POLITECNICO MILANO 1863

TBM lab
Laboratorio di Tecnologie Biomediche

Dipartimento di Elettronica, Informazione e Bioingegneria

# Respiro: le nuove tecnologie

Andrea Aliverti

# Respiratory function

Total ventilation
($O_2$ consumption)

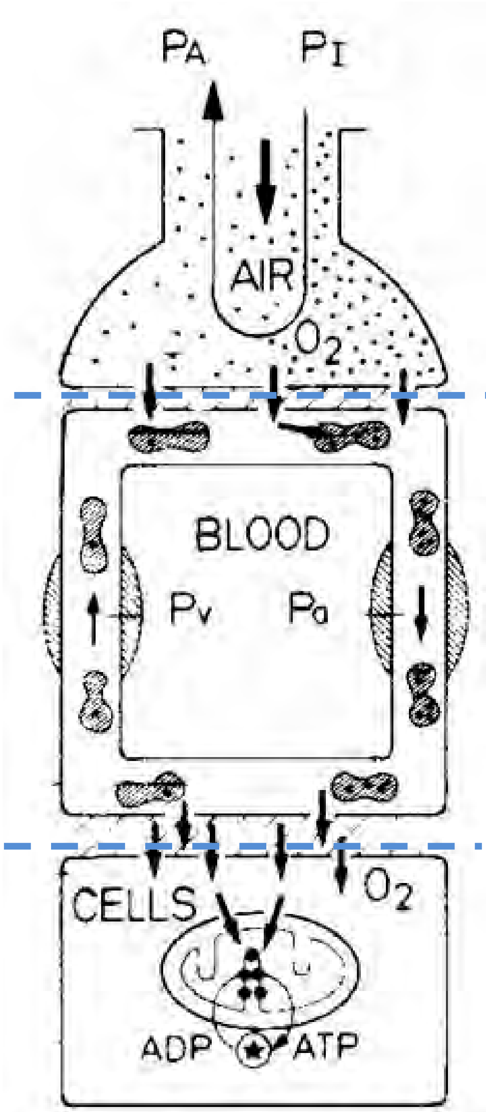
alveolar ventilation
diffusion/gas exchange
lung perfusion

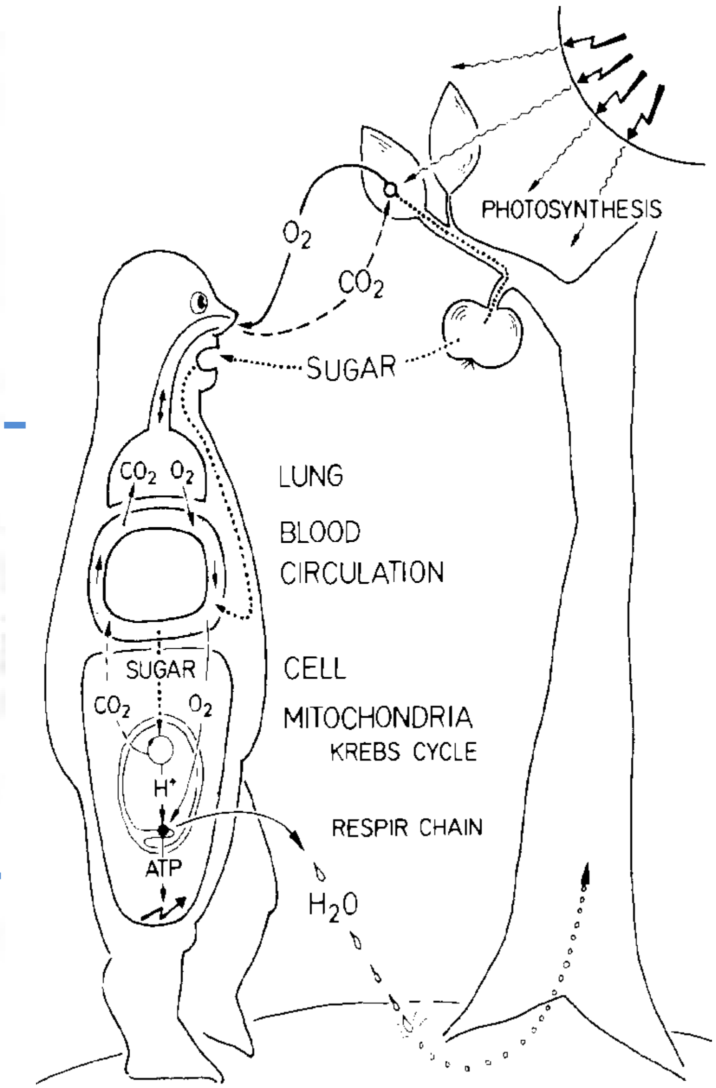
pulmonary circulation

systemic circulation

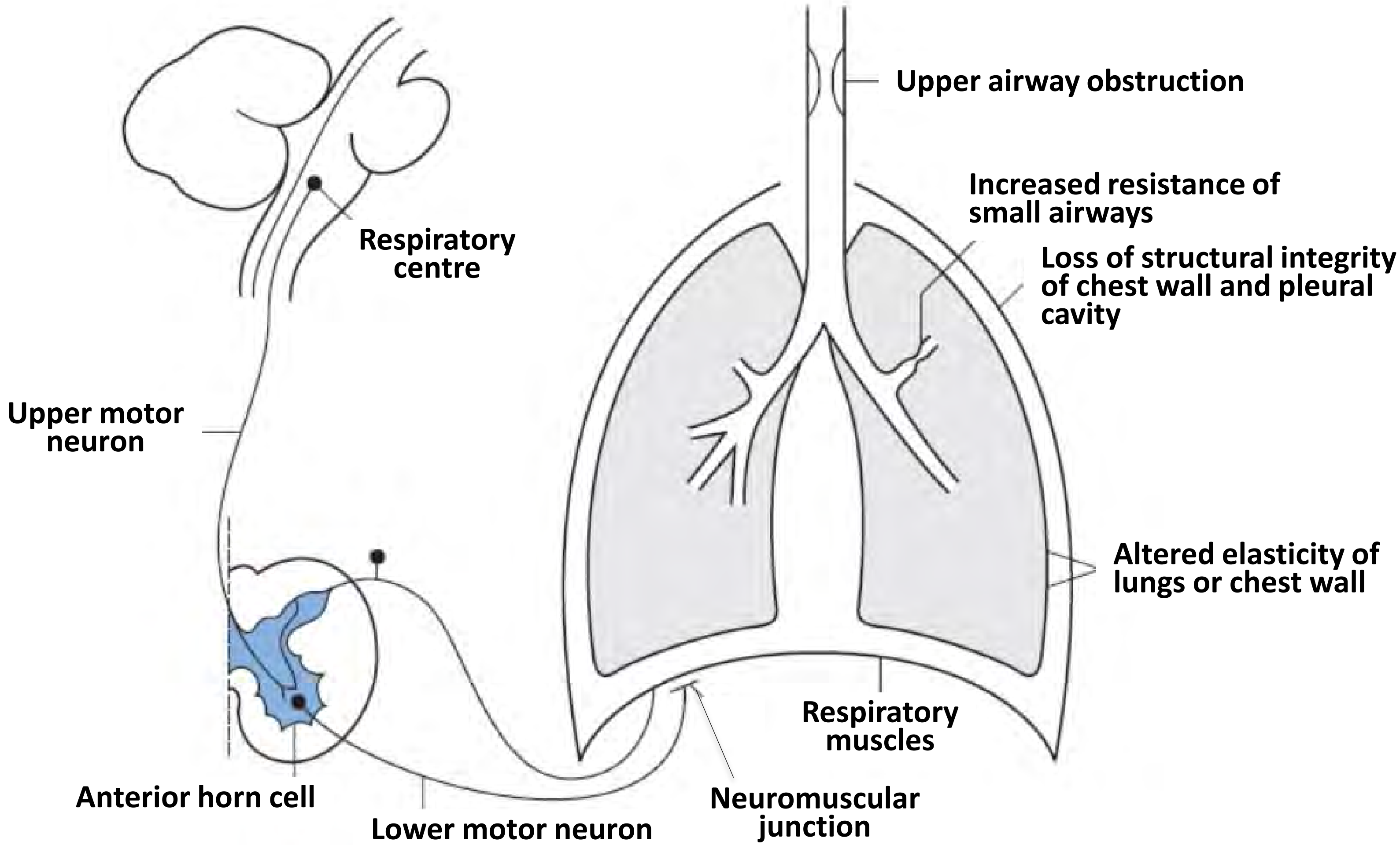
tissue perfusion ($O_2$ delivery)
diffusion/gas exchange
($O_2$ extraction)

cell “respiration”



# CAUSES OF VENTILATORY FAILURE



# Assessment of respiratory function

**ventilation**

**Lung ventilation distribution and inhomogeneity**
(by imaging and single- or multiple-breath inert gas washout techniques)

**Respiratory (lung and chest wall) mechanics**

- Statics
- Kinematics
- Dynamics
- Energetics

BASIC VARIABLES

**Pressure**('force')
**Volume** ('displacement')
**Flow** ('velocity')

**"active" components**

- respiratory muscle action
  - force
  - work
  - power
  - endurance
  - fatigue
  - …

**"passive" components**

- Mechanical properties
  - Compliance
  - Resistance
  - Inertance
  - Impedance
  - …

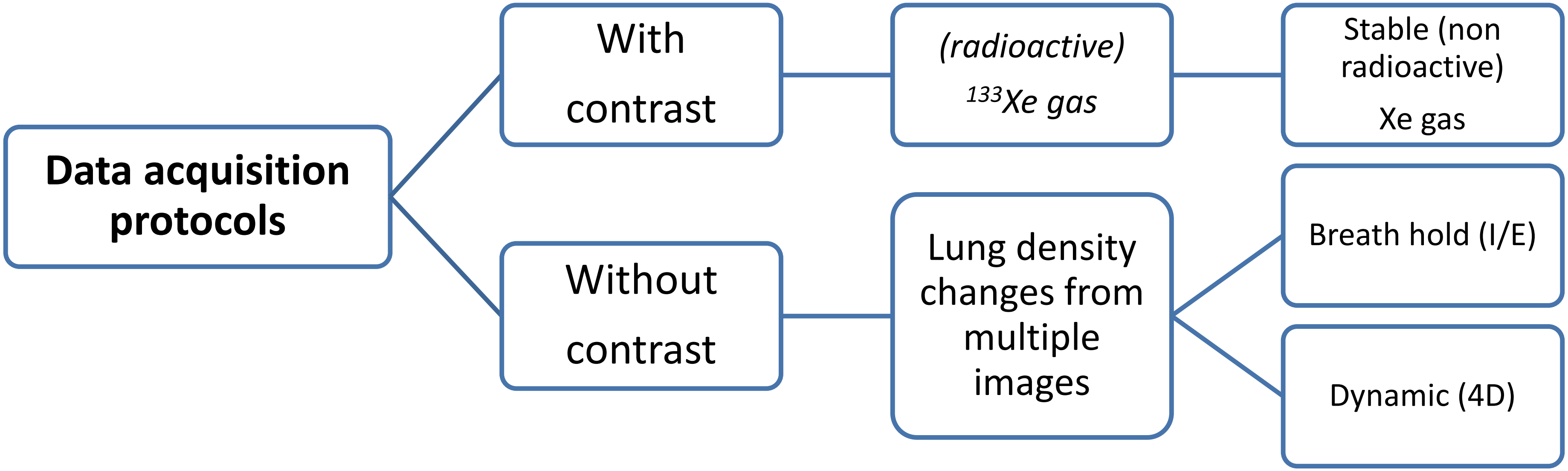
diffusion/
gas exchange

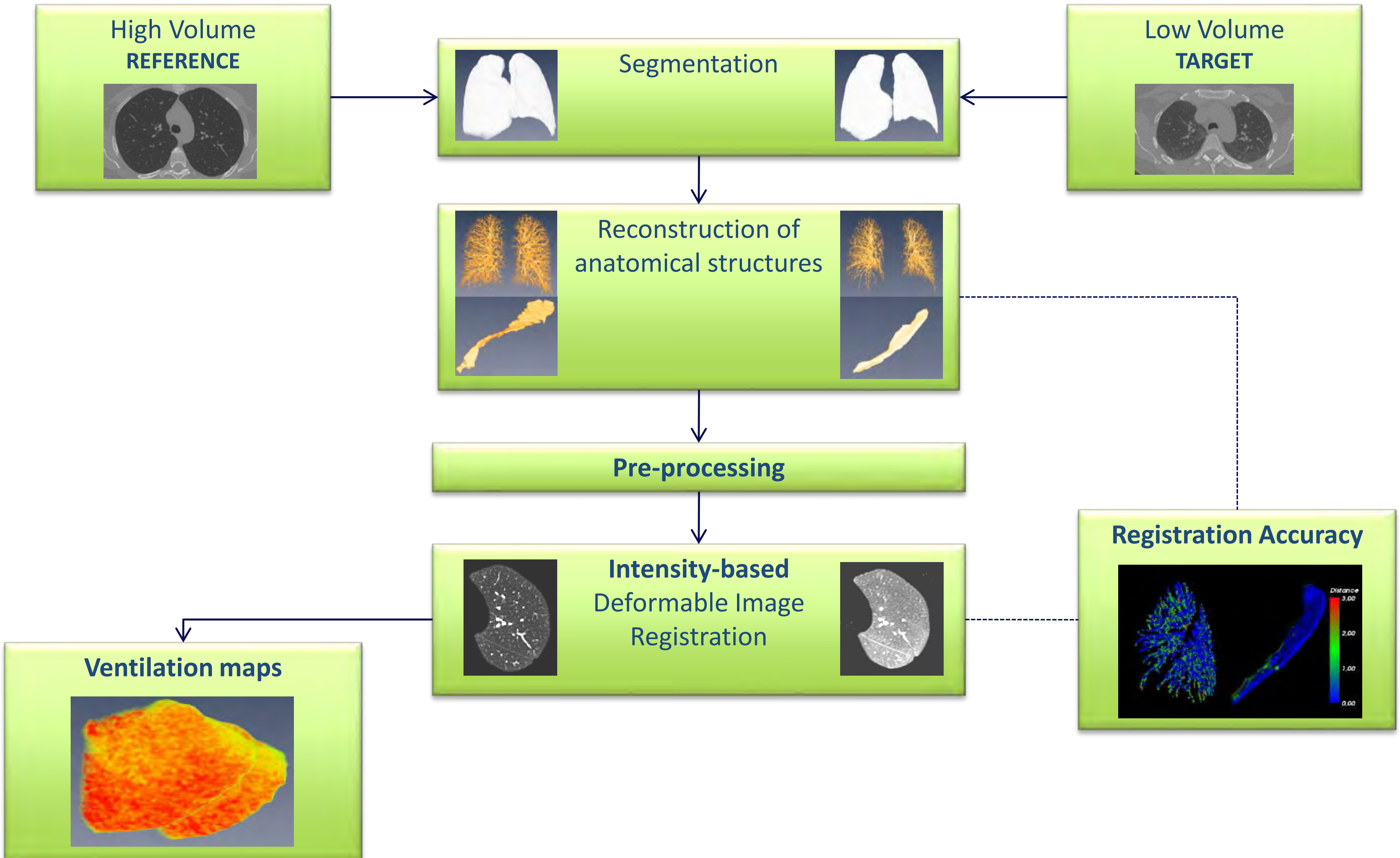
perfusion

diffusion/
gas exchange

cell "respiration"

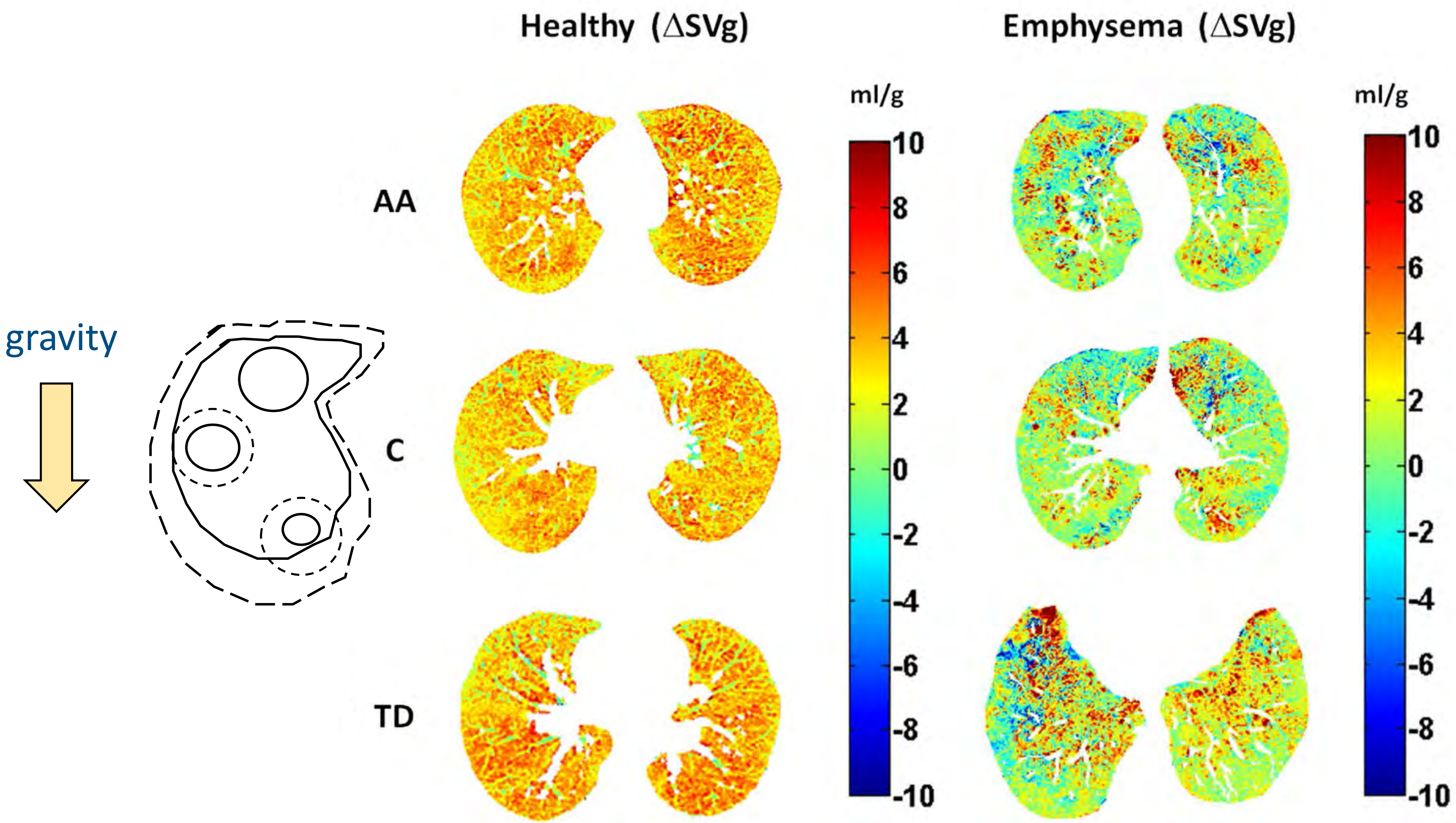
# CT-based functional imaging
# for assessment of regional ventilation




