Journal of Physics: Conference Series

PAPER • OPEN ACCESS

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To cite this article: A Masner *et al* 2019 *J. Phys.: Conf. Ser.* **1272** 012008

IOP Conf. Series: Journal of Physics: Conf. Series **1272** (2019) 012008 doi:10.1088/1742-6596/1272/1/012008

Electrical impedance tomography for neonatal ventilation assessment: a narrative review

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Abstract. Neonatal care has improved dramatically over the last decades thanks to a better understanding of the transition to extrauterine life, especially due to the new respiration condition. A privileged technique to assess the filling of the lungs with air in a non-invasive way is Electrical Impedance Tomography (EIT), which is, therefore, also a tool to monitor ventilation. Out of 2427 papers on EIT from 1985 to 2018, 116 deal with EIT in neonatal care, with both the set and subset increasing at similar rates of 5 and 0.4 additional papers per year (0.03 and 0.05 papers per year) respectively. EIT can be used to determine Body position and Pneumothorax, to guide Endotracheal Tube Positioning and to monitor Ventilation Homogeneity. Moreover, real time EIT gives abundant evidence to develop new techniques such as Sustained Inflation, Protective Intended Ventilation, Minimal Invasive Surfactant Therapy, Less Invasive Surfactant Administration, Intubation-Surfactant-Extubation and Oro Pharyngeal Surfactant during their application to both animal models and patients. The low cost, non-invasive and easy graphic interpretation of EIT leads to the belief that it will have widespread use in Neonatal Medicine.

1. Introduction

Neonates are a very particular type of patient: seldom do we see physiological changes take place as rapidly and suddenly as they do in newborn babies. Moreover, these changes occur all at once. This convergence of processes is known as 'transition to extrauterine life' and entails a series of physiological events. Understanding this transition has been vastly investigated, giving rise to the description of highly sophisticated physiological mechanisms. It becomes clear that the first few days of a newborn´s life have a great influence on the individual's future development, as formulated by Barker´s hypothesis on fetal conditions [1].

Technology plays a major role in helping to gain a better understanding of the complex newborn adaptation to extrauterine life, starting from either prematurity or illness. Namely, within the very promising Non-Invasive Techniques, two research areas such as Cerebral Function Monitoring (CFM) and Near Infrared Spectroscopy (NIRS) address the problem, in addition to Electrical Impedance measurements and the determination of tomographic images using Electrical Impedance Tomography (EIT) [2]. Electrical Bioimpedance can be of great value since it is non-invasive, and low cost. Frequencies of 30 Khz to 50 Khz are not perceived by human physiology and are limited by tissue and air trapped in alveoli [3]. This difference in bioimpedance is the basis of EIT imaging. Thus, EIT is increasingly being used to monitor air thoracic occupation. This paper presents a narrative review of the literature available on neonatal applications of EIT for anatomical and functional exploration.

2. Objective
To describe the state of development of EIT and its neonatal clinical use.

3. Methodology
Our search was carried out on PubMed by entering the keywords and title “impedance” AND “newborn” OR “neonate” OR “neonatal” OR “infant”. A total of 2,341 publications were found. Subsequently, another 86 studies were added by entering the keyword “bioimpedance” as part of the search. A total of 2427 papers were considered, published between 1950 and 2018. We then excluded all studies on adults and adolescents, as well as studies not related to functional aspects obtained by EIT.

Of the 2427 studies, only 63 referred to EIT in newborns. Reading these papers produced the identification of 53 seminal publications in the reference lists. The EIT subgroup *corpus* was, therefore, composed of 116 studies.

