EIT during Mechanical Ventilation Lorentz Center, Leiden, Netherlands 23 Apr 2024

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### EIT: perfusion and V/Q

### Outline

- Definitions
- Measurement of Perfusion
  - Contrast-agent approaches
  - Pulsatility-based approaches
  - Review
  - Issues
- Measurement of V/Q
  - Review
  - Issues
- Open questions
- Pathways forward

### The elephant in the room



<sup>1</sup>openclipart.org/detail/17810/cartoon-elephant



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<sup>&</sup>lt;sup>2</sup>en.wikipedia.org/wiki/Volumetric\_flow\_rate



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- $V \triangleq Air Volume$
- $Q \triangleq$  Blood Flow

<sup>&</sup>lt;sup>2</sup>en.wikipedia.org/wiki/Volumetric\_flow\_rate

$$\frac{\text{ventilation}}{\text{perfusion}} = \frac{\text{air flow } [\frac{\text{mL}}{\text{min}}]}{\text{blood flow } [\frac{\text{mL}}{\text{min}}]} = \frac{\frac{d}{dt}\text{Volume air}}{\frac{d}{dt}\text{Volume blood}} = \frac{\frac{dV_{\text{air}}}{dt}}{\frac{dV_{\text{blood}}}{dt}} = \frac{\dot{V}}{Q}$$

- $V \triangleq$  Air Volume so the air flow is  $\frac{d}{dt}V = \dot{V}$
- $Q \triangleq$  Blood Flow

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In engineering literature<sup>2</sup> Volumetric Flow rate symbols:  $Q, \dot{V}$ 

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• 
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$$V \triangleq$$
 Air Volume – so the air flow is  $\frac{d}{dt}V = \dot{V}$  –

•  $Q \triangleq$  Blood Flow – so the symbol is Q In engineering literature<sup>2</sup> *Volumetric Flow rate* symbols:  $Q, \dot{V}$  With dot

<sup>&</sup>lt;sup>2</sup>en.wikipedia.org/wiki/Volumetric\_flow\_rate

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• 
$$V \triangleq$$
 Air Volume – so the air flow is  $\frac{d}{dt}V =$ 

•  $Q \triangleq$  Blood Flow – so the symbol is Q  $\longrightarrow$  Without dot In engineering literature<sup>2</sup> *Volumetric Flow rate* symbols:  $Q, \dot{V}$ 

With dot

Ŵ

<sup>&</sup>lt;sup>2</sup>en.wikipedia.org/wiki/Volumetric\_flow\_rate

### How to write V

- Word type "V0307" and press "Alt-X"
- HTML type "V̇" (V with Combining Dot Above)
- Latex (text) \.{V}
- Latex (math) \$\dot{V}\$
- Google docs Add equation "\dot{V}" or cut and paste from Internet

Rant: Journals often mess up  $\dot{V}$ . A carefully submitted paper with correct symbols turns into a mess on their websites.

### Part A – Contrast-agent based techniques

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<sup>&</sup>lt;sup>3</sup>makeitgrateful.com/living/celebrate/halloween

#### Regional Lung Perfusion as Determined by Electrical Impedance Tomography in Comparison With Electron Beam CT Imaging

Inéz Frerichs\*, José Hinz, Peter Herrmann, Gerald Weisser, Günter Hahn, Michael Quintel, and Gerhard Hellige

### EIT contrast agents



Fig. 1. Load time-impedance (ix) fel-band diagrams) and time-density curves (four right-hand diagrams) in pie [4 during bolns administration of the hypertosite sating solution and the indigraphic contrast material, respectively. The black crosses in the dosara legistics of the right and left maps in the functional EIT mages of lang ventilation and in the ERCT images (top) indicate the pixel locations at which the data were obtained. Three drawings of the lumps in the functional EIT mages position of the Swame-function and the term of the data drawing the data drawing of the lumps have administred either through the data (upper drawing) or the poximal opening of the catheter with the ballows at the tip of the catheter being inflated (middle mixing) or deflated (lower drawing). The ERCT measurement during the centure verso block administration with deflates ballow were not performed in this animal.

<sup>4</sup>Frerichs *et al* (2002) Regional lung perfusion as determined diversity drawing) we have a state of the diversity of the dintegrel diversity of the diver

<sup>5</sup>McArdle *et al* (1988) An assessment of dynamic images by applied potential tomography for monitoring pulmonary perfusion Clin Phys Physiol Meas 9:87

Adler, EIT: perfusion and V/Q...