High Volume
REFERENCE
Segmentation
Low Volume
TARGET
Reconstruction of anatomical structures
Pre-processing
Intensity-based
Deformable Image
Registration
Registration Accuracy
Ventilation maps

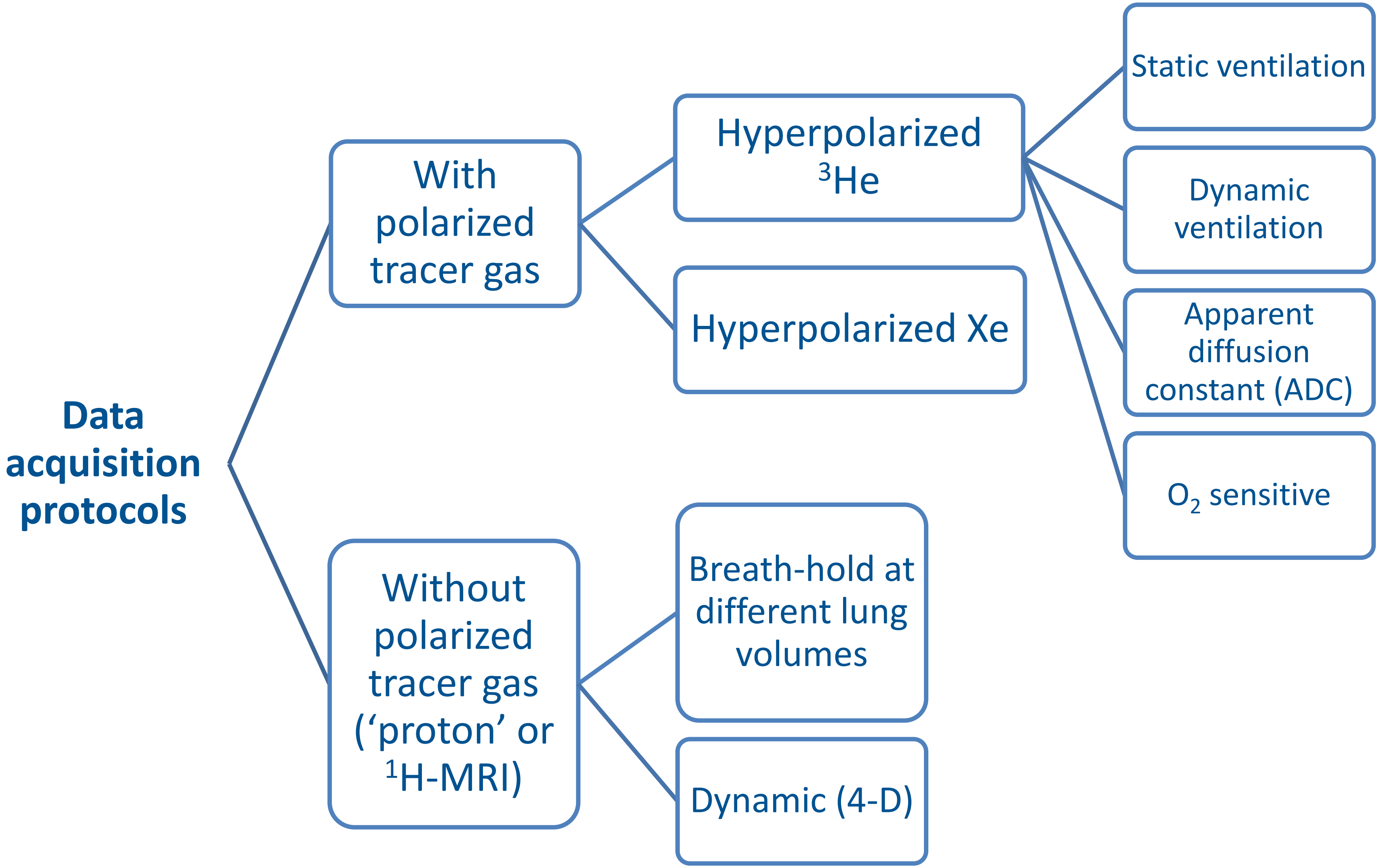
**ITK, VTK, Qt**

# ΔHU and ΔSVg maps in health and emphysema

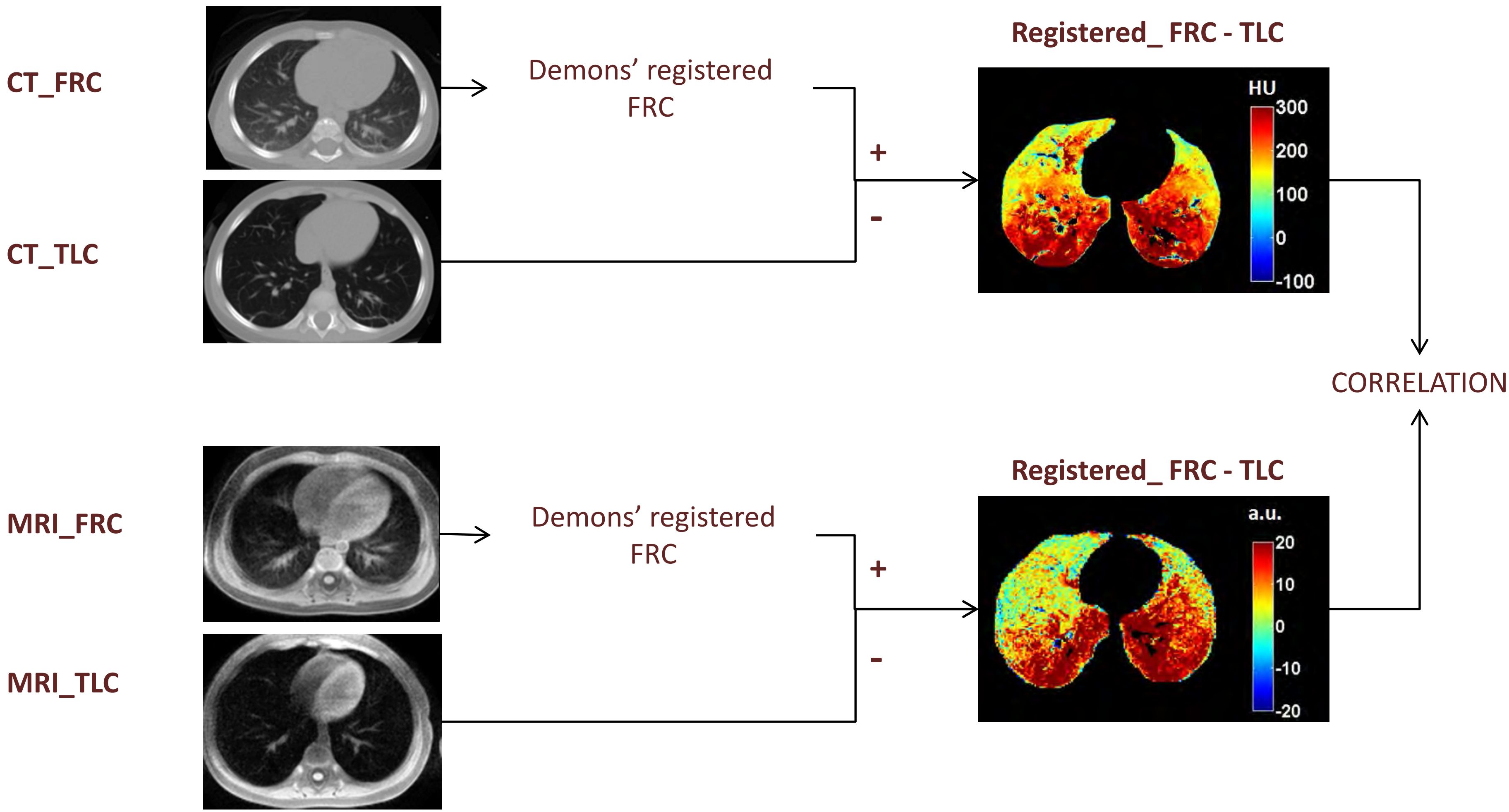



*Eur Respir J*. 2013 - 41(5):1179-88.

# MRI-based pulmonary functional imaging

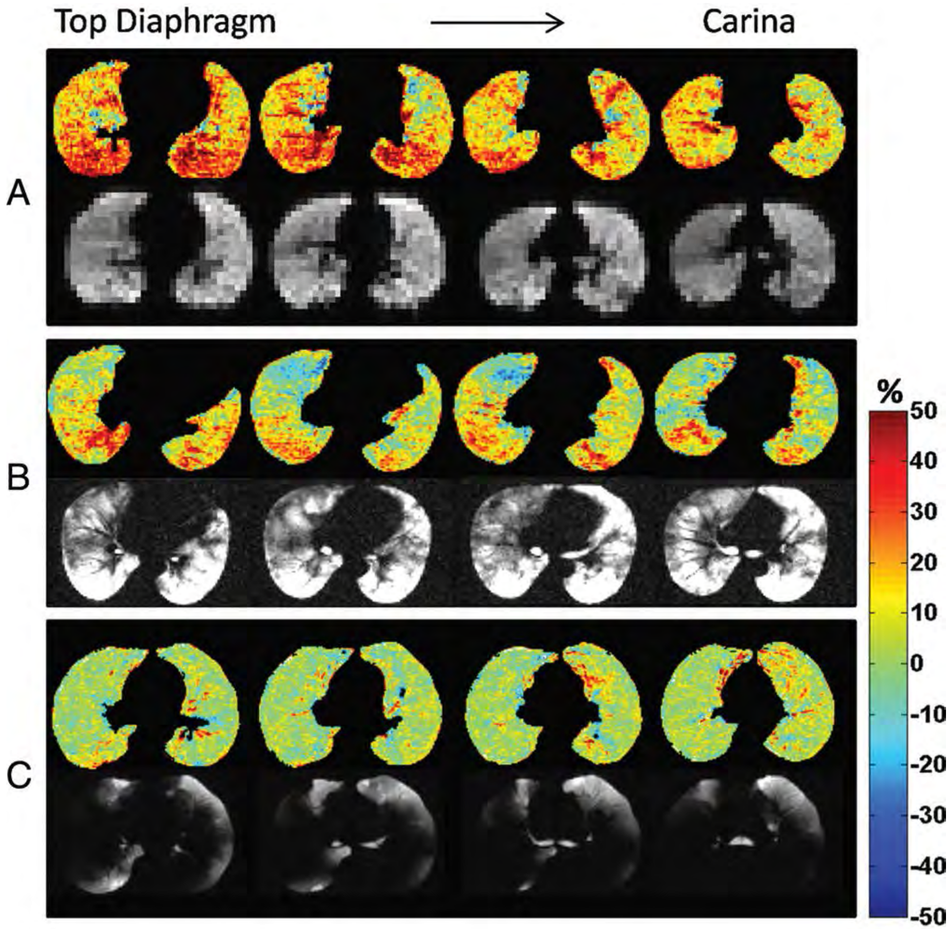


# REGIONAL VENTILATION IN INFANTS QUANTIFIED BY MULTI-VOLUME COMPUTED TOMOGRAPHY (CT) AND MULTI-VOLUME PROTON MAGNETIC RESONANCE IMAGING (MRI) *(ERS, 2015)*



# Maps of proton-signal-density difference

**Proton signal change** within the lung between different lung volumes (TLC and registered RV) is a reliable estimate of regional lung function




Multi-volume MRI as estimate of regional ventilation is:

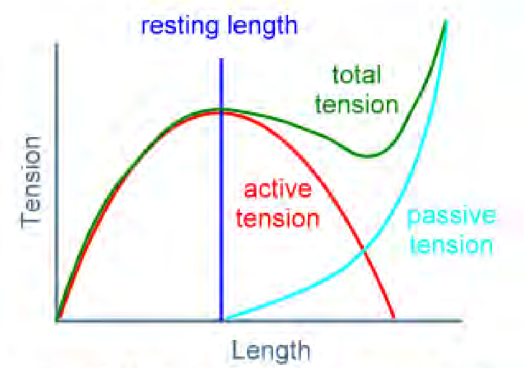
- highly correlated to $^{3}$He-MRI
- gravity-dependent in health (A)
- sensitive to disease-related heterogeneities in emphysema (C) and asthma (B)

F Pennati, J Quirk, D Yablonskiy, M Castro, A Aliverti, J Woods. Assessment of regional lung function by multi-volume 1H-MRI in health and obstructive lung disease: comparison with 3He-MRI. Radiology 2014.

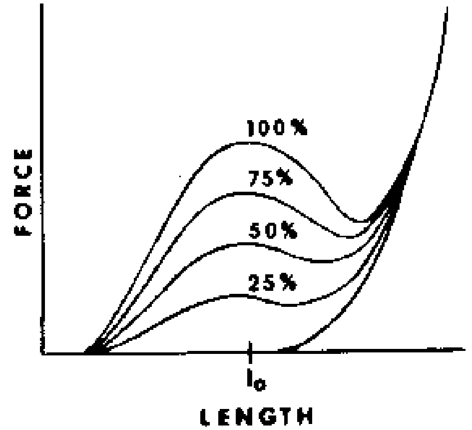
# Assessment of respiratory muscles

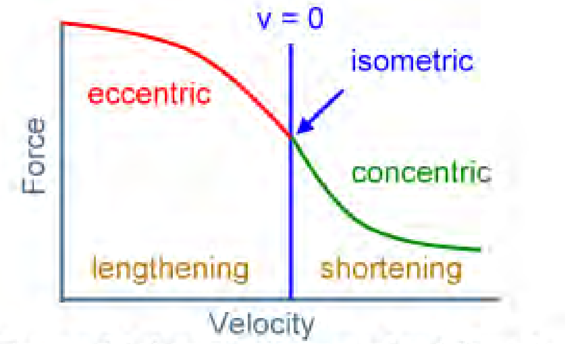
When ventilatory failure depends on the **altered action of the respiratory muscles**, like in the neumomuscular diseases, it is important to assess their:

- force F (→ pressure measurements)
- length L (→ imaging or volume measurement)
- velocity of shortening Vel
  (→ flow, dynamic imaging, volume variations)
- activation (→ mechanical power=F·Vel, EMG)




Length-Tension Curve of a Muscle




Force-Velocity Curve of a Muscle

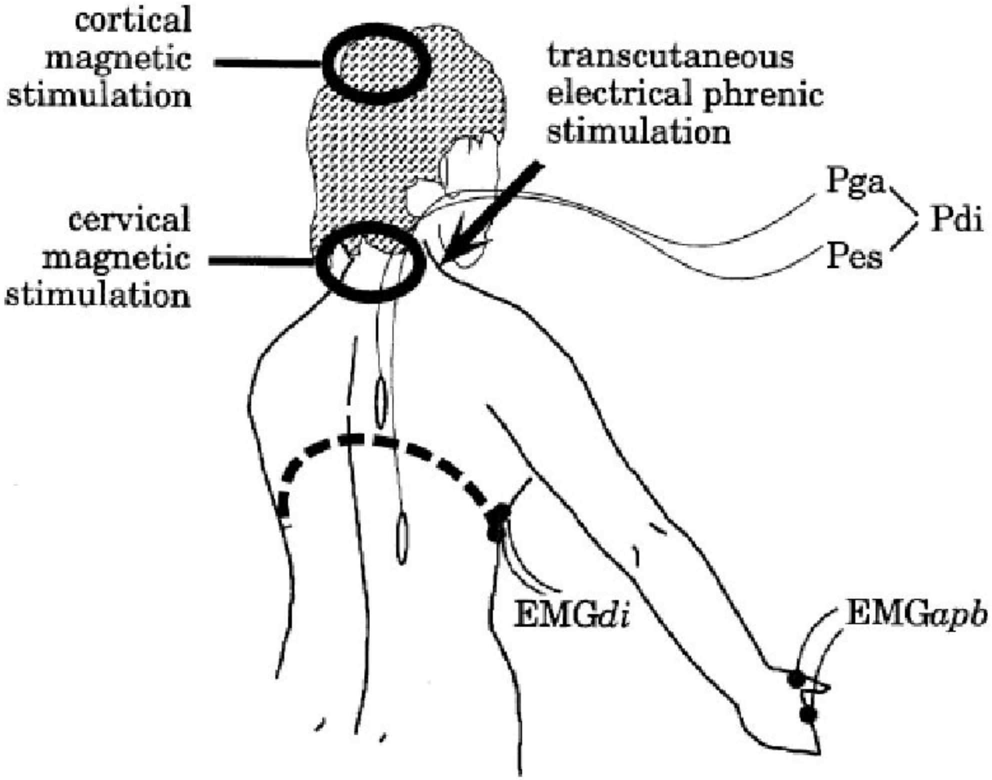
# Assessment of ventilatory function in neuromuscular disorders

