Fraction of reverse impedance change (FRIC): a quantitative electrical impedance tomography measure of intrapulmonary pendelluft

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Abstract: Pendelluft is the movement of air between lung regions, and EIT has shown an ability to detect and monitor it. In this note, we propose a functional EIT measure which quantifies the reverse airflow seen in pendelluft: the *Fraction of Reverse Impedance Change* (FRIC). FRIC measures the fraction of reverse flow in each pixel waveform (as an image) or globally (as a single parameter). Such a measure is designed to be a more specific measure than previous approaches, to enable comparative studies of the pendelluft, and to help clarify the effect of ventilation strategies.

Objective: Pendelluft refers to movement of air between lung regions. It is the consequence of spatial inhomogeneities in the distribution of lung compliance and/or airway resistance between different lung regions (Otis et al, 1956). The presence of pendelluft is associated with lung disease severity. However, there is considerable debate over its clinical significance: perhaps pendelluft is a sign of underlying lung stresses, or perhaps it independently stresses lung tissues, and thus contributes to lung damage.

Since electrical impedance tomography (EIT) is capable of determining regional lung gas volume changes with an excellent time resolution such that intrapulmonary redistribution of air can be detected. This was shown for the first time by Yoshida et al (2013) in mechanically ventilated pigs with injured lungs, in which the animals were not paralyzed and spontaneous breathing was not suppressed. Diaphragmatic contractions led to a vertical gradient of pleural pressure and the presence of pendelluft between the non-dependent and dependent lung regions was detected by EIT.

In this paper, we propose a functional EIT measure which quantifies the reverse airflow seen in pendelluft: the *Fraction of Reverse Impedance Change* (FRIC).

Such a measure will facilitate comparative studies of the phenomena, and help clarify the effect of ventilation strategies. It may also eventually become a clinically-useful parameter to guide support settings. Previous work has used different EIT-based measures of pendelluft. For example Sang et al (2020) used measures of regional phase shift (defined as time difference between global and regional impedance-time curves) and amplitude differences (defined as the impedance difference between sum of all regional tidal variation and the global tidal variation). Chi et al (2022) defined the amplitude of pendelluft as the impedance difference between the sum of all regional tidal impedance variation and the global tidal impedance variation. In Liu et al (2024), pendelluft occurrence was defined to be when tidal variation amplitude exceeded 2.5% of global tidal impedance variation. In a review, Su et al (2022) summarized three further EIT-based measures of pendelluft. We believe that these measures are useful, but are also measures of phenomena other than pendelluft. We intend that our parameter

is more specific to pendelluft than other functional EIT parameters (see Frerichs et al, 2017, supplement 4).

Approach

Our measure is motivated as follows: when pendelluft occurs during ventilation, air moving between lung regions will support flow in one region and will be contrary to air flow in another. Thus our measure should quantify the air paradoxically moving in the “wrong” direction in each lung region.

Thus FRIC is the fraction of impedance change in the reverse direction: Figure 1 illustrates the calculation.

