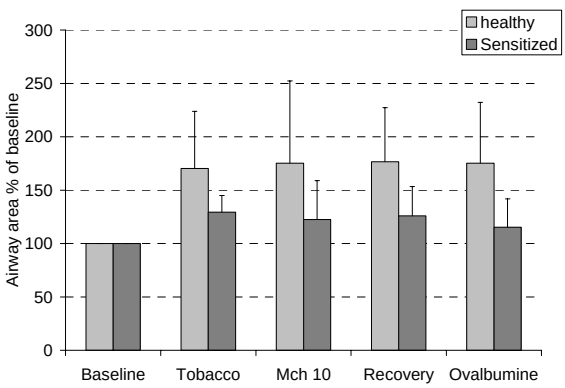

Figure 4. Airway surface areas during tobacco provocation and after Mch challenge. Tobacco smoke dilatates airways, and prevents airway narrowing induced by the Mch, compared to the previous study (fig 2b).