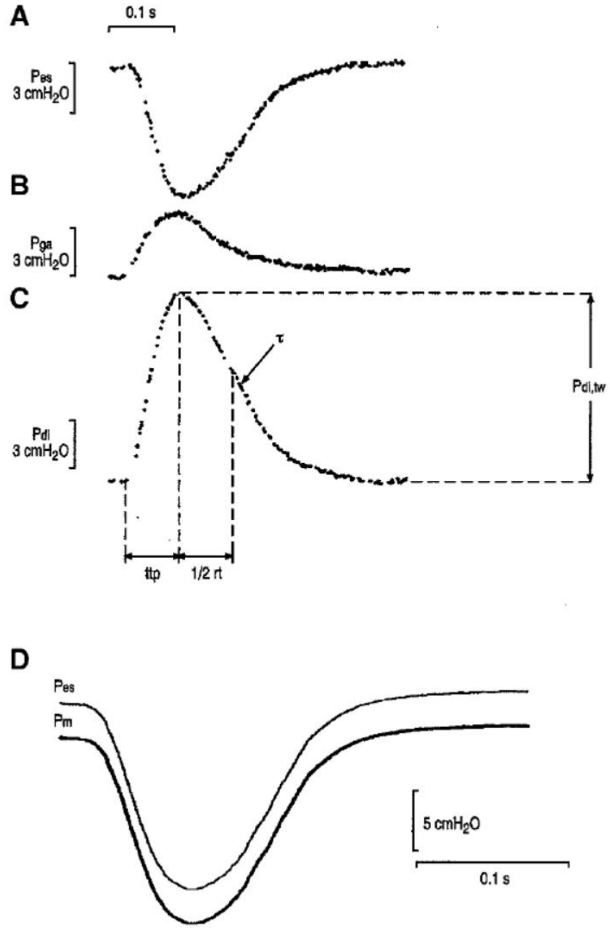
| | |
|---|---|
| **Invasive** | Non-volitional |
| | Volitional |
| **Non-invasive** | Non-volitional |
| | Volitional |

| | | Functional parameter | Measurement method(s) |
|---|---|---|---|
| **Invasive** | Non-volitional | paradoxical breathing index ($\Delta P_{GA}/\Delta P_{DI}$) | oesophageal and gastric balloon-catheters with pressure transducers |
| | | strength of the diaphragm (Peak $P_{DI}$) | oesophageal and gastric balloon-catheters with pressure transducers + magnetic stimulation of the phrenic nerve |
| | | 3D shape of the diaphragm | volumetric computed tomography imaging (CT) |
| | Volitional | strength of the inspiratory muscles (Peak $P_{OES}$) | oesophageal balloon-catheter with pressure transducers during sniff manoeuvre |
| | | strength of the diaphragm (Peak $P_{DI}$) | oesophageal and gastric balloon-catheters with pressure transducers during sniff manoeuvre |
| | | strength of the expiratory muscles (Peak $P_{GA}$) | gastric balloon-catheter with pressure transducers during cough |

# Invasive, non-volitional tests

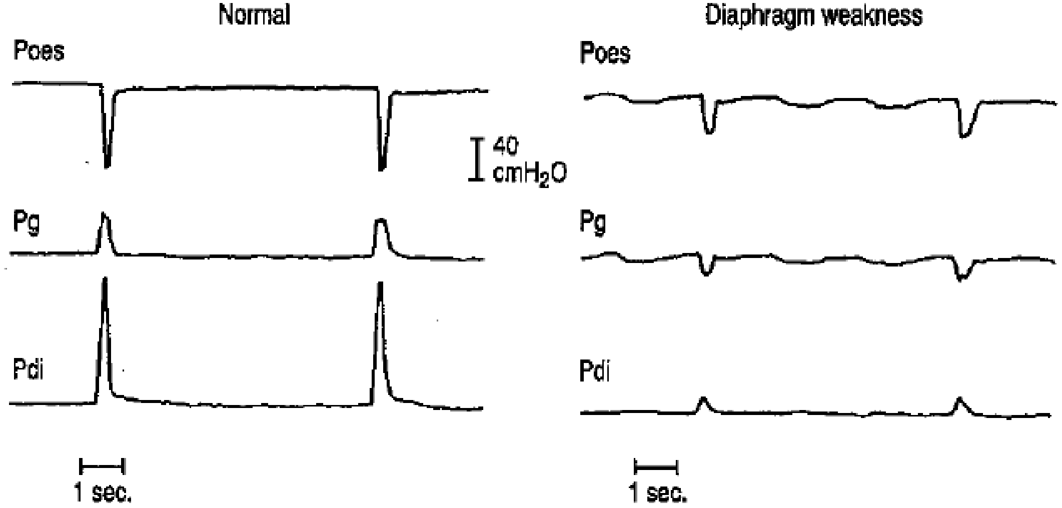
## Transcutaneous magnetic / electrical phrenic nerve stimulation for diaphragm assessment

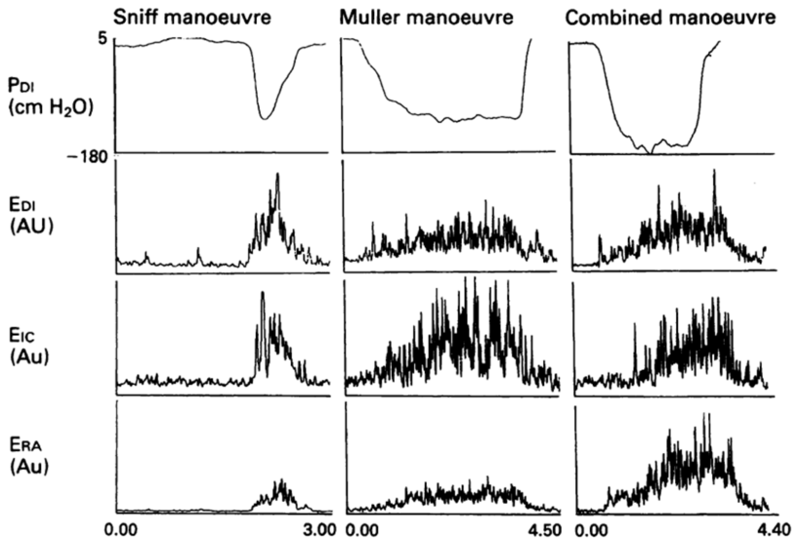


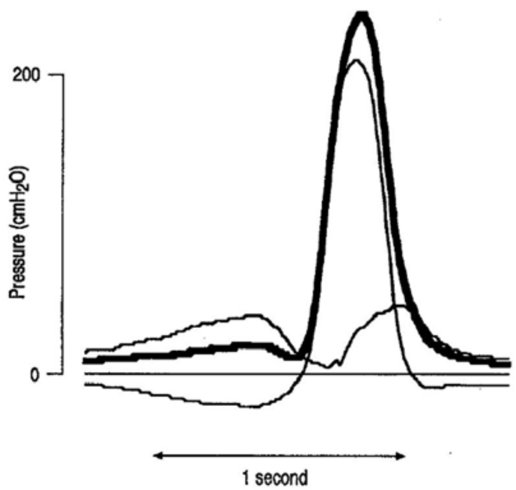
# Invasive, volitional tests

## Sniff maneuver



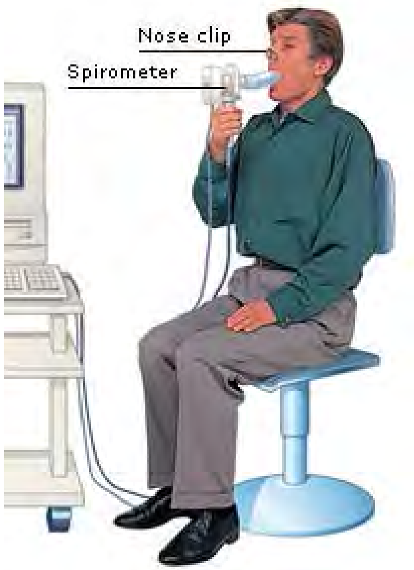

## Maximal voluntary cough maneuver

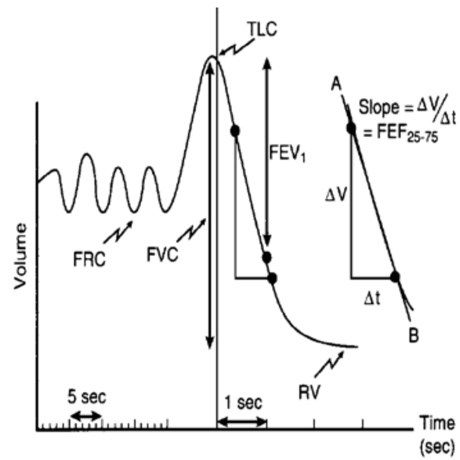


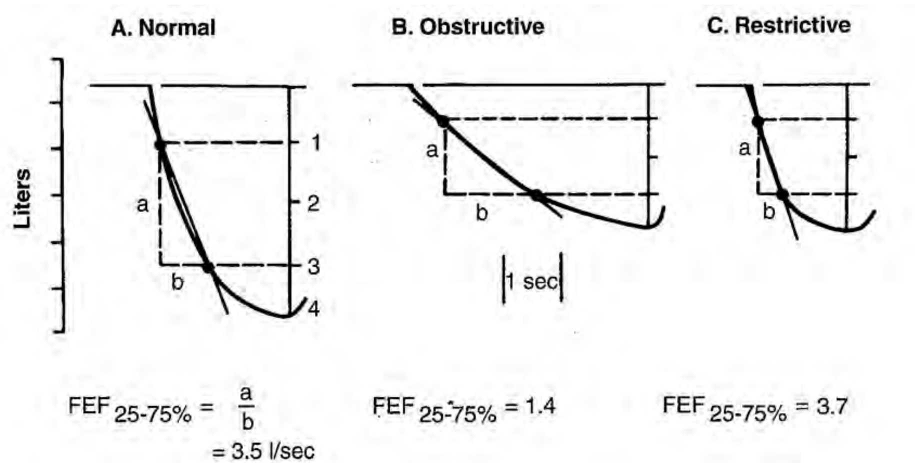
| | | Functional parameter | Measurement method(s) |
|---|---|---|---|
| **Non-invasive** | Non-volitional | electrical activity respiratory muscles | transcutaneous electromyography (sEMG) with surface electrodes |
| | | breath-by-breath ventilatory pattern during quiet breathing at rest | pneumotachograph with mask (or mouthpiece) |
| | | thoraco-abdominal kinematics | magnetometers (diameters), resp. inductive plethysmography (cross sectional areas), opto-electronic plethysmography (total and compartmental chest wall volumes) |
| | | diaphragm shape and displacement | magnetic resonance imaging (MRI) |
| | | displacement of dome, length of apposition zone and thickness of the diaphragm | ultrasound (US) imaging |
| | Volitional | maximal static inspiratory (MIP) and expiratory (MEP) pressures | pressure transducers with mask (or mouthpiece) |
| | | sniff nasal inspiratory pressure (SNIP) | pressure transducers with nostril plug |
| | | forced vital capacity (FVC), forced expiratory volume in 1 second ($FEV_1$), peak expiratory flow (PEF) and cough peak flow (CPF) | spirometer/pneumotachograph with mask (or mouthpiece) |
| | | total lung capacity (TLC), functional residual volume (FRC) and residual volume (RV) | body plethysmography or spirometer + $N_2$ washout techniques |
| | | tension time index ($TT_{0.1}$) | pressure transducers + pneumotachograph with mask (or mouthpiece) |