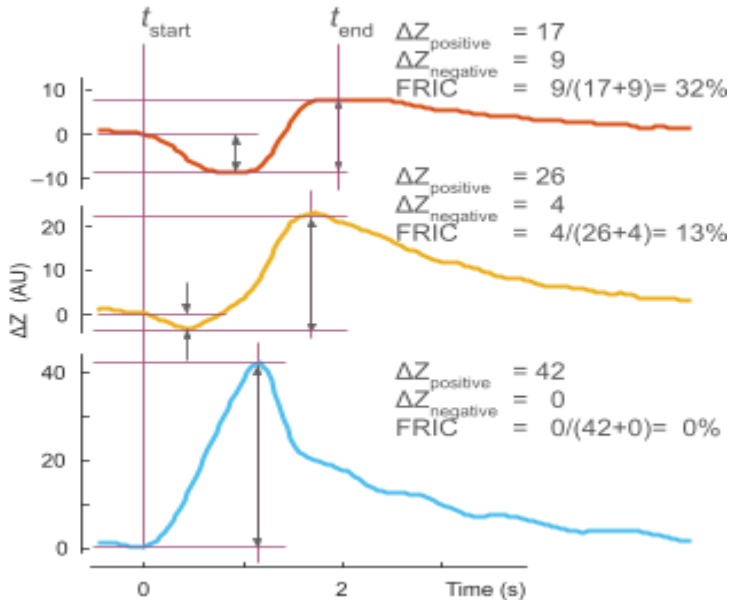

Figure 1: Illustration of calculator of FRIC using three pixel waveforms from figure 2. The start of inspiration (t_{start}) is identified globally, and the end of inspiration in each pixel waveform (t_{end}) is identified as the point of maximum impedance change. FRIC is calculated from the impedance change in the positive ($\Delta Z_{positive}$) and negative directions ($\Delta Z_{negative}$).

Pixel FRIC is calculated via the following steps::

1. Filter out the heart-rate component in the EIT signals by breath averaging or bandpass filtering at the heart rate.

2. Low-pass filter the signals to remove spurious noise that could be misinterpreted as negative impedance change (we use a 6^{th}-order phase-neutral Butterworth filter at 10 Hz)

3. Identify the start of inspiration (t_{start}) in the EIT global waveform using the change in derivative. Pixel waveforms should be analyzed at t_{start} to identify whether any "early pendelluft" ΔZ precedes the global start. If such decreases are detected, t_{start} should be moved to an earlier point to precede all pendelluft-related ΔZ.

4. For each pixel waveform (i) in the lung region-of-interest (ROI), calculate:

a. The end-expiratory point as the point of maximum ΔZ_i in pixel *i* during the breath

b. The pixel waveform end-inspiration point ($t_{end,i}$) as the point of maximum ΔZ_i

c. Calculate a numerical derivative $D_i(t) = (\Delta/\Delta t)\ \Delta Z_i(t)$

d. Calculate: $\Delta Z_{positive,i} = \Sigma_t\ (|D_i(t)|$ for all $D_i(t) > 0)$ for $t_{start} < t < t_{end,i}$

e. Calculate: $\Delta Z_{negative,i} = \Sigma_t\ (|D_i(t)|$ for all $D_i(t) < 0)$ for $t_{start} < t < t_{end,i}$

f. Pixel $FRIC_i = \Delta Z_{negative,i}/(\Delta Z_{positive,i} + \Delta Z_{negative,i})$

From pixel FRIC values, the global $FRIC_g = \Delta Z_{negative}/(\Delta Z_{positive} + \Delta Z_{negative})$, where $\Delta Z_{positiveve} = \Sigma_i(\Delta Z_{positive,i})$ and $\Delta Z_{negative} = \Sigma_i(\Delta Z_{negative,i})$ for all pixels *i* in the lung ROI.

The calculation of the FRIC parameter is illustrated using data from a published study of the effect of positive end-expiratory pressure (PEEP) during pressure-support ventilation (Schroeder et al, 2020). A clinical case was selected of a 52-year old male patient (body height 173 cm and weight 83 kg) treated in the ICU for extrapulmonary adult respiratory distress syndrome (ARDS) due to peritonitis after sigmoid colon perforation. The patient was tracheotomized and examined by EIT (PulmoVista 500, Draeger, Lübeck, Germany) 14 days after endotracheal intubation. He was ventilated with pressure-support ventilation (EVITA XL, Draeger, Lübeck, Germany) with a pressure support of 8 mbar, tidal volume of 600 ml and respiratory rate of 16/min at varying levels of positive end-expiratory pressure (PEEP). The portion of the waveform analyzed had PEEP initially at 5 mbar, and then increased to 10 mbar. Airway occlusion pressure (P0.1) was 7.1 mbar and patient work of breathing was 1.63 J/l. Arterial pressure of oxygen (P_aO_2) was 88 mmHg at fraction of inspired oxygen (F_IO_2) of 0.40, arterial pressure of carbon dioxide (P_aCO_2) was 37 mmHg and pH 7.47. Images were reconstructed using GREIT (Adler et al, 2009) and the above algorithm applied. The patient participated in a clinical study (Schröder et al., 2020), but the PEEP steps analyzed in this publication were performed for clinical reasons outside the study protocol.