#### Measurement of Ground-Water Parameters Using Salt-Water Injection and Surface Resistivity

#### Paul A. White

First published: March 1988 | https://doi.org/10.1111/j.1745-6584.1988.tb00381.x | Citations: 50

ERT contrast agents





Fig. 4. Resistivity change showing the direction and velocity of salt-water flow over a four-hour period after injection using the array arrangement in Figure 2A. Data are from a Rakaia River bed site, South Island, New Zealand.

<sup>6</sup>PA White (1988) "Measurement of Ground-Water Parameters Using Salt-Water Injection and Surface Resistivity", Groundwater: 26:179–186



<sup>&</sup>lt;sup>7</sup>Larrabee *et al* (2023) Am J Physiol: Lung 325:L638–L646



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<sup>&</sup>lt;sup>7</sup>Larrabee *et al* (2023) Am J Physiol: Lung 325:L638–L646

### Perfusion with EIT – Features



- Visualize Anatomy: LV  $\rightarrow$  Lungs  $\rightarrow$  RH
- Signals are fairly large (w.r.t. ventilation)
- Injection must be
  - Rapid
  - Near the heart

### Perfusion with EIT – Filtering effect



- Unfiltered signal shows large cardiogenic changes Perfusion signal is  $\approx 5 \times$  pulsatility
- Bolus: 10 mL of 7.2 % NaCl in  $\approx$ 55 kg pig Conductivity of Saline:  $\approx$ 1.5 S/m/[% saline] Cardiac Ouptut in 2 s =  $\approx$ 100 mL  $\Delta \sigma_{blood} = 7.2 \% \times 0.1 \times 1.5 = 1.1$  S/m compared to  $\sigma_{blood} = 0.65$  S/m (<sup>8</sup>)

<sup>&</sup>lt;sup>8</sup>itis.swiss/virtual-population/tissue-properties

### Indicator Dilution – Theory







### Indicator Dilution: Requirements

Dilution indicator types

- *Diffusible*: will leak out of the capillaries Tend to overestimate cardiac output
- *Non-diffusible*: is retained in the vascular system for a time. Tend to underestimate cardiac output

Requirements	EIT & NaCl	
Measurable (detectable)	$\checkmark$	
Inert	$\checkmark$	(mostly)
Biocompatible (harmless)	$\checkmark$	(mostly)
Stays intravascular	X	(main issue)
and does not leak into tissue spaces		
Economical	$\checkmark$	

### Inert & Biocompatible

• Amounts are small

- the 2300 mg recommended daily Na intake of the American Heart Association corresponds to 23 boluses of 10 mL of 3% saline.

- safety
  - osmotic demyelination syndrome?
  - A report of dropping BP in horses
- Highest concentration used in humans<sup>9</sup> is 10%

<sup>&</sup>lt;sup>9</sup>H He *et al* (2020) "Bedside evaluation of pulmonary embolism by saline contrast electrical impedance tomography method: a prospective observational study" Am J RCCM 202:1464–1468

### Partial-volume effects



<sup>10</sup>Borges *et al* (2012) Regional lung perfusion estimated by electrical impedance tomography in a piglet model of lung collapse J Appl Physiol 112:225–236

### Partial-volume effects: Analysis Tool

#### Select Lung and Heart Pixels



#### Fit gamma functions



<sup>11</sup>Stowe et al V/Q analysis with 3D EIT p. 25, Conf EIT 2023. available at EIDORS.org

# EIT-Perfusion and SPECT



Fig. 2. Regions of interest in healthy lungs. Regions of interest in healthy lungs for the perfusion analysis. Three situations were studied sequentially: bilateral lung ventilation (A), unilateral lung collapse (B; left lung atelectasis), and unilateral lung collapse (C) with sodium nitroprusside infusion.



Fig. 3. Regions of interest in injured lungs. Regions of interest in the piglets with acute lung injury. Three situations are represented sequentially: lung injury condition (A; dependent lung atelectasis), lung injury in conjunction with sodium nitroprusside infusion (B), and open lung condition after lung recruitment (C).

[<sup>12</sup>]

### **EIT Perfusion: Comments**

- Can this be an acceptable clinical technique: in humans? in animals?
- Cold saline? Water tempco  $-2\%/^{\circ}$ C, so 4  $^{\circ}$ C is 70% less conductive



**Figure 2:** EIT images of maximum signed voxel value for C) control, and S) forepaw stimulation. Region outlined in black is the S1 forepaw cortex. Coronal (top) and Saggital (bottom) slices shown.