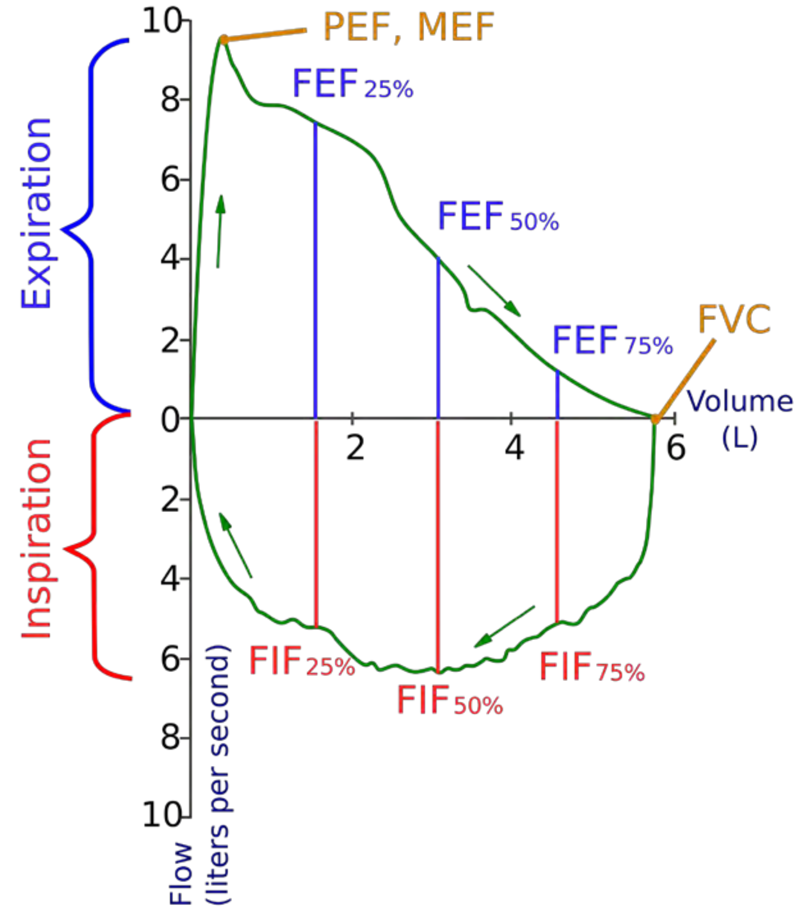
# Noninvasive, volitional tests

## Spirometry



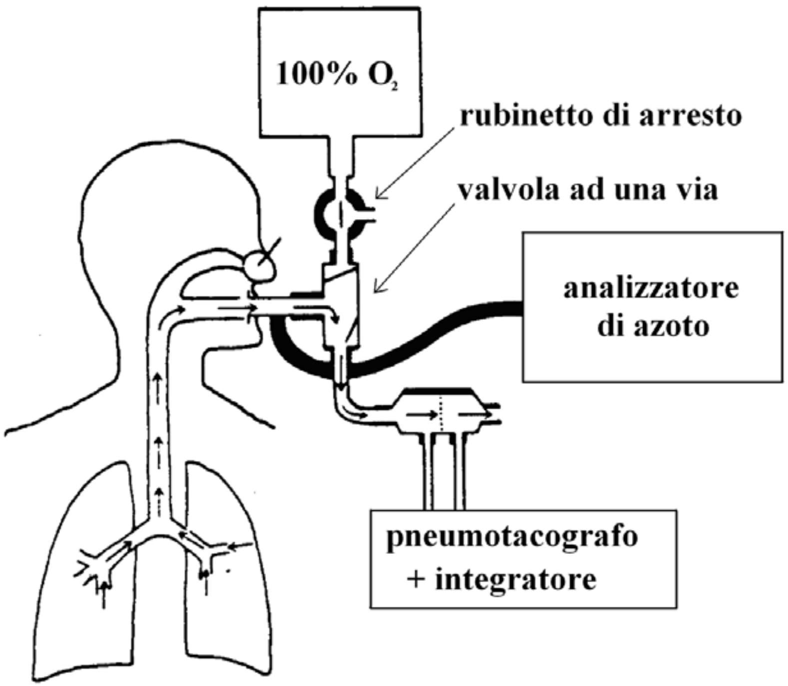



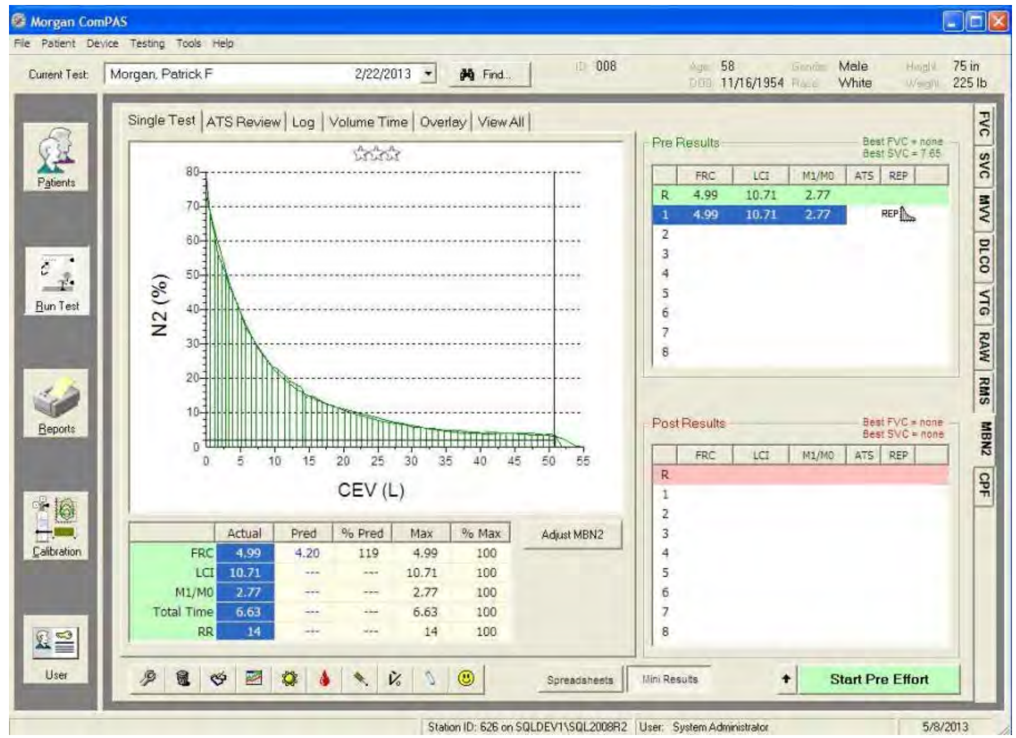



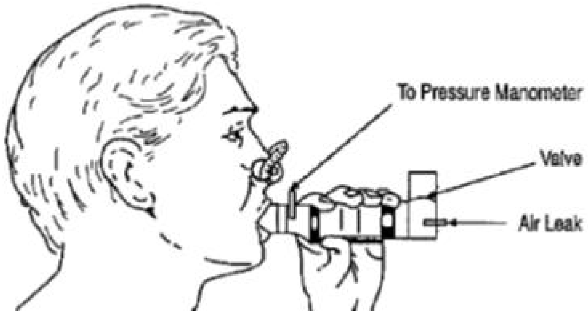
# Noninvasive, volitional tests

## $N_2$ washout test

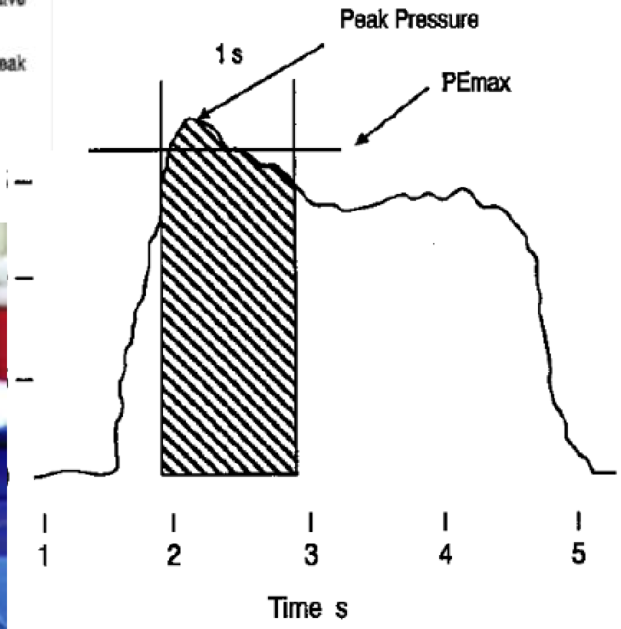


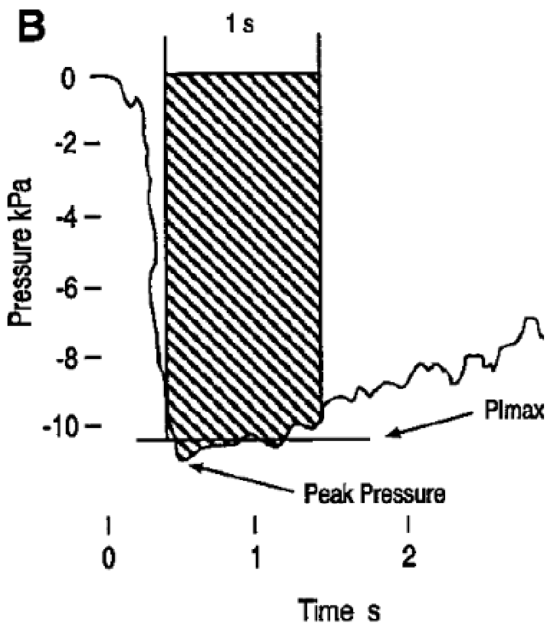
# Noninvasive, volitional tests



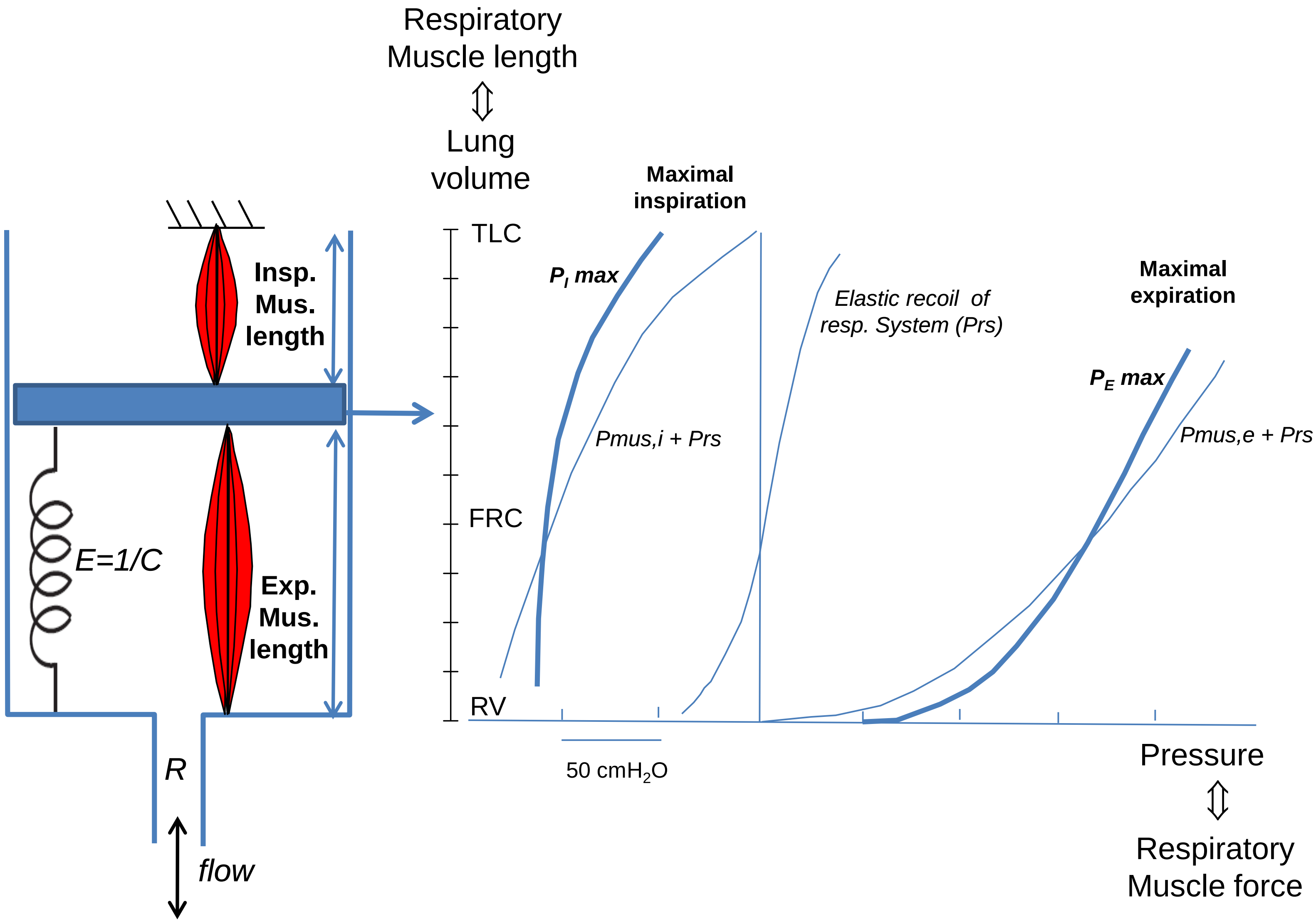

Maximal expiratory pressure (MEP)

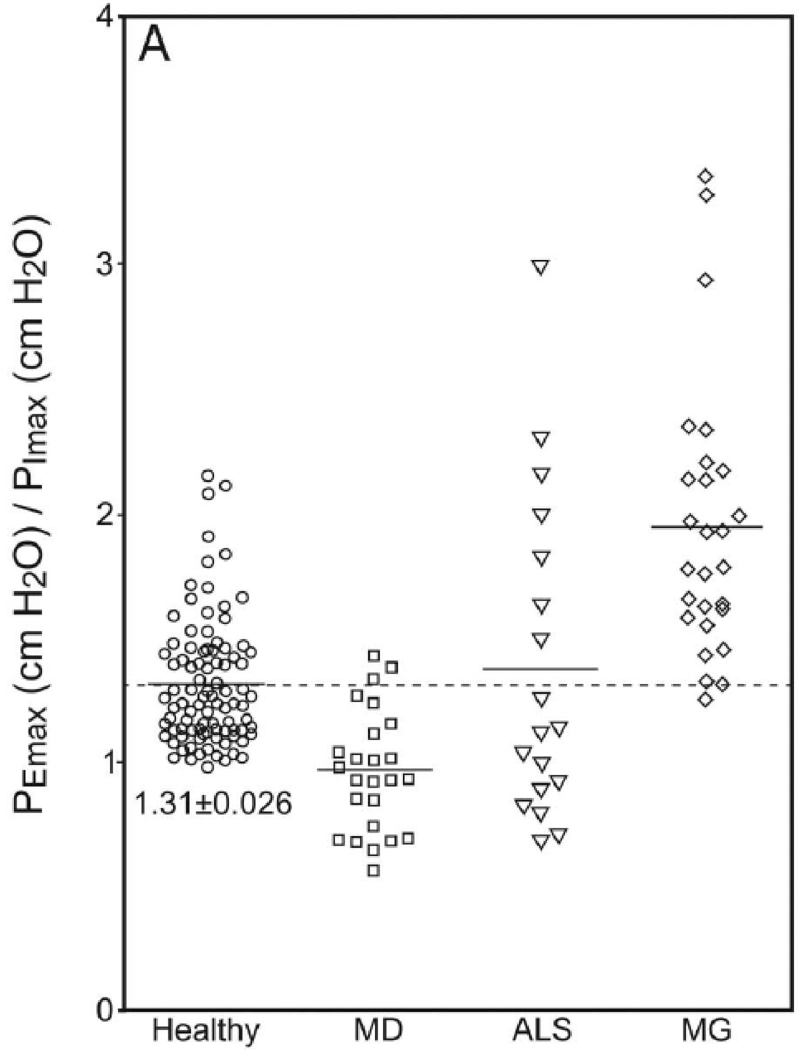



Maximal inspiratory pressure (MIP)



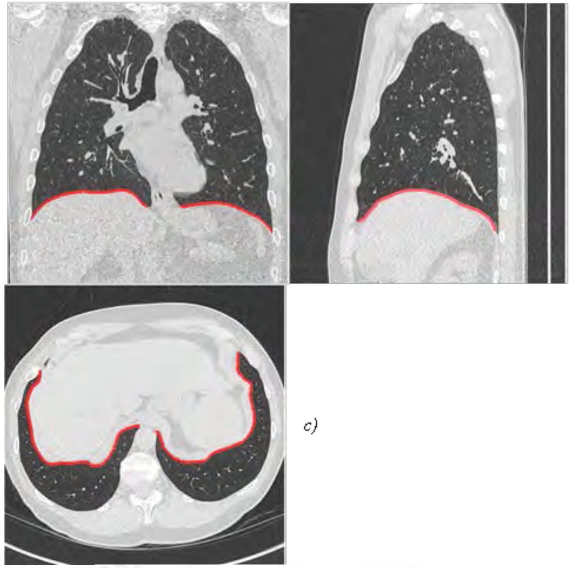
# Respiratory muscle strenght (→pressure) depends on length (→volume)

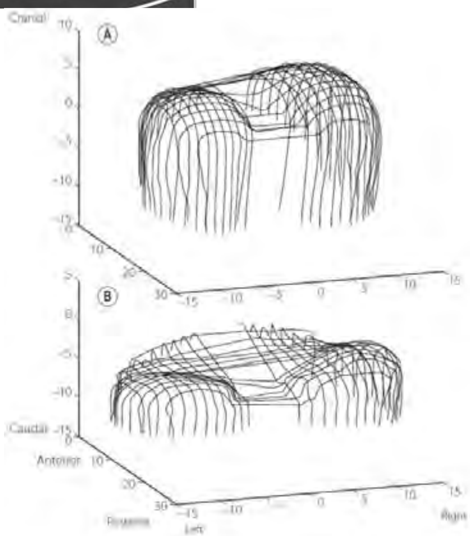


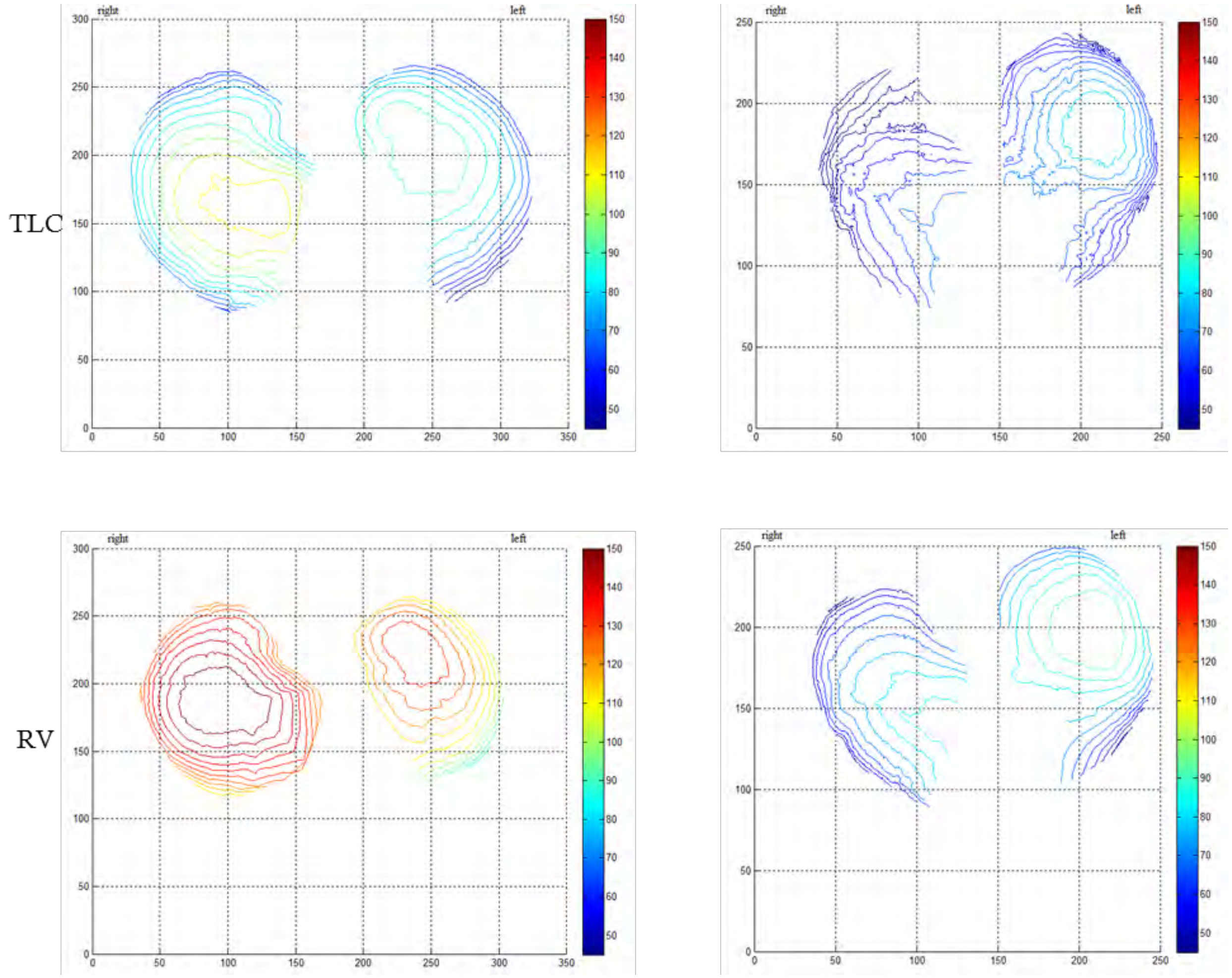



Respir Care, 2015

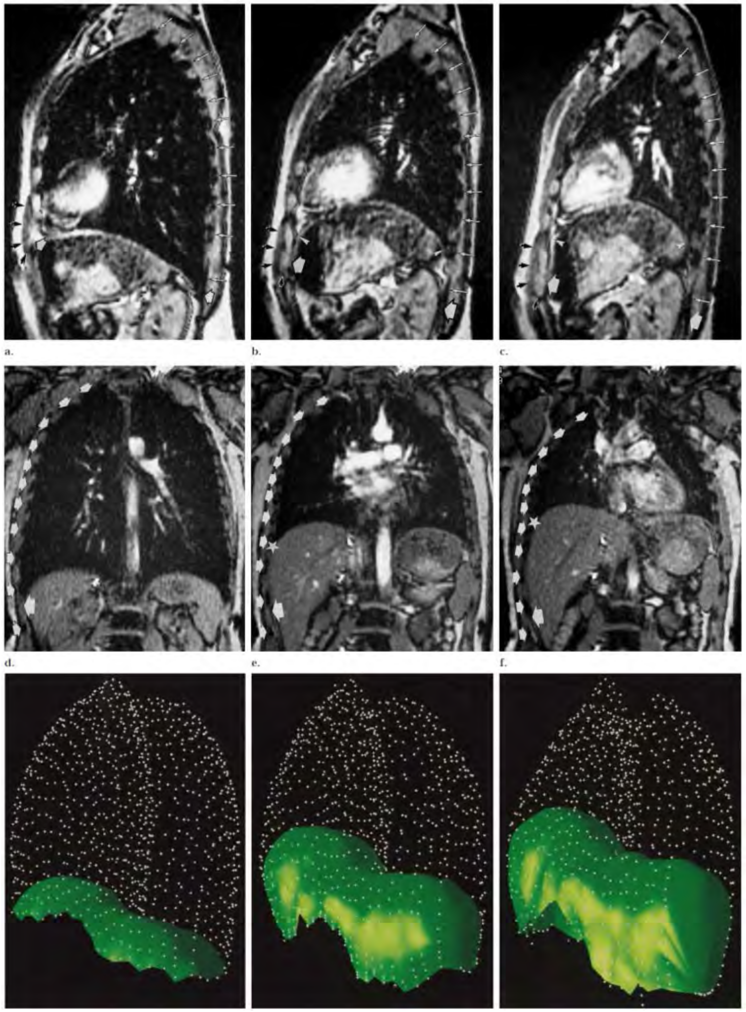
# Assessment of diaphragm geometry by imaging techniques: volumetric HRCT