Main Results

Using the patient data acquired at PEEP 5 and 10 and the calculation steps described above, we calculated pixel-wise and global FRIC values for both PEEP levels. Figure 2 illustrates the EIT waveforms and pixel- and global-wise FRIC calculations. The increase in PEEP from 5 to 10 mbar led to a small increase in global FRIC and an enlarged region of pixel-wise FRIC.

Pixel waveforms with reverse-flow behaviour were identified and the fraction of such flow quantified. The global FRIC value increased as more pixels showed greater levels of reverse flow. The figure also illustrates that other changes due to the PEEP change could be identified, such as the increase in end-expiratory lung impedance (shown by the increase in pixel waveforms above zero at t=114s) which are not reflected in pixel FRIC values.

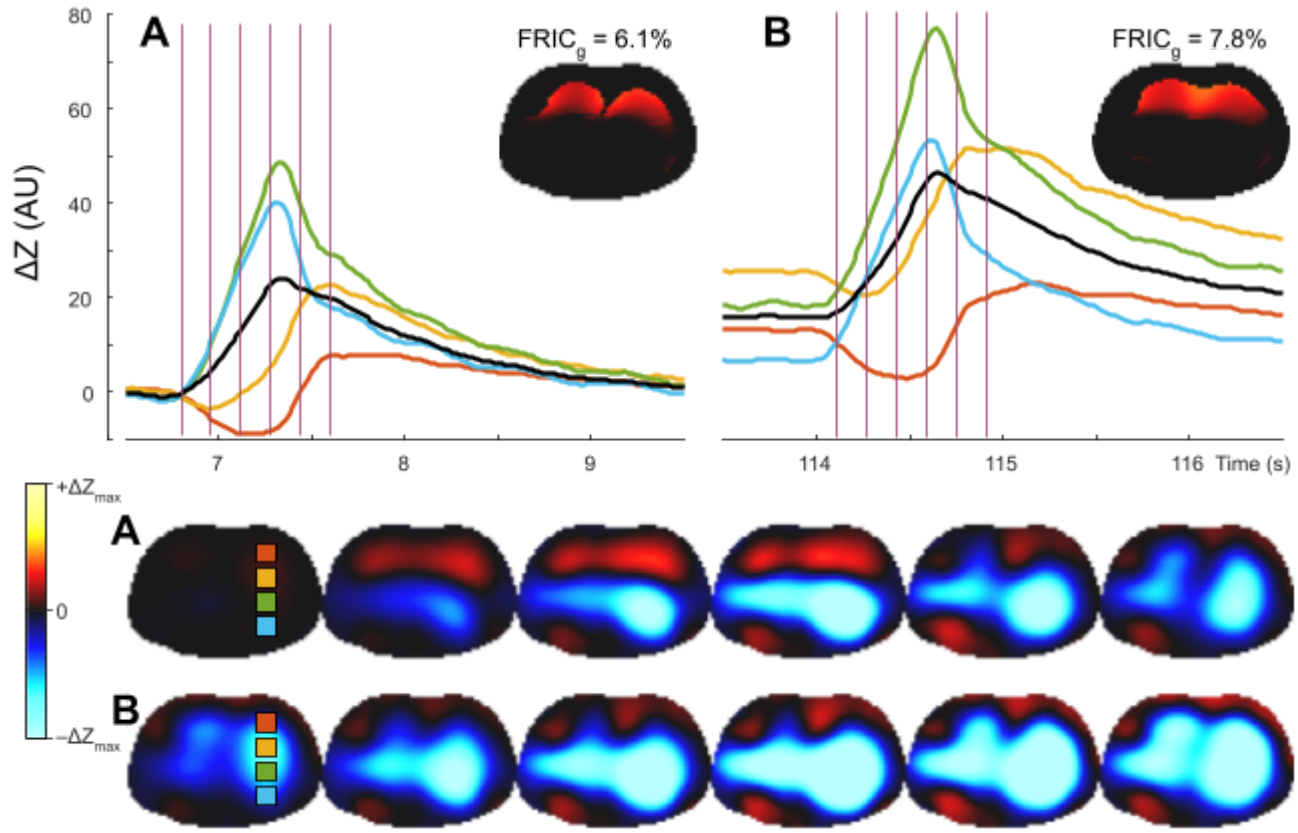

Figure 2: Illustration of pendelluft and FRIC calculation: Upper graphs: pixel waveforms (arbitrary units) vs time (s) (corresponding to the coloured pixels in the images below) before and after an increase in PEEP (time units from start of recording). Vertical bars in upper figures correspond to image sequences A and B, normalized to the first time point, A. Inset graphs, pixel FRIC values and the corresponding FRIC$_g$ value. Lower images: EIT images at each vertical bar referenced to *t*=6.5 s. A small change in global FRC is seen due to the PEEP increase.

Significance

As a bedside, non-invasive imaging technique, one potential use of EIT is to detect and monitor pendelluft and its changes over time and due to treatment. We propose a new functional EIT measure (FRIC), designed to be more specific to pendelluft than other functional EIT parameters.

The clinical significance of pendelluft is poorly understood. It may independently damage lung tissue, or it may be an indicator of the underlying inhomogeneous distribution of lung stresses which are causing damage. In order to untangle such questions, a specific measure is required which quantifies pendelluft independently of other regional inhomogeneities present in the lungs. We believe that previous measures are likely to conflate other effects with pendelluft. For example, measures of regional phase shift (Sang et al, 2020), or regional differences in time-impedance curves (Chi et al 2022, Liu et al 2024) will also measure non-pendelluft variability in regional ventilation.

We have proposed a simple definition which we hope is easy to calculate and understand. Our goal is to estimate the reverse flow associated with pendelluft; however, any EIT-based measure is inherently