4. Results
Figure 1 shows the yearly papers on bioimpedance and neonate, as well as the EIT subset.

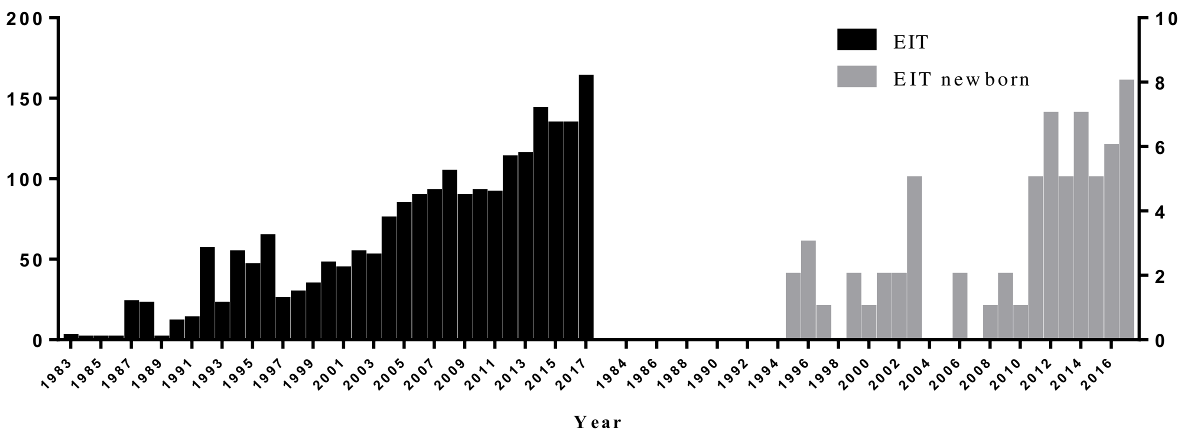

Figure 1. Papers on EIT and “neonate” from 1983 to 2017.

The first studies using impedance in newborns date back to the mid60s, and more than 30 years since the first publications about clinical applications of the Electrical Impedance Tomography (EIT) in medicine by Barber and Brown. The development in this technology continues in the 90s, consolidating its use, and introducing it in newborn babies [4][5][6].

EIT is based on the capability of biological tissues to allow the passage of charged ions as injected by electrical circuits. EIT generates a cross-sectional image of the changes in distribution of electrical impedance measured by skin electrodes. This process is performed by a specialized software which puts into practice mathematical problem resolution [7]. EIT is a technique with several beneficial characteristics: low cost, innocuous, capable of long-term physiological assessment and bedside usability. EIT gives clinically meaningful information in gastric assessment and pulmonary measurement, as well as head and breast imaging [8].

Growing interest in EIT is evidenced by a rising number of publications based on the clinical need for monitoring and, specifically, for the evaluation of regional lung ventilation at the bedside. EIT can be divided into the following sub techniques, as described by Frerichs [9]:

- Chest measurements
- EIT section images
- Region of interest (ROI) signal waveform
- Functional images in sections
- Measurements derived from EIT images

TABLE 1. EIT contributions to newborn baby care.

Authors	Year	Title	EIT and Neonatal Care
Hampshire, A et al	1995	Multifrequency and parametric EIT images of neonatal lungs.	First EIT paper on neonatal lungs
Marven, S S et al	1996	Reproducibility of electrical impedance tomographic spectroscopy (EITS) parametric images of neonatal lungs.	Neonatal lungs EIT reproducibility
Smallwood, R et al	1999	A comparison of neonatal and adult lung impedances derived from EIT images.	Neonatal and adult lungs EIT
Frerichs, I et al	1999	Monitoring regional lung ventilation by functional EIT during assisted ventilation.	Mechanical Ventilation (MV) optimization with EIT
Frerichs, I et al	2001	Non-invasive radiation-free monitoring of regional lung ventilation in critically ill infants.	Monitoring regional lung ventilation with EIT
Frerichs, I et al	2003	EIT: a method for monitoring regional lung aeration and tidal volume distribution?	Regional lung aeration and tidal volume distribution
Frerichs, I et al	2003	Distribution of lung ventilation in spontaneously breathing neonates lying in different body positions	Spontaneously breathing and body positions
Pillow JJ et al	2006	Lung Function Tests in Neonates and Infants with Chronic Lung Disease: Global and Regional Ventilation Inhomogeneity	Ventilation inhomogeneity in acute and chronical respiratory disease
Frerichs, I et al	2006	Lung volume recruitment after surfactant administration modifies spatial distribution of ventilation.	Surfactant instillation and spatial distribution of ventilation
Kribs, A et al	2007	Early administration of surfactant in spontaneous breathing with nCPAP: feasibility and outcome in extremely premature infants	Surfactant instillation and CPAP
Thayyil, S	2008	Optimal endotracheal tube tip position in extremely premature infants.	Endotracheal tube positioning
van Veenendaal	2009	Effect of closed endotracheal suction in high-frequency ventilated premature infants measured with EIT	HFOV and closed ETT suction with EIT
Miedema, M	2011	Changes in Lung Volume and Ventilation during Surfactant Treatment in Ventilated Preterm Infants	HFOV and Surfactant Instillation
Bhatia, R et al	2012	Electrical impedance tomography can rapidly detect small pneumothoraxes in surfactant-depleted piglets	Pneumothorax Identification
Rossi et al	2013	EIT to evaluate air distribution prior to extubation in very-low-birth-weight infants: a feasibility study.	Assessment for Extubation
Hough, J et al	2014	Lung recruitment and endotracheal suction in ventilated preterm infants measured with electrical impedance tomography.	Lung recruitment and endotracheal suction
Thingay et al	2015	An individualized approach to sustained inflation duration at birth improves outcomes in newborn preterm lambs	Sustained Inflation
van der Burg, P et al	2016	Effect of Minimally Invasive Surfactant Therapy on Lung Volume and Ventilation in Preterm Infants	MIST and homogeneous increase in EELV
Frerichs, I et al	2017	Chest electrical impedance tomography examination, data analysis, terminology, clinical use and recommendations: consensus statement of the TRanslational EIT developmeNt stuDy group	EIT TREND Group Consensus