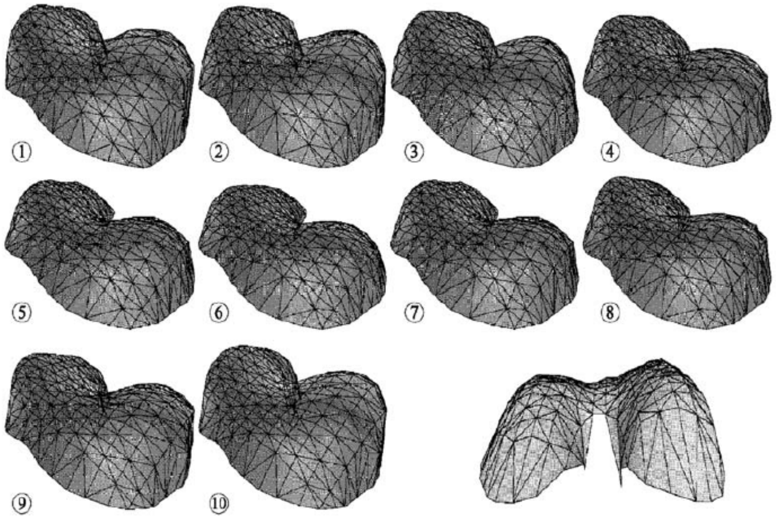


# Assessment of diaphragm function by imaging techniques: dynamic MRI



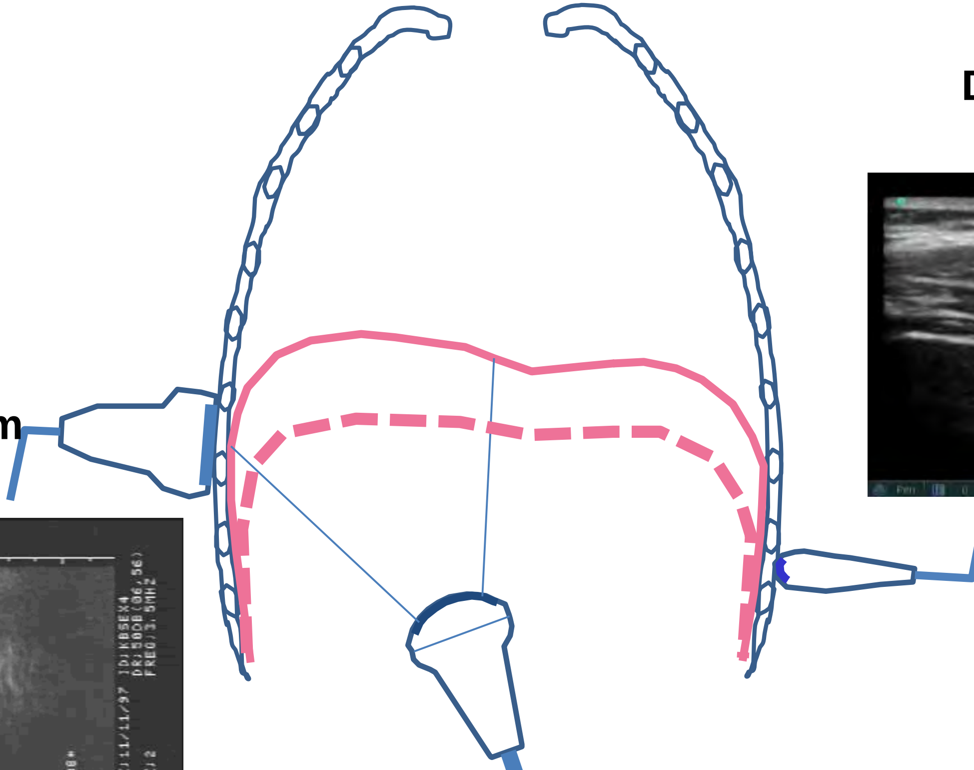



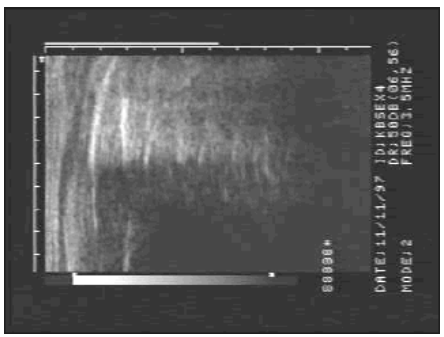
# Assessment of diaphragm function by imaging techniques: dynamic MRI

**Diaphragm thickness**

Ueki, Thorax, 1995

**Length of diaphragm zone of apposition**



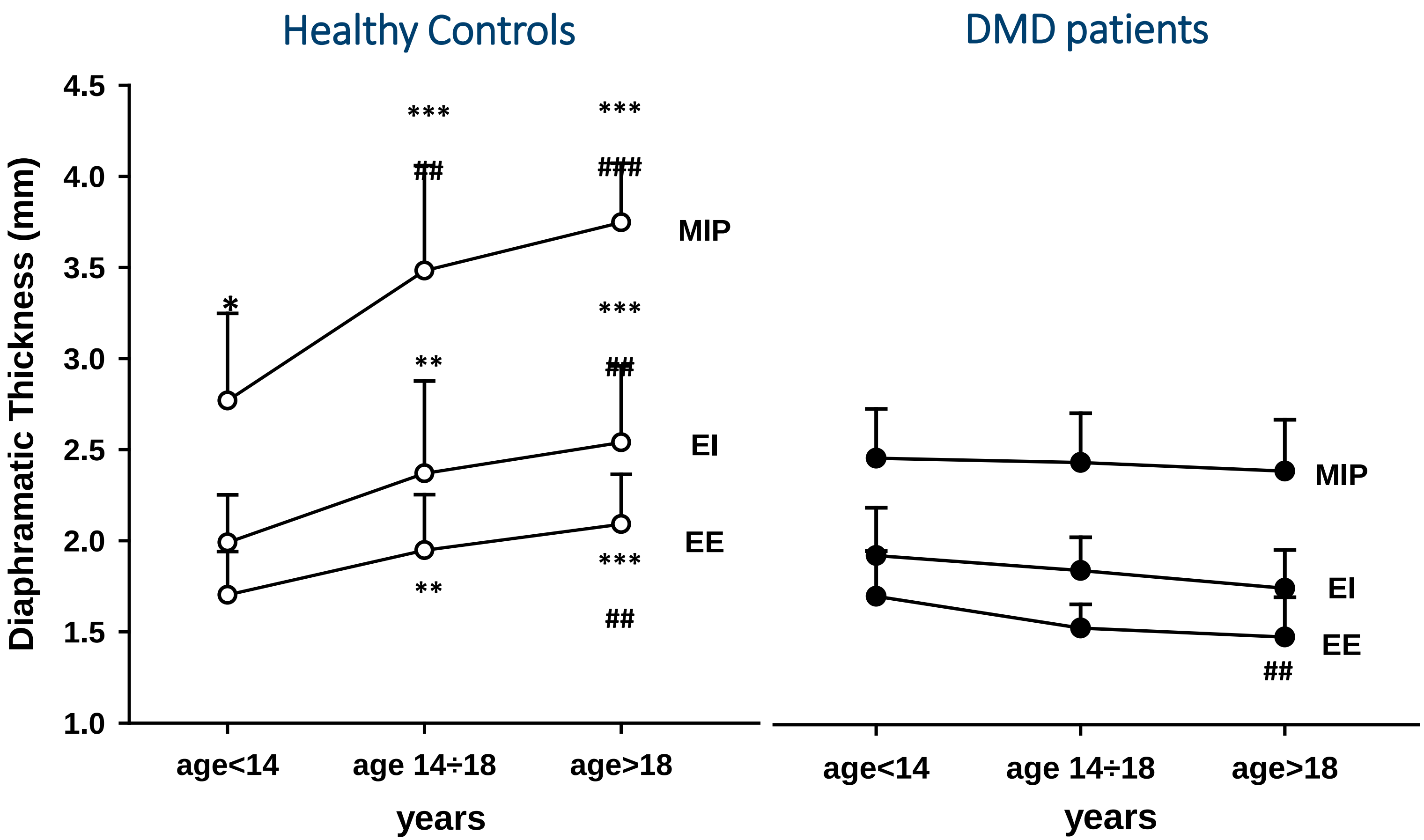


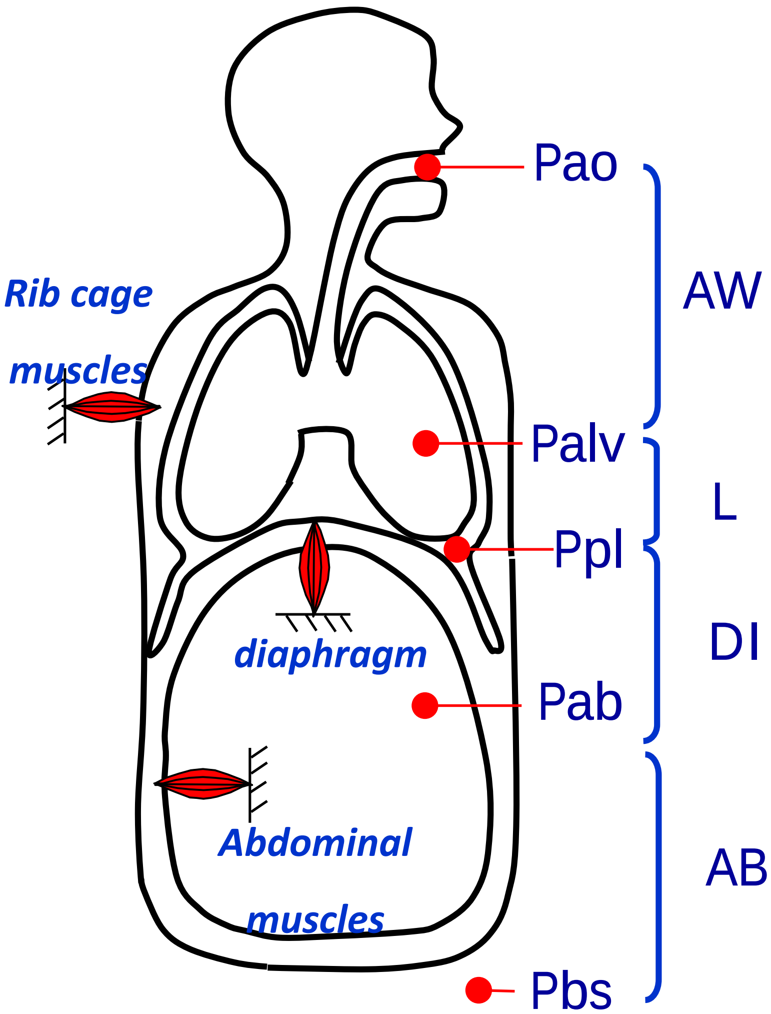
Aliverti, *J Appl Physiol* 2003

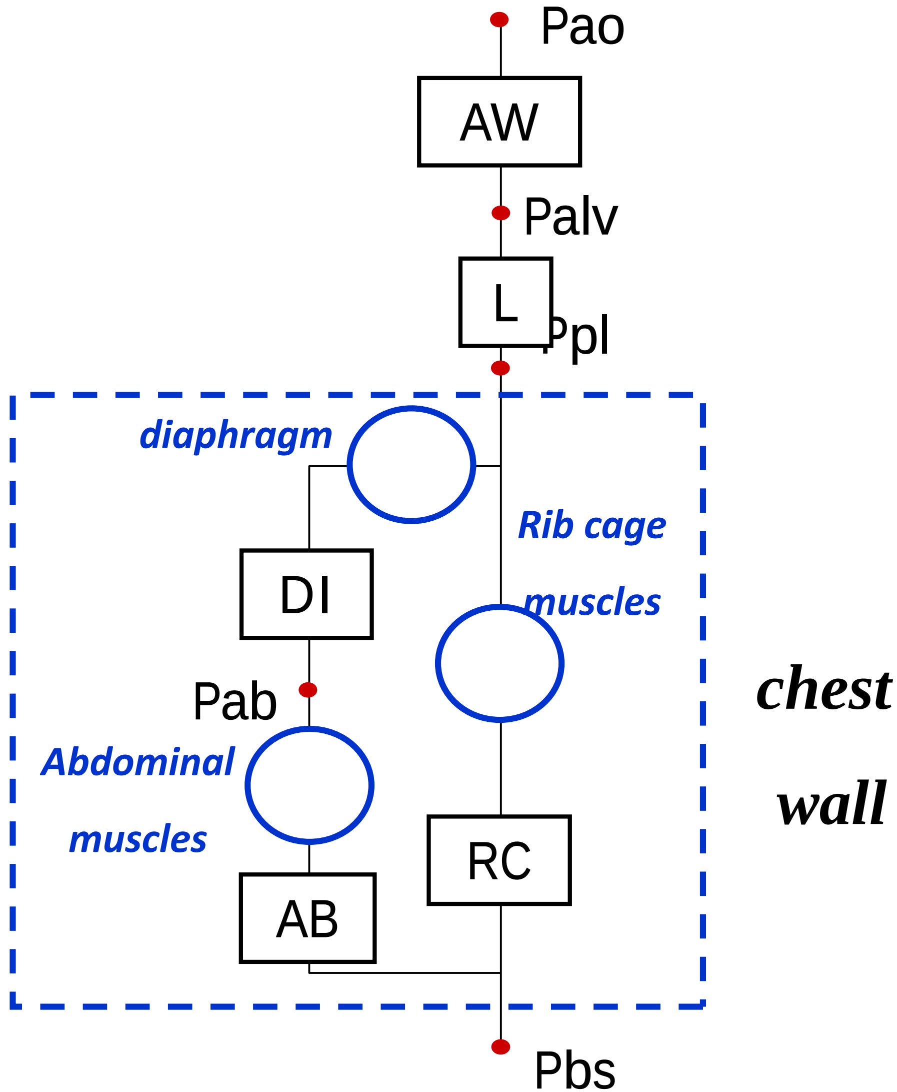
**Displacement of diaphragm dome**

Boussuges *Chest* 2009

# Diaphragm thickness is reduced in DMD




Rib cage
muscles
Pao
Palv
Ppl
Pab
Pbs
AW
L
DI
AB
diaphragm
Abdominal
muscles


Pao
AW
Palv
L
Ppl
diaphragm
Rib cage
muscles
DI
Pab
Abdominal
muscles
RC
AB
Pbs
chest
wall

# Measurement of chest wall displacement

“Chest wall = all parts of the body outside the lung which share changes in the volume of the lungs“

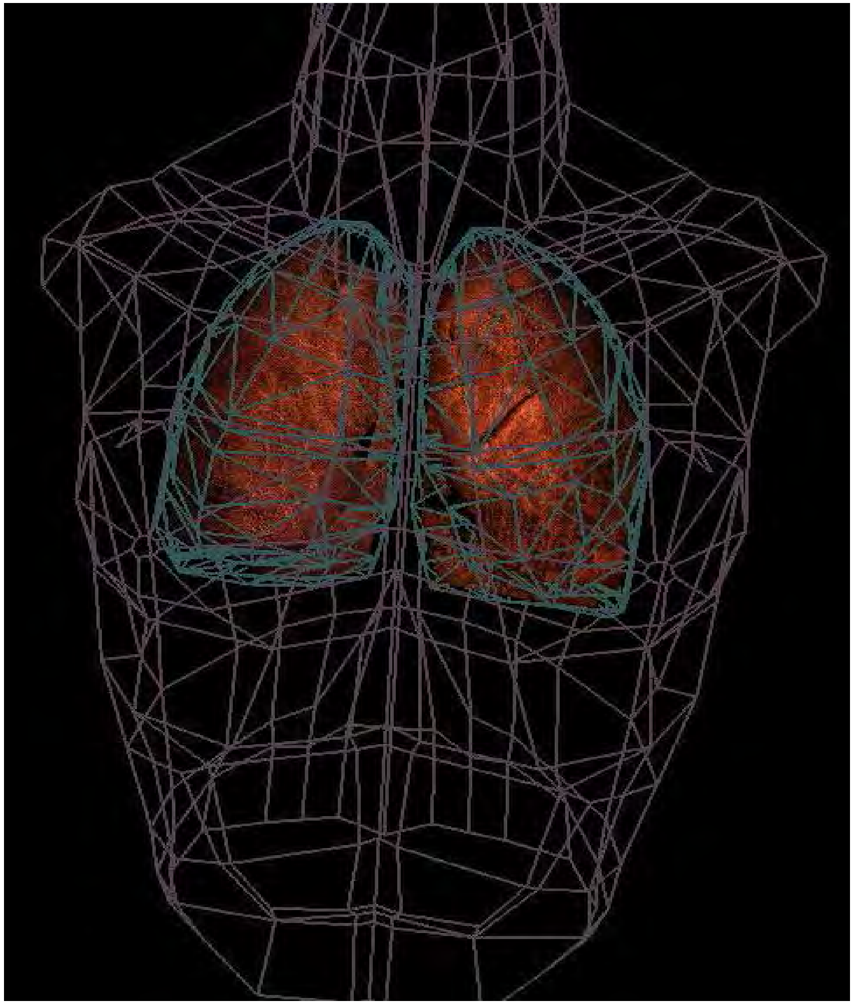
*(Konno and Mead, J Appl Physiol, 22:407-422, 1967)*