limited. Pendelluft is a complex regional phenomenon which should be represented in 3D, rather than in the 2D-plane of a single-belt EIT image.

We make the following notes on this calculation. The heart-rate related EIT signal can lead to non ventilation-related changes, and should be filtered, using an approach such as Wisse et al (2024). In our calculation, we define a t_{end} value separately for each lung pixel; this is important, since the end inspiration varies dramatically throughout the lung. In this paper, we define the lung ROI as 10% of the maximum impedance change; however, other definitions of lung ROI are appropriate and should be mentioned in the calculation. Under normal circumstances, if $\Delta Z_{negative} = \Delta Z_{positive}$, the maximum possible value of FRIC is 50%. It is possible to have even larger values if the signal only decreases during the inspiration phase, which would be an indication of “ringing” in the images or an artefact. We note that FRIC is likely only valid during stable periods of at least 5-10 breaths, and may not be useful during dynamic changes. Finally, since FRIC calculates a ratio, the units of impedance change are irrelevant.

Our proposed measure is also limited in the sense that phase-reversed signals can also occur in non-pendelluft contexts. For example, Becher et al (2018) described phase-inverted impedance changes that frequently occur in the presence of pleural effusion or in the cardiac area and that are most likely not caused by pendelluft but represent some form of "ringing artifacts" related to the reconstruction algorithm's point spread function. In contrast to FRIC, these are completely phase-inverted (they "mirror" the positive global signal) and are therefore almost completely negative. In this case, pendelluft could be differentiated from pleural effusion in two ways: 1) Pendelluft is transient, so the regional decrease in impedance during early inspiration is followed by an increase in impedance during ongoing inspiration in the same region, and 2) Pendelluft during spontaneous efforts appears to occur predominantly in the non-dependent lung regions, whereas out-of-phase impedance changes during pleural effusion naturally occur in the dependent lung region. When using FRIC for assessment of pendelluft, areas with values close to 100% should be considered as potentially caused by ringing or other artifacts.

In summary, we propose a new functional-EIT measure of pendelluft called FRIC, with the hope that this parameter allows useful and specific quantification of the presence and changes in pendelluft in patients’ lungs.

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