

Editorial on the focus collection ‘Advances in Electrical Impedance Tomography and Bioimpedance Including Applications in COVID-19 Diagnosis and Treatment’

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This focus collection of articles published by the journal *Physiological Measurement* introduces the recent advances in Electrical Impedance Tomography (EIT) research. The ongoing COVID-19 pandemic has highlighted clinical settings where EIT may assist in managing the treatment and monitoring of patients suffering from COVID-19 and long COVID. The advent of the pandemic moved the focus of research away from other urgent clinical problems, causing delays in screening and diagnosis of many important conditions. However, the new research presented in this focus collection shows that EIT is still relevant to improving screening and diagnosis in a wide range of clinical conditions.

One key emergence from the pandemic is the urgent requirement for new medical technology to be ready to use on patients. EIT has considerable potential for routine clinical use but improvements in clinical management of EIT use are still needed. Clinical compliance requirements must be considered at the beginning of any research project. However, EIT systems produced in research environments sometimes lack these features. Factors impeding clinical compliance include the need for the device to be approved for use on humans, requiring several ISO standards to be addressed, for example, those relating to biocompatibility (10993) and electrical safety (60601-1-2), as well as software safety compliance (62304). In some cases, CE compliance is also required. Clinically useful EIT systems need to anticipate these requirements as the production of an EIT system and software which cannot be used on human subjects for routine clinical use limits the future adoption of EIT as a key management tool.

This focus collection follows several recent conferences presenting new research outcomes and leading to the development of many research papers. While the 2020 International Conference on the Biomedical Applications of EIT was cancelled, the 21st International Conference on Biomedical Applications of EIT, hosted by the National University of Ireland, Galway was recently held online from 14-16 June 2021. Work presented during the 2021 conference but also of other ongoing EIT research activities will be the subject of a future focus collection on EIT (<https://iopscience.iop.org/journal/0967-3334/page/Advances-and-Emerging-Applications-of-Electrical-Impedance-Tomography>).

Experimental and clinical use of EIT imaging is dominated by the applications on the chest. The predominant use is for monitoring of the spatial and temporal distribution of regional lung ventilation, especially in patients with acute and chronic respiratory disorders, often undergoing mechanical ventilator therapy (Kobylianskii et al., 2016, Frerichs et al., 2017, Zhao et al., 2020, Vasques et al., 2019). The COVID-19 pandemic has sped up the use of EIT in intensive care units even more (Kotani and Shono, 2021). It is therefore not surprising that the recent focus collection of EIT papers lists as many as six papers dealing with its chest applications (Bronco et al., 2021, Haris et al., 2021, Hsu et al., 2021, Jiang et al., 2021, Hentze et al., 2021, Menden et al., 2021a). The articles span physiological and methodological studies, as well as prospective and retrospective clinical studies on the use of EIT.

An extraordinary use of EIT during a space flight, that aimed at the analysis of body fluid shifts in weightlessness, was reported as early as in 1993 (Baisch, 1993). Since then a few reports exploring the effects of gravitational forces on regional lung function using chest EIT have been published. They either explored the impact of their absence during parabolic flights (Frerichs et al., 2001) or their increase during exposure to high accelerations (Borges et al., 2015). Menden and colleagues performed an elegant physiological study exploring the effects of high acceleration on the distribution of tidal ventilation, regional end-expiratory lung volumes and regional lung emptying behaviour (Menden et al., 2021a). The authors examined ten volunteers who were exposed to accelerations of up to 6 G using a human centrifuge. Such accelerations are comparable with those experienced by astronauts during launch and re-entry in suborbital spaceflights. The subjects were studied while supine and the distribution of regional tidal and end-expiratory lung volumes, as well as lung emptying behaviour were analysed within the chest cross-section by EIT in the front-to-back orientation. The authors detected a redistribution of tidal ventilation favouring the ventral regions, faster emptying of the dorsal regions and ventral gas trapping due to regional airway collapse. The effects negatively impacted the pulmonary gas exchange and reduced arterial oxygenation. The results are relevant for our understanding of the individual reaction and adaptation of the respiratory system to hyper gravity.

A new research development in EIT lung monitoring is associated with the recent technological advancements of wearable medical devices. The integration of chest EIT into a wearable medical device has recently been reported (Frerichs et al., 2020, Hong et al., 2015). Such use of EIT might prove valuable in remote examinations of patients suffering from chronic lung diseases like COPD. The perspectives of EIT use in these patients have been lately summarized and deemed promising (Sang et al., 2020). The use of EIT in awake, unsupervised spontaneously breathing patients at their homes can be expected to require robust tools for an automated and reliable analysis of the recorded EIT signals. These tools should identify stable breathing periods in the recordings and generate measures characterizing the distribution of ventilation and detect pathological changes of regional lung function. Haris and colleagues present the results of a study conducted on healthy subjects who were continuously examined by EIT during the total of 690 min (Haris et al., 2021), while performing different occasional manoeuvres like posture change, arm movement, coughing, talking, breath-holding or deep breathing. These voluntary interventions interrupted the normal quiet tidal breathing pattern. The authors proposed a method for automatic respiratory cycle detection with subsequent identification of stable breathing periods based on the coefficient of variation of tidal impedance amplitude, breath duration and end-expiratory lung impedance derived from the regional EIT waveforms. The method exhibited a high accuracy of over 90 %. The authors postulated that the identification of stable breathing periods could be further improved when additional information provided by other wearable sensors, e.g. accelerometers or microphones, and advanced analysis using deep learning was employed.