During breathing, chest wall varies not only volume, but also <u>shape</u>

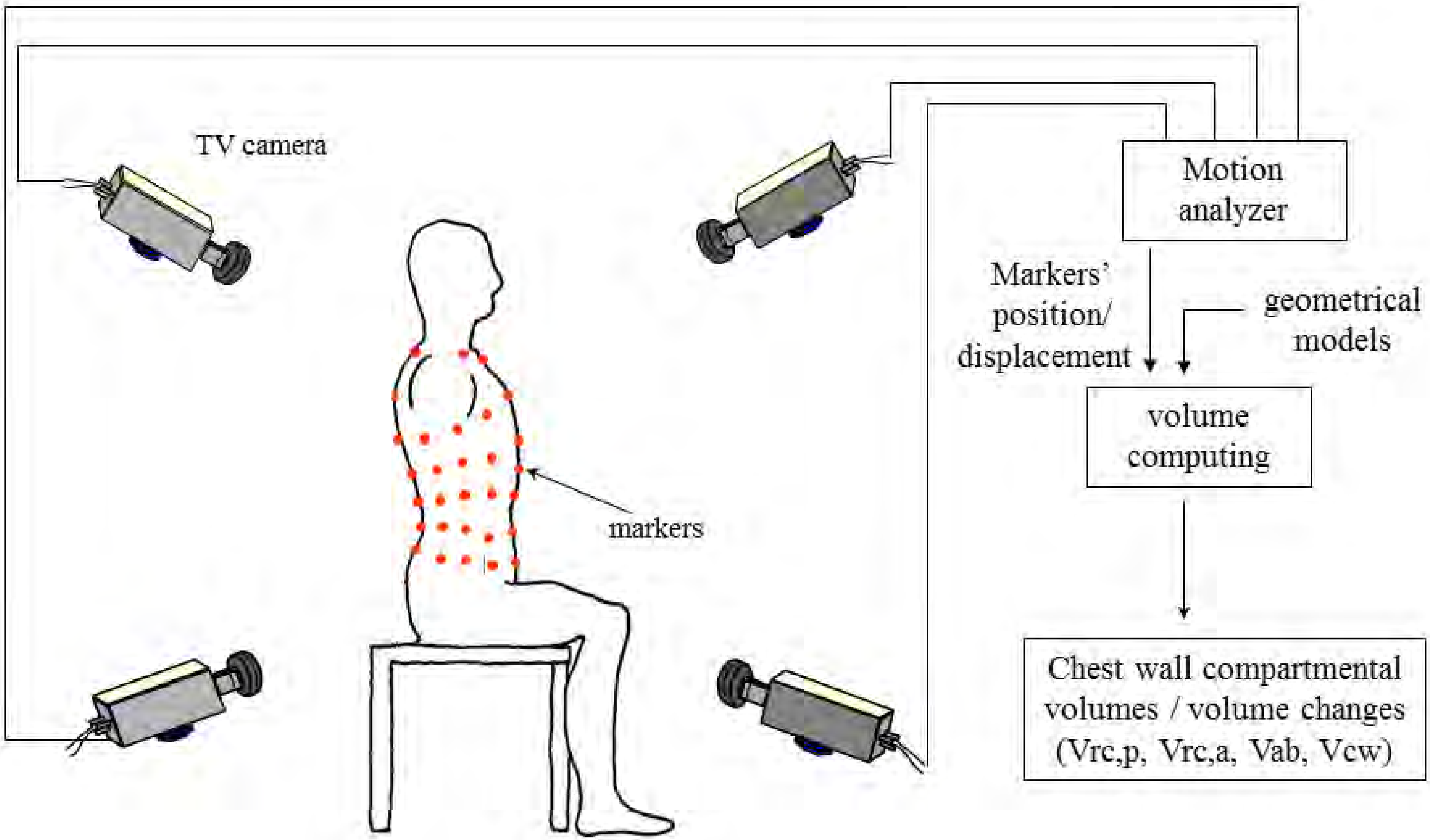
⇒ Measurement has to be done in several points of the thoraco-abdominal wall

Where ?

How any “degrees of freedom” does chest wall have during breathing?

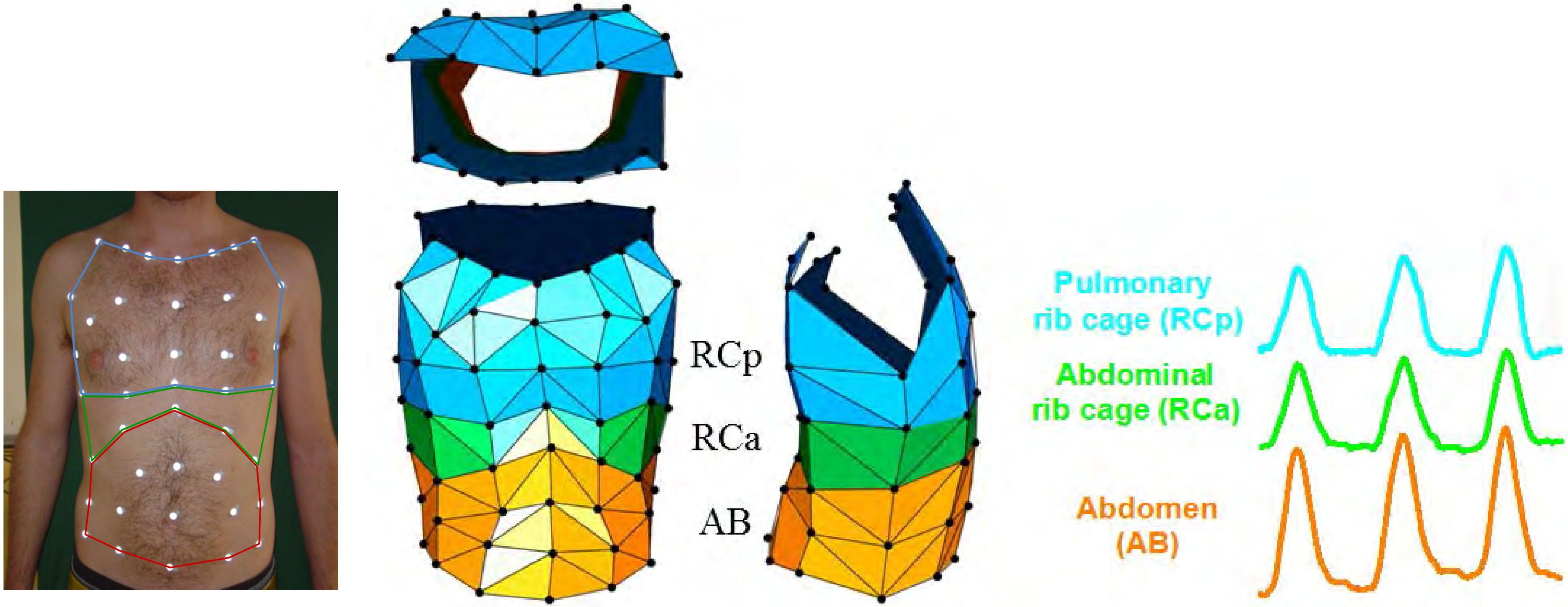


# Opto-Electronic Plethysmography: from respiratory movements to volume computation

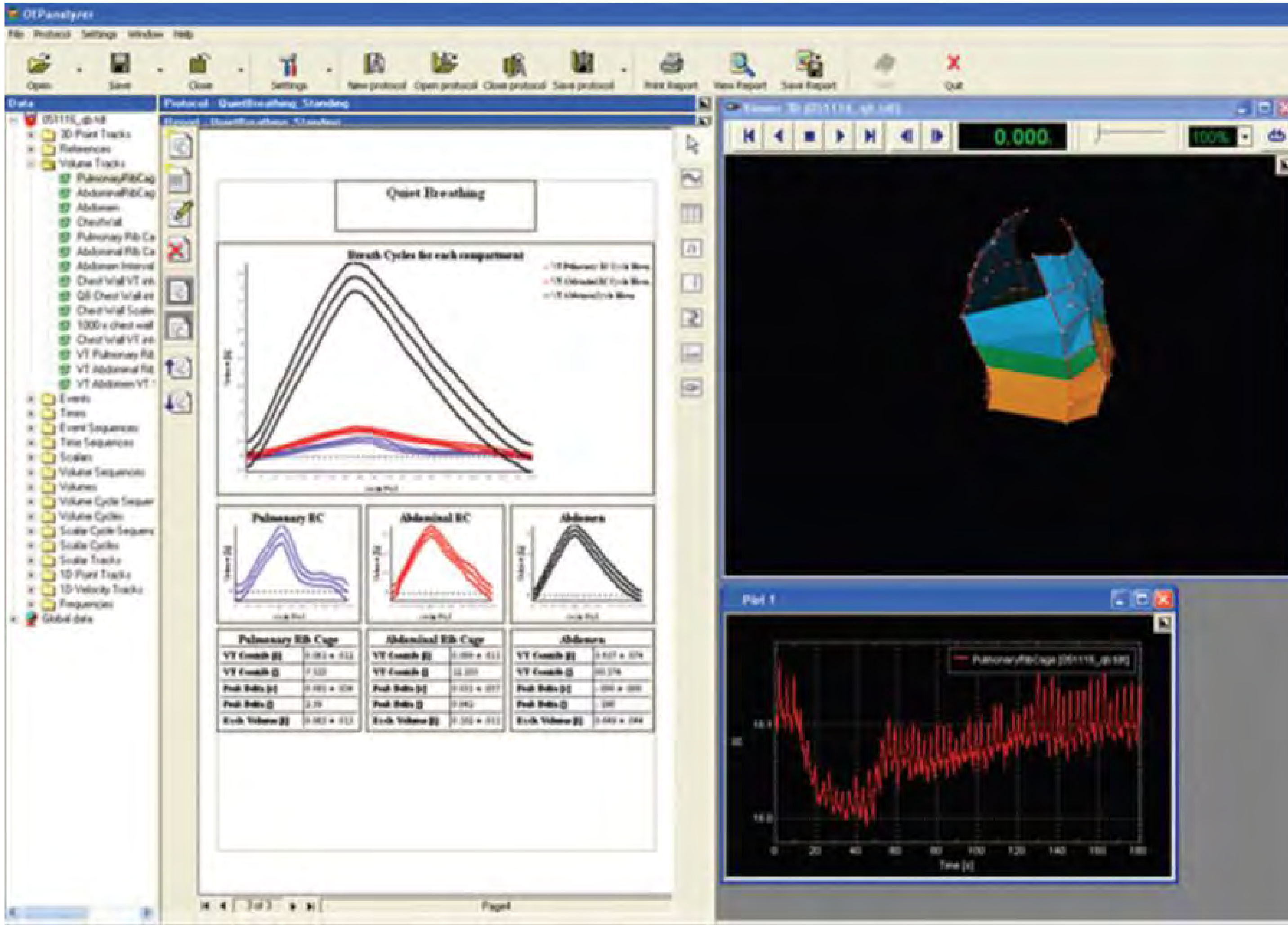



Cala et al, J Appl Physiol, 1996
Aliverti et al, Am J Resp Crit Care Med, 2001
Romei et al, Resp Physiol Neurobiol, 2010

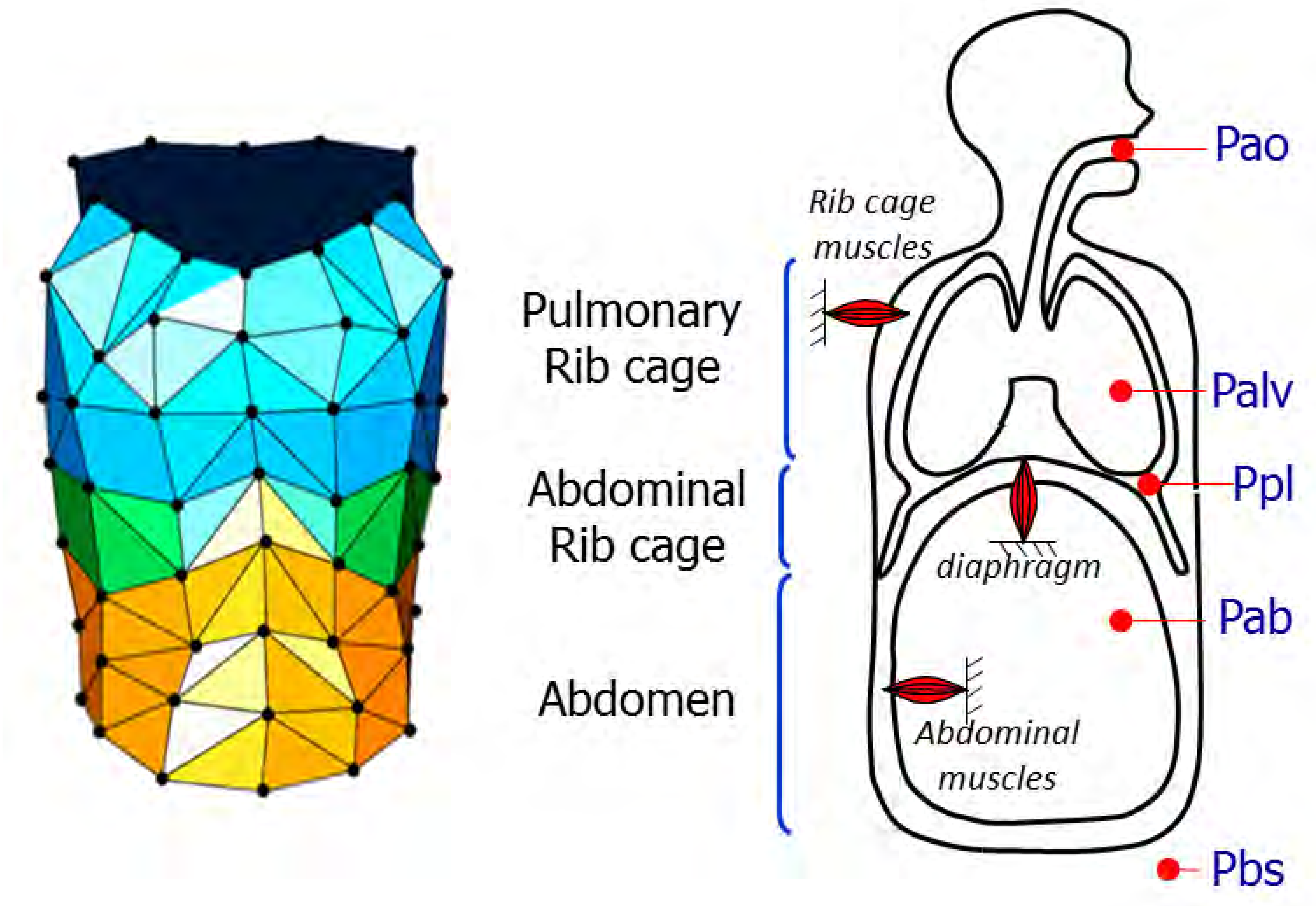
# Opto-Electronic Plethysmography: compartmental volumes



