AirPROM

The AirPROM Project Prospectus: Values, Achievements, Services

Funded by the European Union

Our background and aims

AirPROM stands for 'Airway Disease Predicting Outcomes through Patient Specific Computational Modelling'. This is the name for the 5 year EU-funded project (2011-2016), which has aimed to produce computer and physical models of the whole human airway system. These models will help scientists and doctors predict how people affected by asthma or chronic obstructive pulmonary disease (COPD) will react to different treatments.

Developing accurate models will provide:

- Better diagnosis of different types of asthma and COPD
- Better monitoring of the disease
- Better matching of the right treatment to each patient
- Better tools for more targeted research
- Better understanding of the disease
- Improved quality of life due to personalised medicine

AirPROM Network vision

AirPROM will become recognised as a global leader for the provision of expert services, translational research and development, validation and approval of patient specific computational modelling for airways diseases.

- AirPROM will be independently sustained as an important collaborative organisation
- AirPROM will have an established brand for the provision of global expertise, translational research and the development of patient specific computational modelling products and services
- AirPROM will have a strong influence in the market and be internationally recognised for developing and validating patient specific computational models

Enabling precision medicine

AirPROM has demonstrated how an integrated approach, involving modelling, measurement and clinical validation, can accelerate the development of new therapies and improve existing methods. To build on this AirPROM is taking forward the unique mix of skills and expertise within the AirPROM network.

AirPROM proposes that applying computer modelling can reduce the number of study participants needed in clinical trials, while also leading towards a more precision medicine approach, where patients can be assessed and treated on a more individual basis.

The societal impact of AirPROM, through improved quality of life for airway diseases patients and reduced costs of healthcare, highlights the scope and potential to continue the work within the AirPROM network and connect this learning with the work of other partners.

Taking the partnership forward

AirPROM has brought together 34 partners across Europe from universities, research institutes, the biopharmaceutical industry, patient organisations, small companies and existing research projects with expertise in physiology, radiology, image analysis, bioengineering, data harmonization, security and ethics, computational modeling, systems biology, and health communication.

The AirPROM Network will build on this partnership and its achievements, to turn the AirPROM vision into clinical practice.

Building on success

AirPROM has seen great success, which has demonstrated that significant benefits can be obtained from the AirPROM approach, while also considerably advancing the state of knowledge of asthma and COPD. The key achievements underpinning the continuing work are:

- more than 80 high quality peer-reviewed scientific papers produced by partners and presented at key medical and industry conferences, including the ATS Congress and ERS Congress from 2012 to 2016
- the generation of a comprehensive Knowledge Base of patient details, clinical evaluations, scans and derived data, such as the 3D segmented geometries, and outcomes, as well as creating new data mining tools

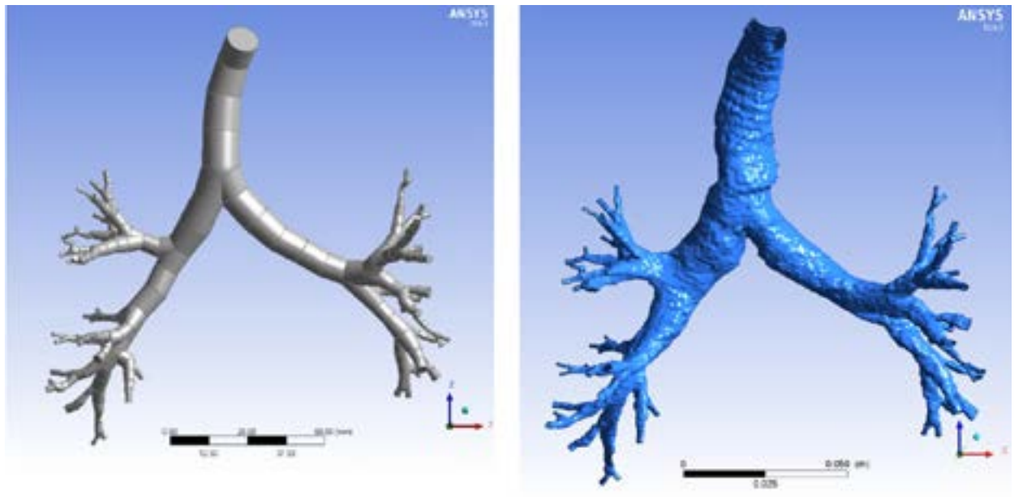

Figure 1: Skeletonisation and surface CFD mesh (credit: ANSYS - produced within the AirPROM project)

- production of enhanced software, models and workflows. These include specific models for particular issues, and integrated models, to predict the interactions between the phenomena from cellular scale to organ scale
- validation of its key models
- participation in several key, ground breaking clinical trials, to demonstrate increased value for clinical trials through the AirPROM approach, adding in complementary modeling to give greater understanding of the trial results.