<sup>&</sup>lt;sup>13</sup>Adler et al (2017) Cerebral perfusion imaging using EIT p. 44 Conf EIT 2017

### Part B – Pulsatility based techniques

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<sup>&</sup>lt;sup>14</sup>CC0 public domain

### Pulsatile signal in EIT data



<sup>&</sup>lt;sup>15</sup>Heinrich *et al* (2006) "Body and head position effects ..." Int Care Med, 32:1392–1398.



<sup>&</sup>lt;sup>16</sup> Frerichs *et al* (2003) Electrical Impedance Tomography – a method for monitoring regional lung aeration and tidal volume distribution? Int Care Med 29:2312–2316 Adler, *EIT: perfusion and V/Q...* 

### Origins of cardiosynchronous EIT signals



<sup>&</sup>lt;sup>17</sup>Adler et al (2017) "Origins of cardiosynchronous signals in EIT", Conf EIT2017, p73

### **Heart Motion**

- Simulations based on 4D MRI
- Heart motion/deformation is 56% of EIT signal
- Strong correlation motion blood flow
- However: ∆ with disease? ∆ with posture?



<sup>&</sup>lt;sup>18</sup>Proença *et al* (2015) Influence of heart motion on cardiac output estimation by means of electrical impedance tomography: a case study Physiol Meas 36:1175–1192.

### Flow-induced RBC orientation



• Effect should be important (20%)

Figure 2.7: Relative change in resistivity of human blood as a function of the reduced average velocity for different haematocrit values (Visser 1989)

Have never been able to see or reproduce

<sup>&</sup>lt;sup>19</sup>R L Gaw, The effect of red blood cell orientation on the electrical impedance of pulsatile blood with implications for impedance cardiography, PhD Thesis, Queensland University of Technology, 2010.

### Does EIT measure perfusion or pulsatility?

The EIT community debate in<sup>20</sup>:

- not all blood flow leads to ΔEIT signal
   e.g.blood flowing continuously through a capillary bed: No changes over time, no EIT signals variations.
- not all ΔEIT signal originate in blood flow.
   e.g. movement of the heart in the chest accounts for a large fraction of the signal, which will vary with the patient, posture, and electrode placement



<sup>20</sup> Frerichs *et al* (2017) "... TRanslational EIT developmeNt stuDy group" Thorax, 72:83–93

### Does EIT measure perfusion or pulsatility?

Pulsability seems to be a fairly good measure of perfusion <sup>21,22,23</sup>.

Clearly for *marketing* of EIT, it's best to say it measures perfusion.

Recommendation: perfusion-related EIT signal,

- scientifically accurate
- easy to understand for non EIT specialists.

<sup>&</sup>lt;sup>21</sup>Borges et al (2012) "Regional lung perfusion estimated by electrical impedance tomography in a piglet model of lung collapse" J Appl Physiol 112:225–236

<sup>&</sup>lt;sup>22</sup> Reifferscheid *et al* (2011) "Regional ventilation distribution determined by electrical impedance tomography: Reproducibility and effects of posture and chest plane" Respirology, 16:523–531

<sup>&</sup>lt;sup>23</sup>Stowe et al (2019) "Comparison of bolus- and filtering-based EIT measures of lung perfusion in an animal model" Physiol Meas, 40:054002

### Impedance Cardiography



- Easy to understand
- Stroke-volume correlates nicely

https://ispub.com/xml/journals/ija/vol11n2 (No longer available 8-( )

 Unfortunately: "poor correlation between ... invasive measurements of cardiac output, especially in heart failure ... limited data demonstrating any improved outcomes"<sup>24</sup>

<sup>&</sup>lt;sup>24</sup>Wang *et al* (2006) Impedance cardiography: More questions than answers 8:180–186

### Stroke-Volume with 3D EIT

• SV estimation ±15.2 mL (subject-specific calibration)

Fig 7. ECG-gated 3D EIT (end systole vs end diastole). One subject



Fig 5. 3D EIT [ L1 (highest) to L5 (lowest) ] of SD respiration – supine position.



<sup>25</sup>Braun et al (2018) Accuracy and Reliability of Noninvasive Stroke Volume Monitoring via ECG-Gated 3D Electrical Impedance Tomography in Healthy Volunteers PLoS One, 13:e0191870

[<sup>25</sup>]

### What is Pulsatility / Perfusion-related EIT good for?

- Timing of signals is useful
  - Stroke-volume variation
  - Pulse-Transit time —> Pulmonary-arterial pressure
- Need work to understand when reliable<sup>26</sup>
  - Waveform shape?
  - Waveform timing?