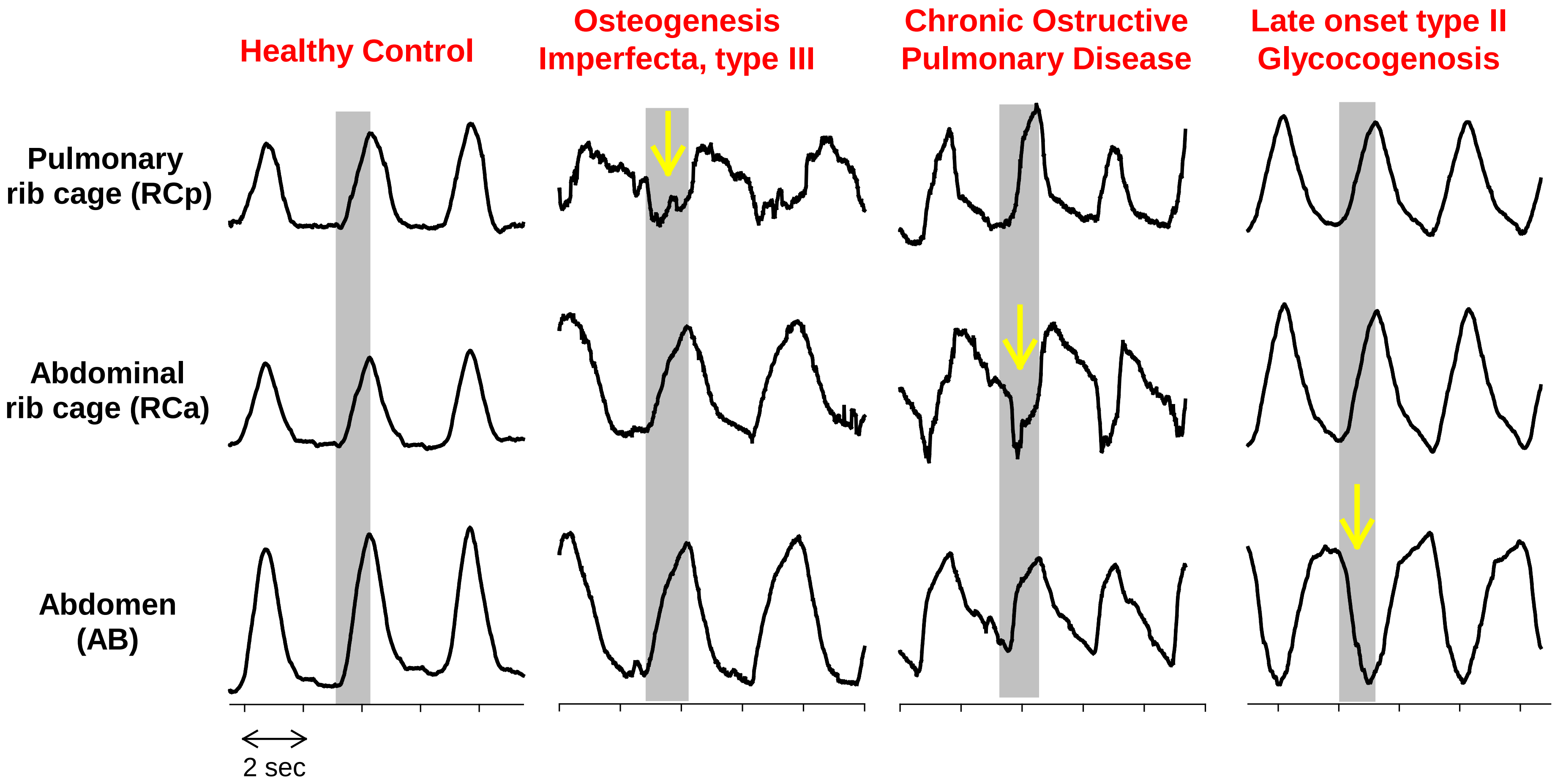
# Opto-Electronic Plethysmography



# Assessment of respiratory musce action from thoraco-abdominal kinematics

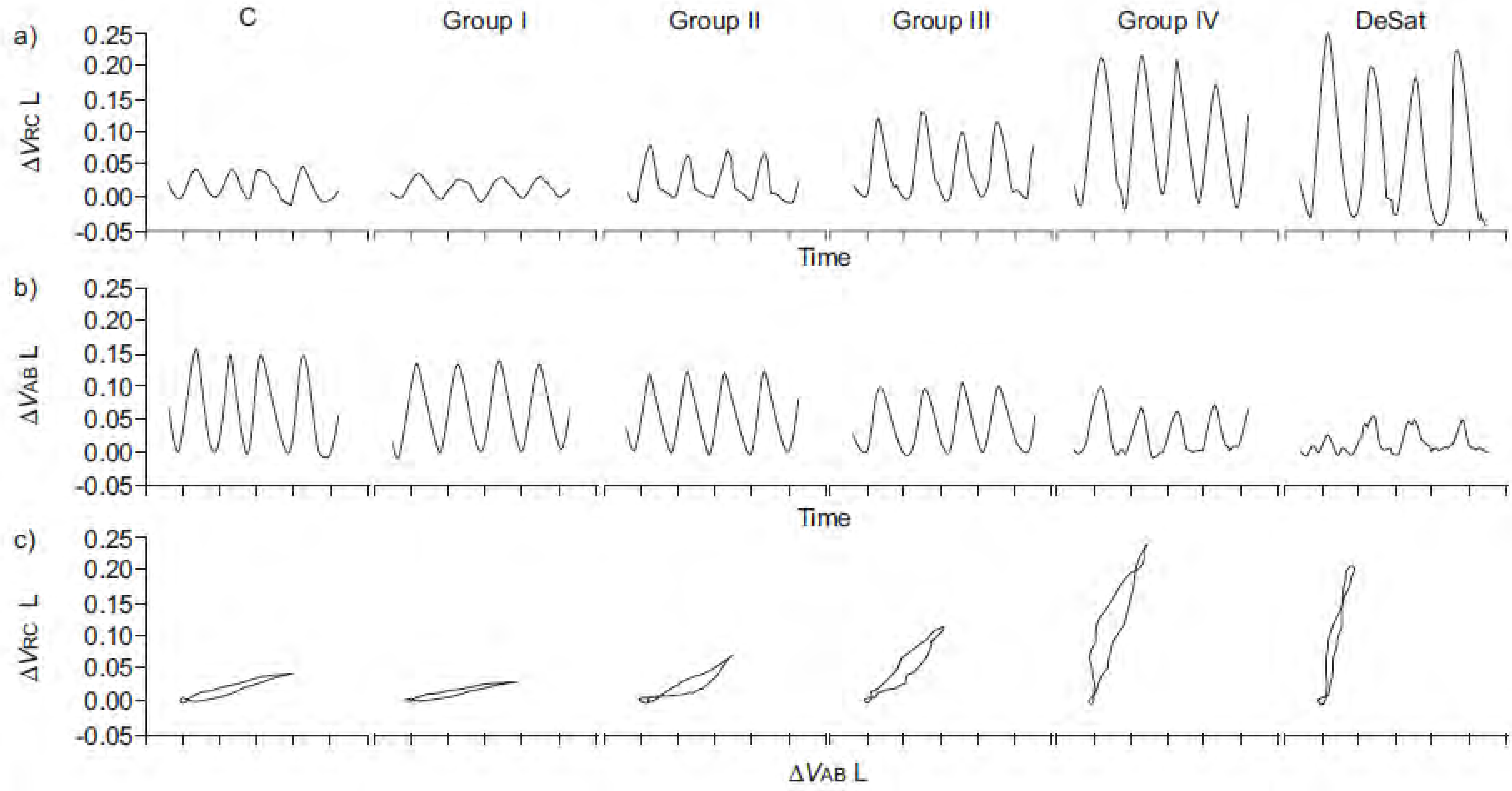


# Asynchronies among the different thoraco-abdominal compartments reflect respiratory muscles uncoordinated action



# Abdominal volume contribution to tidal volume is an early indicator of diaphragm impairment in DMD

*Eur Respir J, 2010*



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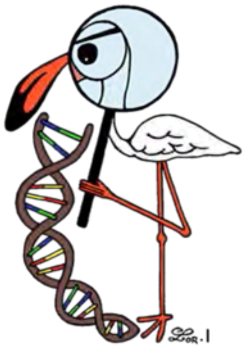
journal homepage: www.elsevier.com/locate/jns

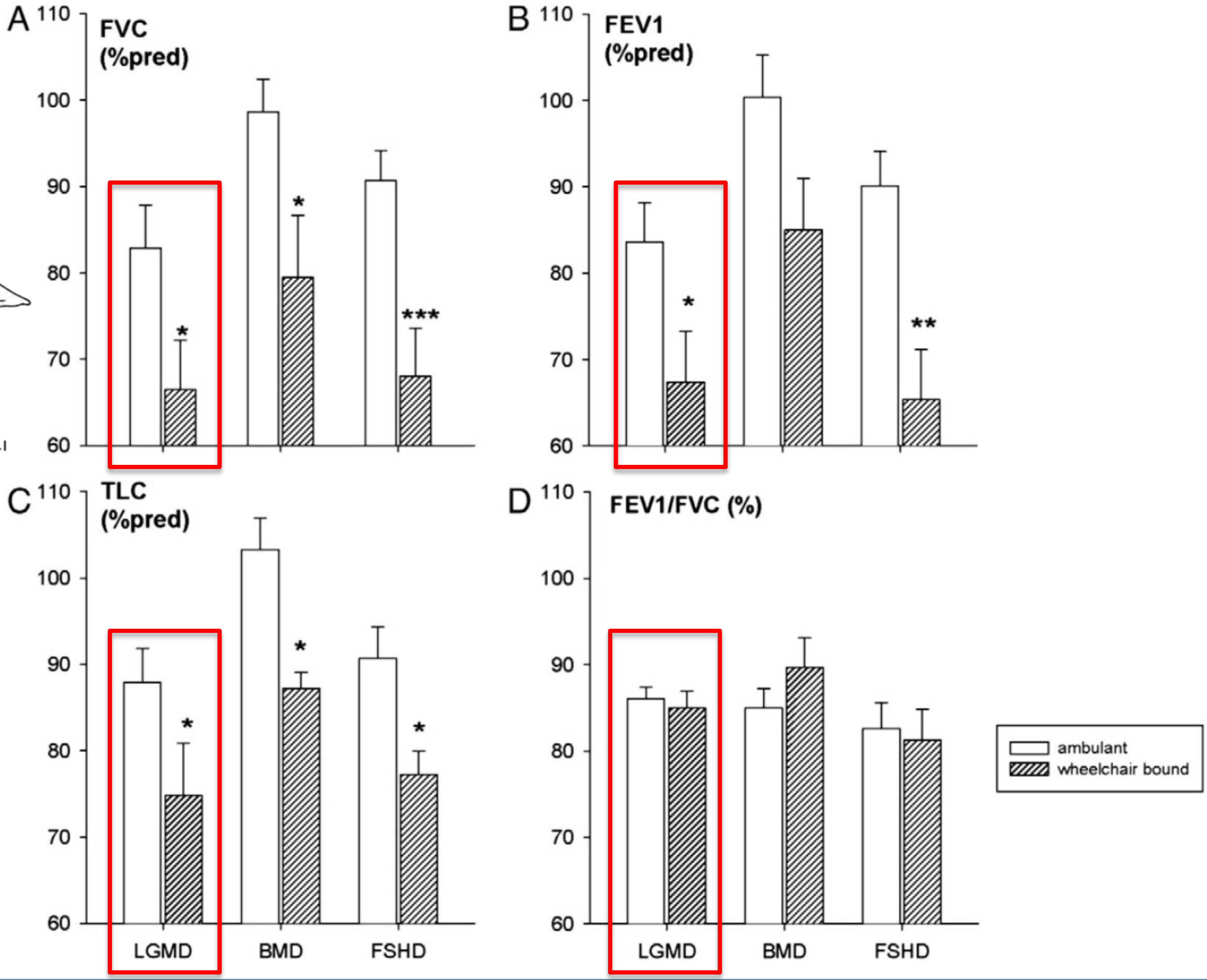
# Respiratory pattern in an adult population of dystrophic patients

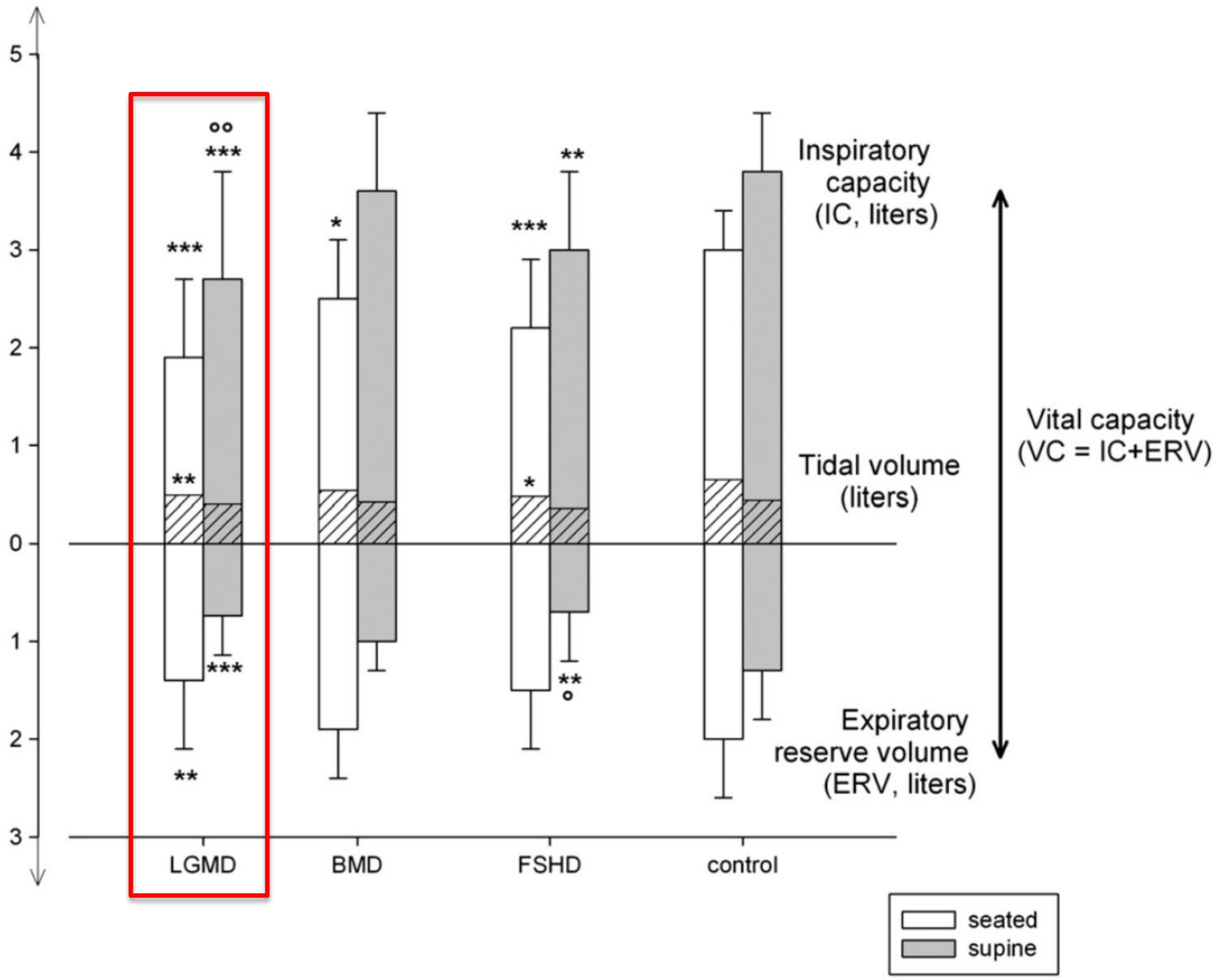
M.G. D'Angelo [a,*,1], M. Romei [a,1], A. Lo Mauro [b], E. Marchi [c], S. Gandossini [a], S. Bonato [a], G.P. Comi [d], F. Magri [d], A.C. Turconi [a], A. Pedotti [b], N. Bresolin [a,d], A. Aliverti [b]

[a] IRCCS E.Medea, Bosisio Parini, Lc, Italy
[b] TBM Lab, Dipartimento di Bioingegneria, Politecnico di Milano, Milano, Italy
[c] IRCCS INRCA Casatenovo, Lc, Italy
[d] Dino Ferrari Centre, Department of Neurological Sciences, University of Milan, I.R.C.C.S. Foundation Cà Granda, Ospedale Maggiore Policlinico, Milano, Italy

| | | N | Sex f:female m:male | Age(years) | Weight (kg) | Height (cm) | Disease duration (years) | Onset (years) | AMS |
|---|---|---|---|---|---|---|---|---|---|
| LGMD | All | 38 | 17 f, 21 m | 37.6 ± 12.5 | 64.6 ± 16.3 | 168.8 ± 8.4 | 18.5 ± 8.3 | 19.1 ± 11.4 | 4.5 ± 1.3 |
| | A | 24 | 10 f, 14 m | 36.2 ± 10.7 | 63.0 ± 12.0 | 168.5 ± 8.7 | 15.6 ± 7.3 | 20.7 ± 11.5 | 5.1 ± 1.0 |
| | W | 14 | 7 f, 7 m | 39.9 ± 15.2 | 67.4 ± 22.1 | 169.4 ± 8.0 | 23.5 ± 7.9 | 16.4 ± 11.3 | 3.3 ± 1.1 |
| BMD | All | 20 | 20 m | 32.7 ± 12.2 | 66.1 ± 8.9 | 170.7 ± 6.2 | 16.0 ± 7.3 | 16.8 ± 11.1 | 5.8 ± 1.9 |
| | A | 16 | 16 m | 32.1 ± 12.6 | 66.6 ± 9.3 | 170.6 ± 6.3 | 14.0 ± 5.8 | 18.1 ± 12 | 6.5 ± 1.5 |
| | W | 4 | 4 m | 35.5 ± 11.4 | 64.5 ± 8.2 | 171.5 ± 7.0 | 24.0 ± 7.6 | 12.0 ± 4.3 | 3.2 ± 1.1 |
| FSHD | All | 30 | 14 f, 16 m | 43.7 ± 17.5 | 70.5 ± 13.3 | 169.8 ± 9.1 | 18.9 ± 12.6 | 24.5 ± 15.8 | 5.1 ± 2.4 |
| | A | 20 | 9 f, 11 m | 45.2 ± 17.3 | 72.8 ± 13.2 | 169.9 ± 9.2 | 16.8 ± 13.7 | 27.9 ± 16.9 | 6.3 ± 1.8 |
| | W | 10 | 5 f, 5 m | 40.7 ± 18.3 | 65.8 ± 12.9 | 169.6 ± 9.3 | 23.1 ± 9.4 | 17.7 ± 11.3 | 2.9 ± 1.7 |
| CG | All | 20 | 6 f, 14 m | 32.7 ± 9.3 | 71.1 ± 14.6 | 174.9 ± 7.6 | | | |




A
FVC
(%pred)
B
FEV1
(%pred)
C
TLC
(%pred)
D
FEV1/FVC (%)
110
100
90
80
70
60
*
***
**
LGMD
BMD
FSHD
ambulant
wheelchair bound