5. Clinical relevance of EIT in Newborn Babies

The clinical importance of EIT has been established in adults and children, but for the ventilated and non-ventilated newborn there is still a need for technology development and new knowledge.

Survival is rising in preterm infants due to the advance in physiological knowledge, but this viability is linked to long term morbidities. Focusing on the lung, new strategies are available to assist acute pulmonary illness and, at the same time, to minimize pulmonary temporal impairment. In the last few years there has been a trend towards increased use of non-invasive forms of respiratory support such as nasal continuous positive airway pressure (nCPAP), nasal intermittent positive-pressure ventilation, heated and humidified high-flow nasal cannula (HFNC), as well as new forms of surfactant administration. All these therapeutic approaches need studies with non-invasive EIT [10].

Assessing pulmonary function at the bedside is difficult and even more difficult in newborns. Today, most of the tools in use include chest X-ray, CT scan, blood gases and static MRI. All these techniques produce static evidence and some expose newborns to radiation in addition to being difficult for use at the bedside. Assessment of pulmonary function is, at most, general and seldom informs about regional ventilation. Other monitoring tools like oximeter, capnography, NIRS or clinical examination are appropriate for longitudinal assessments but they are not specific of the pulmonary function. EIT lacks the spatial resolution of other imaging modalities but it is compact in size, uses no ionizing radiation and gives functional images. This is a superior perspective for the comprehension of the newborn pulmonary function [11][12].

Several clinical studies have been carried out on the newborn baby (and newborn animal models), making use of the characteristics of EIT and a selection of these are presented in Table 1.

5.1. Body posture and positioning

Effects of body posture was studied in preterm babies with no respiratory disease by Frerichs with EIT, aimed at breathing patterns and posture in relation to spatial distribution in preterm infants with no lung disease and a significant relationship was found between them, suggesting that EIT can easily determine regional ventilation [13].

Hough *et al*. studied different positions in ventilated premature infants and found that a change in body position facilitates an improvement in lung function [14]. Hough also found that ventilated infants had significantly more ventilation inhomogeneity than the healthy infants, which is not gravity dependent but follows an anatomical pattern. In supine and prone positions, gravity had little impact on regional ventilation distribution both in ventilated infants or infants breathing spontaneously. However, there was no improved oxygenation in relation to position [15].

Prone positioning with nCPAP is often used after extubating. Van der Burg monitored differences in EELV and tidal Volume (TV) with EIT and evidenced that infants were able to maintain their EELV and increase TV in ventilatory mode transition, on prone position, suggesting this as a preferred initial posture [16]. This is also seen in a ventilated piglet model of PEEP titration prone position that leads to improved oxygenation and ventilation parameters in a lung injury model and EIT monitoring may help visualize optimal PEEP [17].

5.2. Pulmonary Mechanics

Miedema *et al.* report changes in regional lung volume implosion occurring during a spontaneous left-sided pneumothorax in a preterm animal model. EIT is able to identify pneumothorax onset and place in real time, long before clinical signs of cardiorespiratory distress, therefore, shortening treatment onset delays. This study also reveals a delayed increase of the End of Expiratory Lung Volume (EELV) that may help distinguish pneumothorax (higher EELV) from atelectasis (lower EELV). EIT is also good for the recognition of small pneumothoraxes [18][19].

Endotracheal tube management is always a concern in clinical practice. In normal mechanical ventilation (MV), suctioning the tube is a standard maintenance maneuver which inevitably entails a temporary loss of lung volume. EIT, for the first time, was able to demonstrate that there is a significant lung volume increase for at least 90 min after an initial and brief loss of lung volume [20]. Similarly, during High Frequency Oscillating Ventilation (HFOV), closed Endotracheal Tube (ETT) suctioning causes a transient and heterogeneous loss of lung volume in premature RDS infants, with a median residual loss of 3.3% of maximum volume [21].