Figure 2: For each of the nine subjects (S1 to S9) we show: (Top) cardio-synchronous activity (CA) image as the pixel-wise temporal standard deviation of the EIT plane L2 with the lung ROI delineated in black. (Bottom) Spatial distribution of the pulmonary PAT in the lung ROI and on the same EIT plane with the five vertical segments separated by dashed red lines.

<sup>&</sup>lt;sup>26</sup>Stowe *et al* (2019) Comparison of bolus- and filtering-based EIT measures of lung perfusion in an animal model Physiol Meas, 40:054002
<sup>27</sup>Braun *et al* (2019) Distribution of Pulmonary Pulse Arrival in the Healthy Human Lung EIT Conf 2019, p.64



<sup>28</sup>Proença *et al* (2020) Non-invasive pulmonary artery pressure estimation by electrical impedance tomography in a controlled hypoxemia study in healthy subjects Sci Reports, 10:21462

### EIT-PAP in neonatal lambs



**Figure 1:** PAP and PAP EIT (top row) and systemic arterial pressure (SAP) and HR data (bottom row) for a representative animal. A: FiO<sup>2</sup>=21% B: FiO<sup>2</sup>=100%, C: FiO<sup>2</sup>=12–14%, D: FiO<sup>2</sup>=21%, E: FiO<sup>2</sup>=12–14%+hypoventilation, F: FiO<sup>2</sup>=100%+epinephrine.

<sup>&</sup>lt;sup>29</sup>Braun et al (2019) EIT measurement of pulmonary artery pressure in neonatal lambs p.33, Conf EIT 2019

### Part C - Ventilation / Perfusion matching

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<sup>&</sup>lt;sup>30</sup>CC0 public domain

### V/Q: Holy grail?

- Physiological "Goal" of lungs is gas exchange  $\longrightarrow$  accomplished by  $\dot{V}/Q$  matching
- Holy grail<sup>31</sup>  $\triangleq$ 
  - (A) the cup Jesus drank from at the last supper,
  - (B) treasure with miraculous healing powers,
  - (C) elusive object or goal of great significance<sup>32</sup>
- If EIT can provide V/Q it will be (C) and maybe (B) but not (A)

<sup>&</sup>lt;sup>31</sup>Leonhardt & Lachmann (2012) Electrical impedance tomography: the holy grail of ventilation and perfusion monitoring? Int Care Med 38:1917–1929.

<sup>32</sup>Not statistical

# Concept: $\dot{V}/Q \triangleq \dot{V}$ [ml air/min] $\div Q$ [ml blood/min]



- V: Ventilation Image
   EIT Tidal Ventilation [unitless]
  - Q: Perfusion Image EIT Perfusion – Partial Volume effects [unitless]

•  $\dot{V}/Q$ : Ventilation  $\div$  Perfusion in lung ROI Should be in log units:  $\log(\frac{\dot{V}}{Q}) = \log(\dot{V}) - \log(Q)$ [unitless – unless using Bohr eqn, next slide]

### **Bohr Equation**

Voxel V/Q ratio calculated using:

- ventilation:  $\Delta Z_{\dot{V},vox}$ ,
- perfusion:  $\Delta Z_{\dot{Q},vox}$

Bohr<sup>34</sup> equation leads to:

$$rac{\dot{\mathrm{V}}_{\mathrm{vox}}}{\dot{\mathrm{Q}}_{\mathrm{vox}}} = rac{rac{\Delta Z_{\mathrm{\dot{V}},\mathrm{vox}}}{\Delta Z_{\mathrm{\dot{V}},\mathrm{tot}}} imes V_{\mathcal{T}} imes \textit{RR} imes (1 - rac{V_{D}}{V_{\mathcal{T}}})}{rac{\Delta Z_{\mathrm{\dot{Q}},\mathrm{vox}}}{\Delta Z_{\mathrm{\dot{Q}},\mathrm{tot}}} imes \textit{CO}}$$

tidal volume ( $V_T$ ), resp rate (*RR*), cardiac output (*CO*) and dead-space frac ( $\frac{V_D}{V_T}$ ).

Motivation: impedance ratios represent the unitless fraction of impedance change in each voxel. Conversion to  $\dot{V}$  and Q units requires multiplication by air and blood flows:  $V_T \times RR \times (1 - \frac{V_D}{V_T})$  represents effective alveolar ventilation.