Jiang and colleagues conducted a prospective clinical study on a group of 35 hospitalised patients suffering from community or hospital acquired non-severe pneumonia (Jiang et al., 2021). The patients were still breathing spontaneously without the need of mechanical ventilatory support. They were examined by EIT in the supine posture on the first and the sixth day of their treatment. The authors used various EIT measures to characterise the spatial and temporal ventilation distribution: the global inhomogeneity index (Zhao et al., 2009), the centre of ventilation (Frerichs et al., 1998), the inter-quadrant ventilation image heterogeneity and the regional ventilation delay (Muders et al., 2012). The study confirmed that the initial high ventilation heterogeneity with pronounced regional ventilation dispersion was reduced by the sixth day of therapy. The authors postulated that EIT imaging might become an additional method for clinical patient assessment with the potential for reducing the use of conventional radiological methods associated with radiation exposure.

Another prospective clinical study was conducted on 87 intubated intensive care patients suffering from moderate to severe acute respiratory distress syndrome (ARDS). The patients exhibited no spontaneous breathing activity (Hsu et al., 2021). The authors randomised the patients into two groups. In one group, EIT was applied for the selection of positive end-expiratory pressure (PEEP) during the decremental PEEP trial while utilising the procedure based on the calculation of regional respiratory system compliance (Costa et al., 2009). In the other group, a pressure-volume manoeuvre was performed with

a constant low-flow inflation and passive deflation. The selected PEEP equalled the airway pressure measured at the time point of maximal hysteresis. After two days of intensive care treatment, the patients exhibited similar oxygenation and lung mechanics in both groups, however, driving pressures were significantly lower in the EIT group. Moreover, the EIT group exhibited higher hospital survival rates. Hsu and colleagues concluded that EIT was a suitable tool for guiding PEEP titration in ARDS patients and recommended a larger study to validate the findings.

Bronco and colleagues performed a retrospective observational study where they analysed the use of EIT in a single centre specialised in the treatment of patients with acute respiratory failure and of patients requiring veno-venous extracorporeal oxygenation (Bronco et al., 2021). The authors reported the use of EIT in 41 patients for 54 times over a period of two years. In 70 % of cases, EIT was applied for PEEP setting using both the incremental and decremental PEEP trial. The PEEP selection was based on the analysis of end-expiratory lung impedance or regional lung compliance. (In the latter case, the procedure was identical to the one reported in the study by Hsu and colleagues and mentioned above.) In the remaining 30 % of cases, EIT was applied with the aim of assessing lung recruitment, the setting of sighs, the effect of prone positioning, the efficacy of bronchial airway block and the effect of inhalation of helium-oxygen mixtures on ventilation distribution in asthma exacerbation. The authors concluded that EIT was a useful bedside tool allowing individually tailored ventilator settings, first of all pertaining to the selection of PEEP. In other situations, the capacity of EIT to describe ventilation distribution in the chest allowed the assessment of the efficacy of specific therapeutic interventions.

The chest applications of EIT for the assessment of regional lung perfusion are far less frequent than those pertaining to lung ventilation (Nguyen et al., 2012, Xu et al., 2021). The most promising approach enabling the measurement of lung perfusion by EIT is based on the central venous bolus administration of an EIT contrast agent, the hypertonic saline solution. The recent experimental validation studies using advanced reference imaging methods (Kircher et al., 2021, Bluth et al., 2019) and the clinical reports on its use in patients with pulmonary emboli (He et al., 2020) and COVID-19 (Mauri et al., 2020) support further research activities in this field. The primary aim of this research should be the refinement of the indicator-based signal analysis. With this respect, the study by Hentze and colleagues is highly topical (Hentze et al., 2021). The authors used a sophisticated animal model, where lung perfusion was either intact or altered directly by blocking regional blood flow or indirectly by inducing regional hypoxic pulmonary vasoconstriction. Computed tomography was applied as a reference imaging method. A model-based algorithm was then developed allowing a reliable extraction of lung perfusion images from the indicator-based signal obtained with 5.84% saline solution. The proposed algorithm improved the detection of regional lung perfusion by EIT which might enable better monitoring of ventilation-perfusion matching in a clinical setting in the future.

Hardware developments in EIT have mostly emphasized development of precise current sources and multiplexing voltage measurements over multiple channels using serial or parallel methods. While most systems are configured to deliver EIT currents over a large frequency range, most studies use a single frequency. Relatively fewer advances have been made in performing true multi-frequency studies, principally because of difficulties and uncertainties inherent in system calibration using multiple frequencies and electrodes. The work presented by Menden et al. (Menden et al., 2021b) presents a method for performing multiple frequency measurements using orthogonal baseband shifting (OBS). OBS may prove a viable path to obtaining spectroscopic EIT information using an efficient hardware configuration. In practical tests of their prototype over the range between 45-180 kHz, amplitude and phase precisions of 0.65% and around 0.8° respectively, and measurements on a silicone heart phantom were also promising. In future work the authors suggest hardware adaptations to further increase full-spectrum frame rates.

Several papers deal with other research areas which include the imaging of slow brain activity during neocortical and hippocampal epileptiform events with electrical impedance tomography (Hanna et al., 2021). The authors present findings that suggest slow impedance response are a reliable marker of hypersynchronous neuronal activity during epileptic seizures and can thus be utilised for investigating the mechanisms of epileptogenesis in vivo and for aiding localisation of the epileptogenic zone during

presurgical evaluation of patients with refractory epilepsies. Also, the development of an EIT set-up for the quantification of mineralization in biopolymer scaffolds (Cortesiet al., 2021) show results for the potential of EIT for the non-destructive quantification of matrix mineralization in 3D scaffolds, and the possible long-term monitoring of osteogenic differentiation in hybrid tissue engineered constructs.

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