Outputs in focus

- Basic discovery genetics and bio-statistical modelling:
  - The largest study of severe asthma genomics
  - The largest study of COPD airway transcriptome
  - The first study of genomics and trait analyses in severe asthma for inflammation and CT-determined airway remodelling

- Clinical trials and computational modelling:
  - The first study to demonstrate efficacy of anti-DP2 upon airway inflammation and remodelling
  - The first computational model of eosinophilic airway inflammation and remodelling
  - Ehanced computational model of thermoplasty validated by a clinical trial in severe asthma

Figure 2 shows flow streamlines in the airways, and the blockage effect of the catheter and electrodes. For the smaller airways, the catheter will be much larger compared to the airway radius, and hence the flow blockage effects would be much greater.

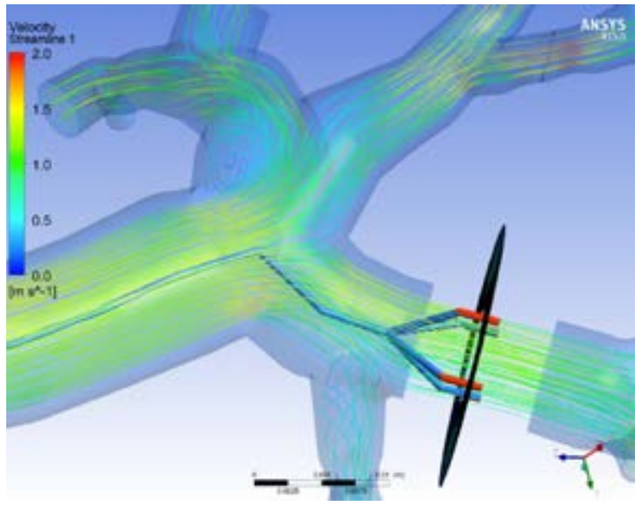

Figure 2: 3D CFD model of the thermoplasty showing flow streamlines.
(credit: ANSYS - produced within the AirPROM project)

- Computational models of airway physiology
  - First computational models of oscillometry, multiple breath washout and spirometry open access through CHASTE (Cancer, Heart and Soft Tissue Environment software developed by University of Oxford)

- Functional Respiratory imaging
  - Development of a new work flow to enable high throughput 3D mesh generation from CT scans and computational fluid dynamics to inform our understanding of heterogeneity of airways disease and response to therapy

- Commercialisation
  - New CT segmentation software
  - Advanced functional respiratory imaging
  - Software for multiple-breath washout analysis
  - Suite of computational tools to enhance early development of new therapies (anti-DP2 programme accelerated to Phase III)
  - Commercial software (Mimics, ANSYS) has been developed and is available under commercial licensing arrangements.

Way forward for Computational Modelling in clinical research

AirPROM has shown that computational modelling offers real and high potential in both moving towards precision medicine and increasing the efficiency of clinical trials, thereby minimising the burden on patients.

- AirPROM computational modelling successfully predicted that the mechanism of action of mepolizumab and fevipiprant would have differential effects upon airway smooth muscle function.

- AirPROM models suggested that DP2 would reduce airway smooth muscle whereas mepolizumab would not. Data from clinical trials undertaken by AirPROM partners have found that indeed airway smooth muscle mass was reduced by fevipirpant and potentially provide a mechanistic explanation for its greater effects upon lung function. This is the first study in a randomised placebo controlled trial to demonstrate reduction of airway smooth muscle mass in asthma which hitherto has been considered an irreversible feature of asthma.

Value and Services

- The AirPROM network and models offers the ability to plug in clinical, mathematical, statistical, imaging and computational modeling expertise into clinical trials or other respiratory or airflow related projects.

- AirPROM's strength comes from its partners. The figure below shows the client groups who can benefit from AirPROM's expertise

Figure 3: The AirPROM core service and prospective partners

AirPROM would be pleased to develop a tailored offer for your project, following an initial exploratory discussion. For more information on how we can help you, please contact airprom@europeanlung.org.