<sup>&</sup>lt;sup>34</sup>Christian Bohr, father of Niels

### 3D V/Q



<sup>35</sup>Larrabee et al (2023) Am J Physiol: Lung 325:L638–L646



<sup>36</sup>Kircher et al (2020) Regional Lung Perfusion Analysis in Experimental ARDS by EIT IEEE T Med Imag 40:251–261



Fig. 5. Regional blood flow distribution before and after regional lung injury by endotoxin. Gravscale CT images (A) are depicted together with computed MDCT blood flow q<sub>er</sub> (B) and computed EIT blood flow q<sub>er</sub> (C) for the healthy state (upper) and for the injured lung (middle) Perfusion changes ( $\Delta q_{c\tau}$  and  $\Delta q_{err}$ ) after regional lung injury compared to the healthy state (bottom).

both MDCT and EIT. LoA: limits of agreement

analysis in four ROIs, the mid-ventral and ventral, as well as the dorsal and mid-dorsal

graphs in plots (C) and (F) represent the dorsoventral profiles and right-to-left profiles for

ROIs are combined. Graph (B) and (E) shows the same analyses for eight ROIs. The

[<sup>37</sup>]

left

<sup>&</sup>lt;sup>37</sup>Kircher et al (2020) Regional Lung Perfusion ...

### **Different Contrast Agents**



Figure 2 (left) Exemplary global signals captured by Electrical Impedance Tomography after bolus injection of different contrast agents. Normalized changes in global conductivity over time after filtering and drift compensation; (right) relative signal strength of different contrast agents calculated from the maximum amplitude of the regional lung perfusion images. Horizontal solid lines indicate mean values and standard deviation. The dotted line indicates the reference (signal strength of the mean image of NaCl 5.84 injections).

<sup>38</sup>Muders *et al* (2023) Evaluation of Different Contrast ... J Clin Med 12:2751.

### Human Results (3D)

A TEE image of the mid-esophageal bicaval view. The red arrow indicates a massive embolism in the right atrium. B TEE image of the mid-esophageal ascending aortic short-axis view. The red arrow demonstrates that the color Doppler found no blood perfusion signal in the right pulmonary artery. C Chest CT image indicated that the lung was almost normal. D Lung ventilation image of EIT in coronary, sagittal, and axial planes with low-ventilated regions marked in dark blue and high-ventilated regions in light grev. E Lung perfusion image of EIT in coronary, sagittal, and axial planes. Regions with low perfusion are displayed in dark red and high perfusion in white. F Ventilation/perfusion (V/Q) image of FIT



<sup>39</sup>Gao et al (2024) Feasibility of 3D-EIT in identifying lung perfusion defect and V/Q mismatch in a patient with VA-ECMO Crit Care 28:90

418/3.02%

7625/55.17%

12/1 20%

521/52.05%

Shunt

Pixels No./%

V/O Match

Pixels No./%

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11/2.06%

325/60.75%

15/2 85%

470/89.35%

15/3 22%

120/25.75%

### Other recent work

- Xu *et al* (2021) Lung Perfusion Assessment by Bedside Electrical Impedance Tomography in Critically III Patients Front. Physiol, 12:748724
- He *et al* (2021) Three broad classifications of acute respiratory failure etiologies based on regional ventilation and perfusion by electrical impedance tomography: a hypothesis-generating study Ann Int Care 11:134
- He et al (2023) New application of saline contrast-enhanced electrical impedance tomography method for right ventriculography besides lung perfusion: detection of right-to-left intracardiac shunt QJM: Int J Med 2023:hcad147
- He *et al* (2020) Detection of Acute Pulmonary Embolism by Electrical Impedance Tomography and Saline Bolus Injection Am J Respir Crit Care Med 202:881–882.
- Hentze *et al* (2018) Regional lung ventilation and perfusion by electrical impedance tomography compared to single-photon emission computed tomography Physiol Meas 39:065004
- Bluth *et al* (2019) Measurement of relative lung perfusion with electrical impedance and positron emission tomography: an experimental comparative study in pigs Br J Anaes 128:246–254

### $\dot{V}/Q$ – thoughts

- Holy Grail ... would provide unique capability
- Can we use contrast agents for human medicine?
- Need to understand pulsatility signal ... when is it reliable? EIT community harming self by not understanding difference
- Lots more technical innovation possible
  - Cardiac Output monitors (e.g. PiCCO) use pulse-contour analysis, which could be done with EIT
  - Compartment models / source separation techniques from PET/SPECT
- $\dot{V}/Q$  is a 3D effect  $\rightarrow$  use 3D EIT