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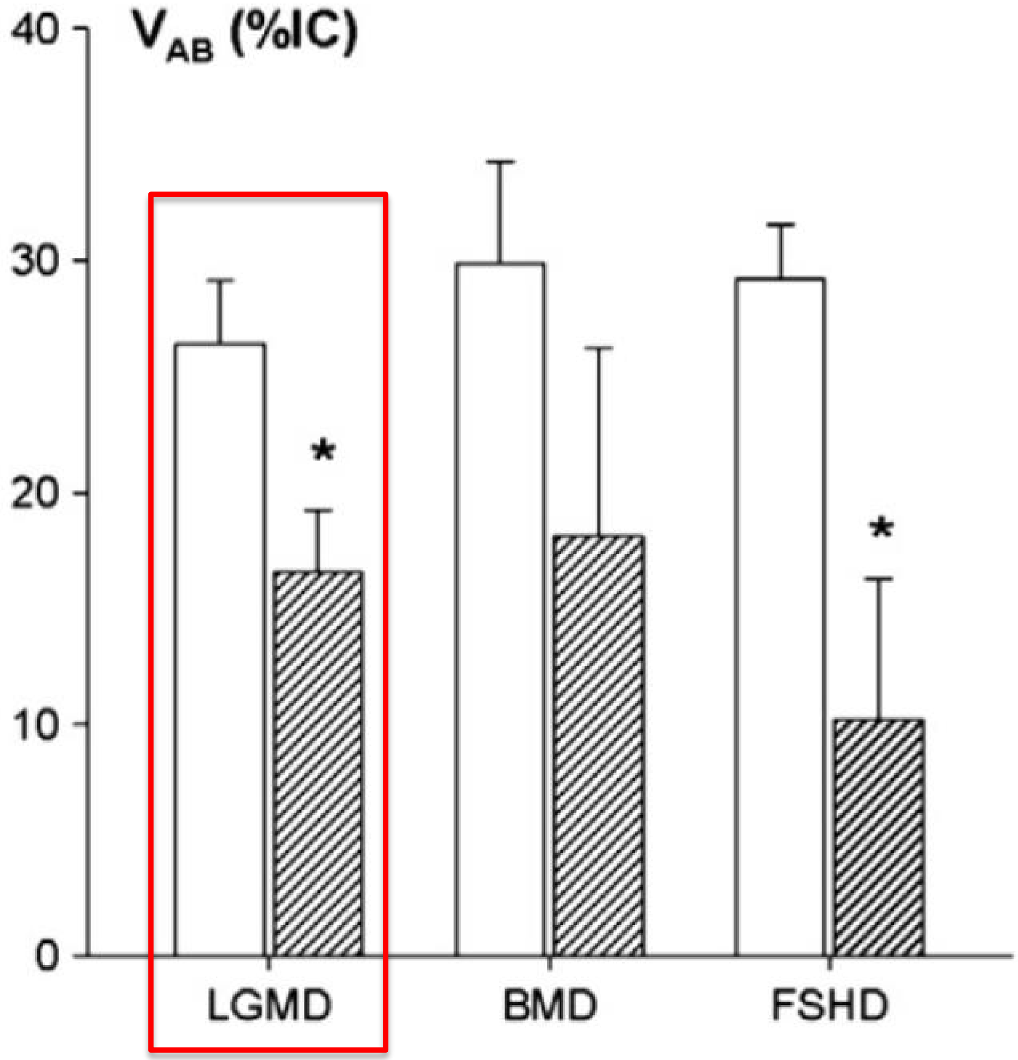
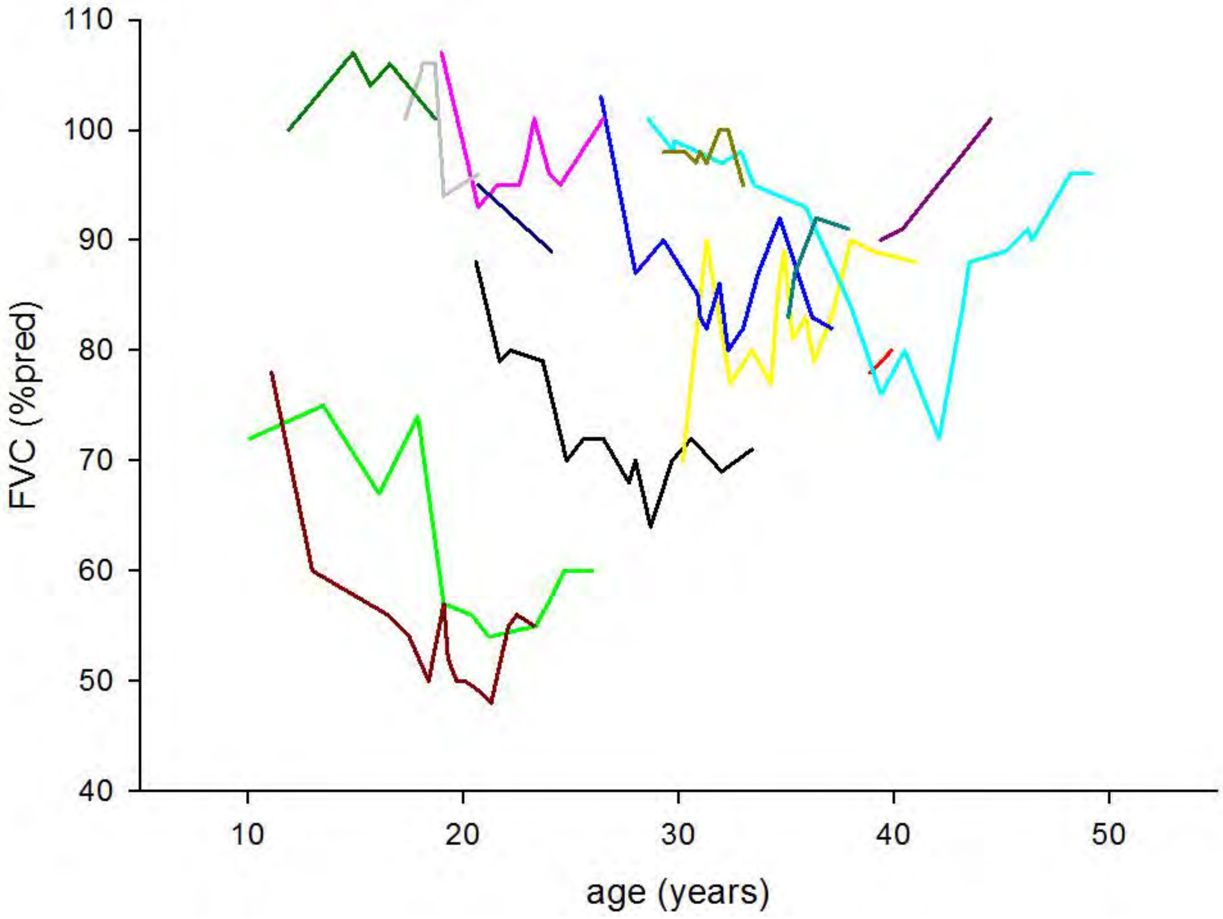
o
Inspiratory capacity (IC, liters)
Tidal volume (liters)
Expiratory reserve volume (ERV, liters)
Vital capacity (VC = IC+ERV)
LGMD
BMD
FSHD
control
seated
supine



$V_{AB}$ (%IC)
40
30
20
10
0
*
*
LGMD
BMD
FSHD

# Progression of FVC in LGMD2A



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D'Angelo MG, Romei M, Lo Mauro A, Marchi E, Gandossini S, Bonato S, Comi GP, Magri F, Turconi AC, Pedotti A, Bresolin N, Aliverti A. **Respiratory pattern in an adult population of dystrophic patients.** J Neurol Sci. 2011;306(1-2):54-61.

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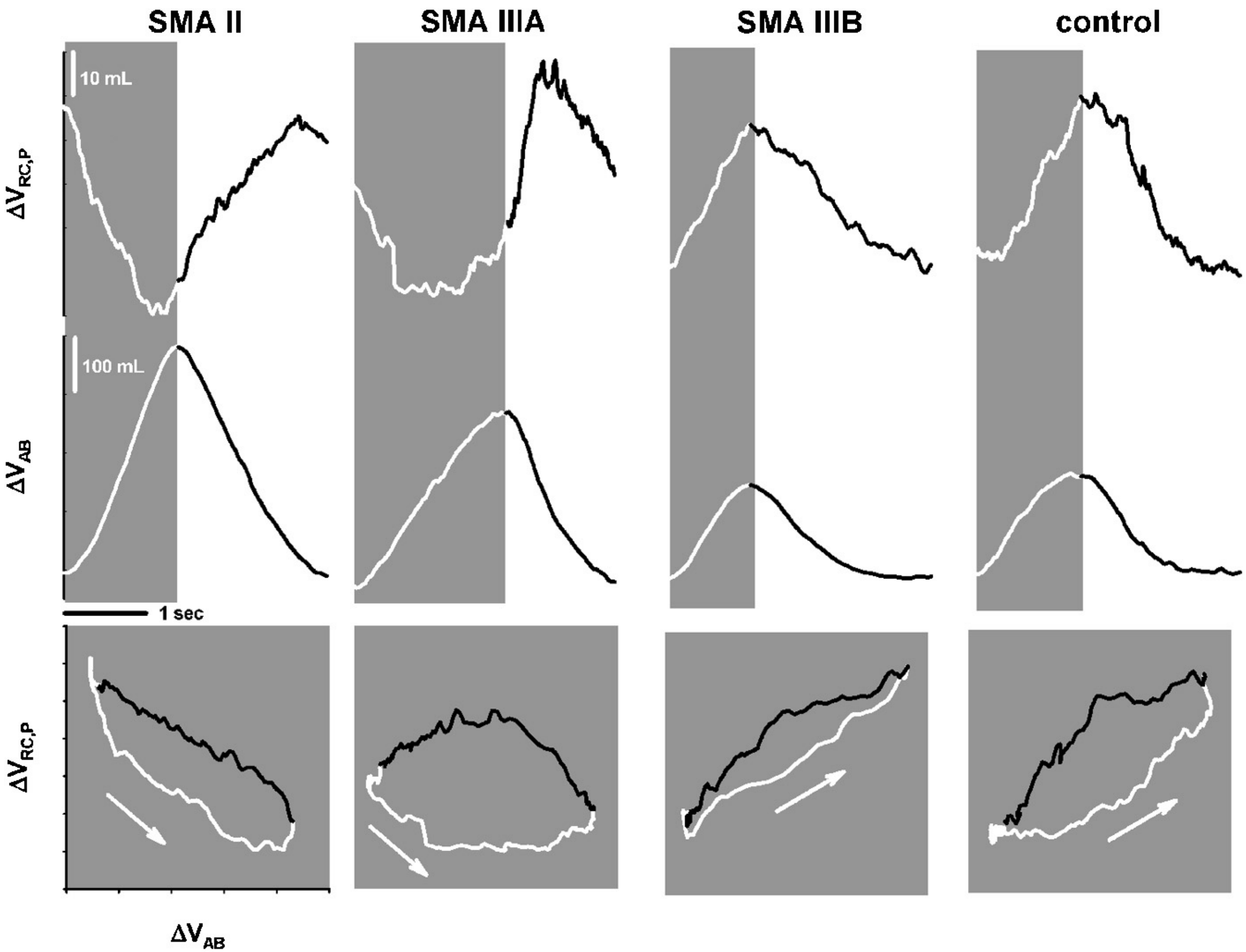
Lo Mauro A, D'Angelo MG, Romei M, Motta F, Colombo D, Comi GP, Pedotti A, Marchi E, Turconi AC, Bresolin N, Aliverti A. **Abdominal volume contribution to tidal volume as an early indicator of respiratory impairment in Duchenne muscular dystrophy.** Eur Respir J. 2010;35(5):1118-25.

# Alterations of thoraco-abdominal volumes and asynchronies in patients with Spinal Muscle Atrophy

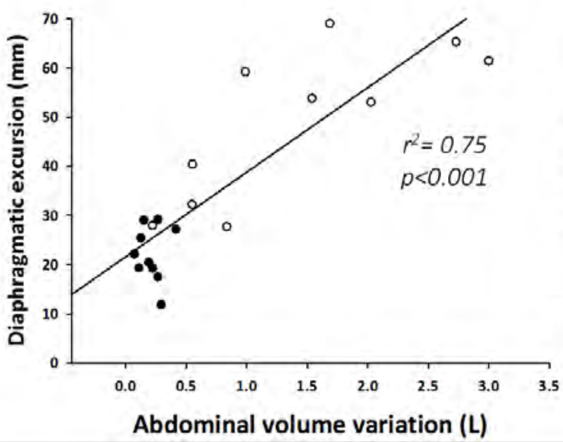
*Resp Physiol Neurobiol, 2014*

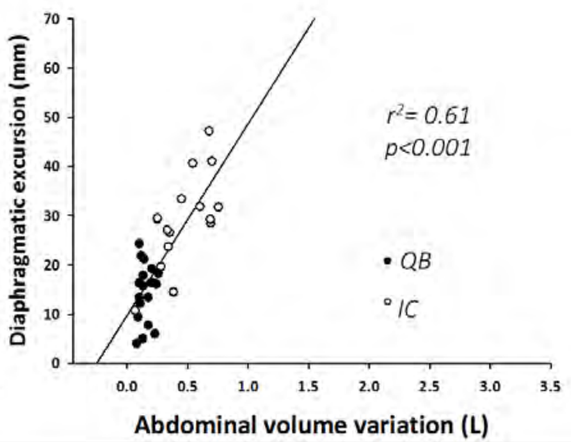


# Relationship between diaphragm excursion / thickness and abdominal volume variations

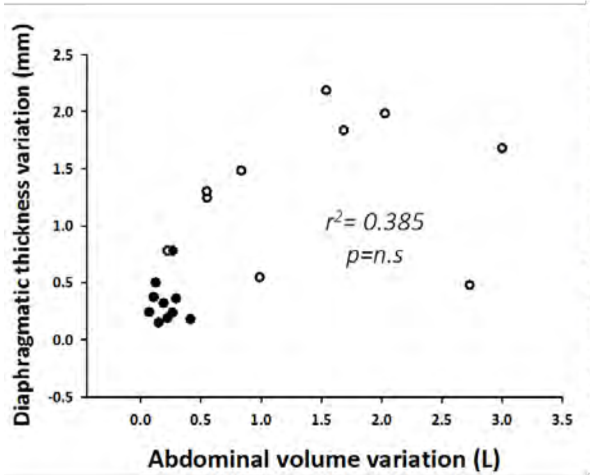
Healthy Controls

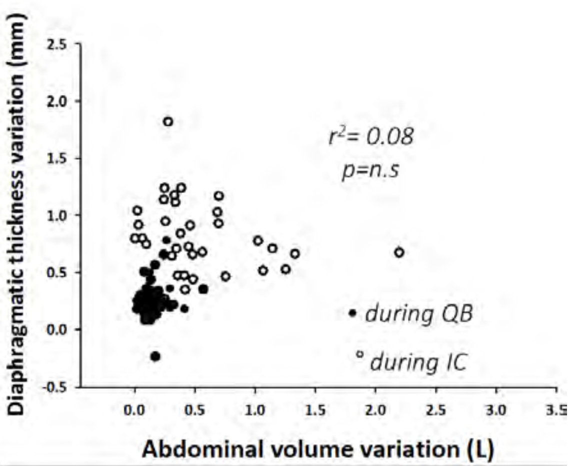
DMD patients




**Diaphragm excursion** is linearly correlated to abdominal volume variations

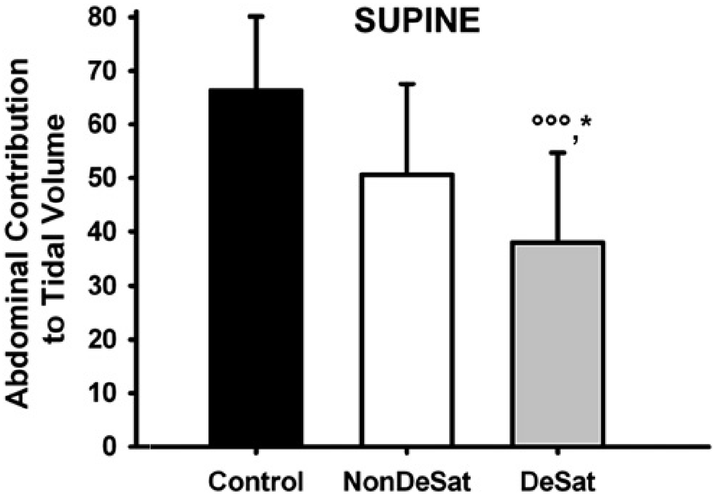


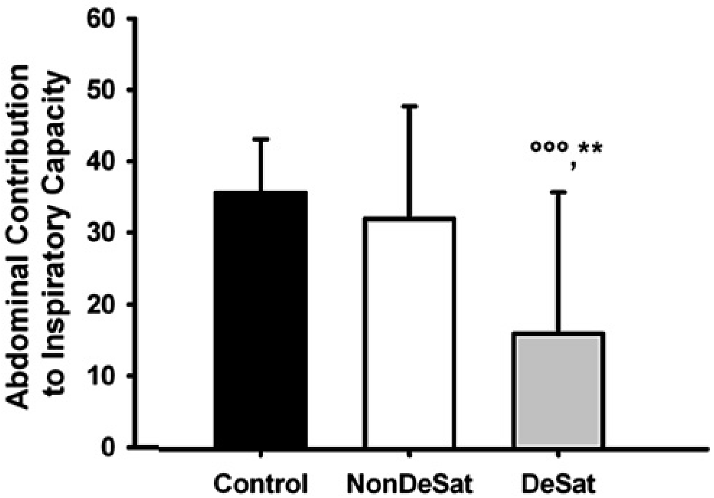



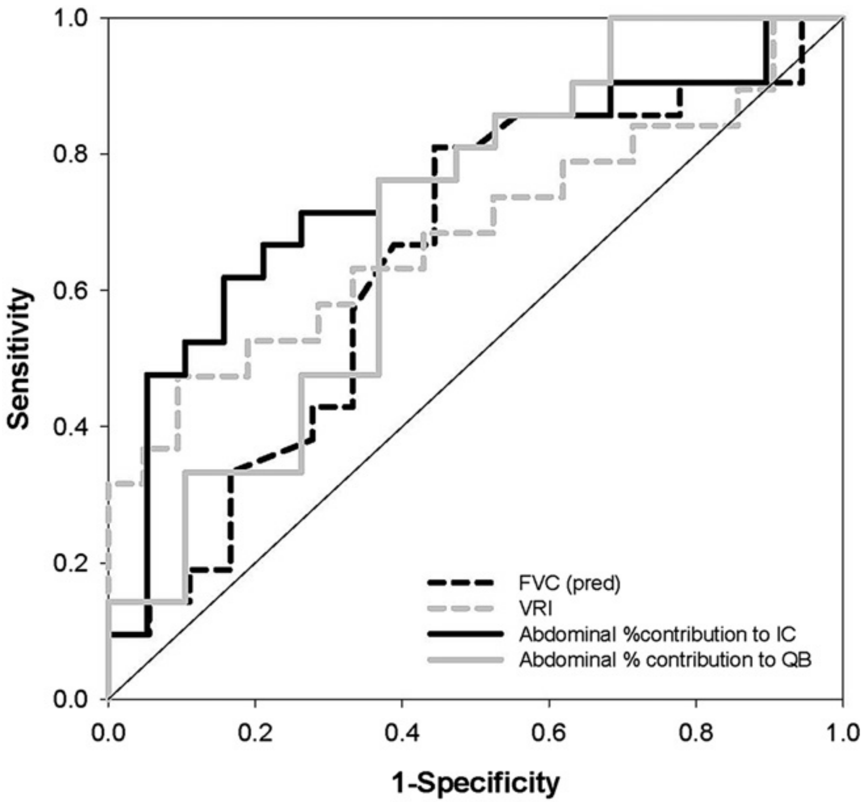

**Diaphragm thickness** is NOT correlated to abdominal volume variations

# Low abdominal contribution to breathing is a daytime predictor of nocturnal desaturation in adolescents and young adults with Duchenne Muscular Dystrophy

*Respir Med, 2012*



# Low abdominal contribution to breathing is a very good predictor of cough inefficiency in young adults with DMD

***Pediatr Pulmonol, 2014***