AirPROM benefits for the patients

People with severe asthma are often unable to walk and talk without coughing; the main challenges are poor sleep, tiredness, exhaustion, no sense of smell, managing side and adverse effects of medications. Other exacerbation triggers, which prevent patients having a normal life are cigarette smoke, air conditioning or air fresheners.

This is the reason why patients are at the centre of AirPROM: to improve and tailor treatments better to individual patient needs. Thanks to the participation of patients, AirPROM scientists were able to develop models that can help them study the characteristics of the airways, how they work and how they are affected by asthma and COPD without the need to conduct consuming tests or examinations on patients.

AirPROM partners also studied how airways react to conditions and therapies, enabling healthcare professionals to recommend which therapies will be most effective for each patient.

"Being an active patient advocate at national and EU level has been a great chance for increasing my knowledge about asthma and allowed me to raise the awareness on chronic respiratory diseases and even to contribute to research studies.
Had tools like 'AIRPROM model' been available for my doctor 20 years ago, I would have been able to know and see what's happening in my lungs, and have more personalized treatment much earlier."

Breda Flood, severe asthma patient advocate

List of partners

University of Leicester
UNIVERSITY OF LEICESTER

amc
ACADEMISCH MEDISCH CENTRUM
BIJ DE UNIVERSITEIT VAN AMSTERDAM

Imperial College London
IMPERIAL COLLEGE OF SCIENCE,
TECHNOLOGY AND MEDICINE

THE QUEEN'S UNIVERSITY OF BELFAST

UNIVERSITY OF OXFORD
THE CHANCELLOR, MASTERS AND SCHOLARS
OF THE UNIVERSITY OF OXFORD

The University of Nottingham
THE UNIVERSITY OF NOTTINGHAM

The University Of Sheffield.
THE UNIVERSITY OF SHEFFIELD

INSTITUT Mines-Télécom
INSTITUT MINES-TELECOM

THE UNIVERSITY OF WARWICK

Parc Científic de Barcelona
FUNDACIO PRIVADA PARC CIENTIFIC
DE BARCELONA

Materialise
MATERIALISE NV

ANSYS
ANSYS UK LIMITED

PSNC
INSTYTUT CHEMII BIOORGANICZNEJ PAN

FLUIDDA
FLUIDDA NV

biomax informatics ag
BIOMAX INFORMATICS AG

ERS EUROPEAN RESPIRATORY SOCIETY
every breath counts
EUROPEAN RESPIRATORY SOCIETY

BioSci Consulting
BIOSCI CONSULTING

University of Southampton
UNIVERSITY OF SOUTHAMPTON

UNIVERSITÀ degli STUDI di CATANIA
UNIVERSITA DEGLI STUDI DI CATANIA

SEMMELWEIS EGYETEM

MANCHESTER 1824
THE UNIVERSITY OF MANCHESTER

Aix+Marseille université
UNIVERSITE D'AIX-MARSEILLE II

UMEA UNIVERSITET
UMEA UNIVERSITET

Karolinska Institutet
KAROLINSKA INSTITUTET

OBJET
OBJET GEOMETRIES GMBH

UNIVERSITÀ DEGLI STUDI DI FERRARA
UNIVERSITA DEGLI STUDI DI FERRARA

EUROPEAN FEDERATION OF ALLERGY
AND AIRWAYS DISEASES PATIENTS' ASSOCIATIONS

INSTYTUT GRUZLICY I CHOROB PLUC

UNIVERSITY OF BIRMINGHAM
UNIVERSITY OF BIRMINGHAM

University of Glasgow
UNIVERSITY OF GLASGOW

DART
KÖMMUNICKATIONS OCH DATARESURSCENTER

ESMO
EUROPEAN SOCIETY FOR MEDICAL ONCOLOGY

cea
COMMISSARIAT À L'ENERGIE ATOMIQUE

cea CNG
COMMISSARIAT À L'ENERGIE ATOMIQUE
CENTRE NATIONAL DE GENOTYPAGE

ELF EUROPEAN LUNG FOUNDATION
EUROPEAN LUNG FOUNDATION

cnag
CENTRE NACIONAL D'ANALISI GENOMICA

University Hospitals Coventry and Warwickshire NHS
UNIVERSITY HOSPITALS COVENTRY & WARWICKSHIRE

HelmholtzZentrum münchen
HELMHOLZZENTRUM MUNCHEN

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