A frequent concern is tube positioning in all newborns but especially in those below 28 weeks [22]. Schmolzer *et al.* compare EIT with five other non-invasive techniques to spot ETT position in a piglet model. EIT was able to correctly identify the location of the tube within the trachea, at the bedside [23]. Steinmann el al also found that EIT is appropriate for the recognition of correct ETT placement [24].

Rossi *et al.* used EIT in very-low-birthweight infants prior to extubation and demonstrated that EIT can be safely and successfully used in patients ready for extubation. This happens when the best ventilation homogeneity is reached, which is influenced by the level of expiratory pressure applied. Extubation failure is one of the most common concerns in premature newborns (25% of neonates of 32 weeks or less) [25]. Miedema *et al.* assessed regional changes in lung volume during HFOV, after surfactant administration to respiratory distress syndrome babies (RDS). EIT showed a rapid increase and stabilization of lung volume [26].

Sustained Inflation (SI) consists of the application of pressure above positive end-expiratory pressure (PEEP) values to help recruit alveoli of non-compliant lungs, followed by normal PEEP [27][28]. Tingay *et al.* studied different strategies for SI in an animal model, for which they changed inflation time with a view to trying to understand the volume response of this model using EIT. In this animal model they evidenced that standardized SI protocols based on fixed times and pressures may not always be beneficial and could have the potential to be harmful. This may explain the inter-subject variability in the time constants of the respiratory system at birth and the subsequent volume response. This is an example of how EIT is an excellent tool for evaluating possible benefits or the harmfulness of new strategies [29]. Other animal models presented by the same author explored the influence of surfactant status at birth on the ability of an SI to facilitate lung aeration, establishment of Functional Residual Capacity (FRC) and uniform ventilation, and subsequent protection of the lung from severe injury. The author demonstrated improved FRC during an SI and persistent uniform distribution of ventilation if exogenous surfactant was delivered to the lung prior to an SI [30].

Chatziioannidis *et al.* in 2013, used EIT to study regional air ventilation in premature babies with RDS after surfactant therapy, low pressure recruitment maneuvers and minimal adjustment of ventilator setting. The authors conclude that surfactant administration in the recruited lung with RDS modifies regional ventilation, as assessed by EIT, contributing to a more homogeneous air distribution [31].

Frerichs *et al.* studied the effect of surfactant and lung volume recruitment on the distribution of regional lung ventilation in a newborn piglet model of induced lung injury. They found evidence that early lung volume recruitment after surfactant therapy may improve pulmonary gas exchange efficiency by modifying spatial distribution of regional lung ventilation [32].

One of the main modes of respiratory support in preterm infants is the Nasal CPAP, which benefits babies with less effort to breathe, less paradoxical respiratory pattern and apnea, as well as improved gas exchange [33][34]. Despite the fact that more preterm infants are using Nasal CPAP for treatment of RDS, many still need invasive ventilation. Assessing global ventilation inhomogeneity is essential in the evaluation of bronchopulmonary dysplasia. Infant End-expiratory lung volume (EELV) changes, with Nasal CPAP, studied by Miedema *et al.* evidenced a homogeneous increase in EELV with nCPAP in preterm infants, which is extremely important because we have good quality data that failed to show a clear benefit of early nCPAP vs Mechanical ventilation. In this study EIT was used to monitor regional changes in EELV [35].

Protective intended ventilation modes are also studied by EIT. Synchronized volume-targeted ventilation (SIPPV + VTV) assessed by EIT in preterm infants shows differences in regional distribution of ventilation according to maturity and a significant variety between breaths, even with ventilation strategies that attempt to standardize lung mechanics [36]. High frequency oscillation ventilation HFOV, as a ventilation mode, was also evaluated. This is a protective intended ventilation mode and EIT is a promising tool to evaluate this [37].

5.3. Respiratory Treatment

Surfactant therapy and RDS is addressed by several studies including EIT and it wasn't until the late 1950s that surfactant was identified as critical to maintaining lung inflation at low pulmonary volumes. Avery and Mead discovered that lungs from premature newborns with RDS lack the low surface tension of pulmonary surfactant [38]. The first newborn successfully reported regarding surfactant administration was by Fujiwara *et al.* in 1980. In Uruguay, the first use is dated 1991 [39][40][41].

Most infants below 32 weeks need help in the delivery room, generally assistance to physiological transition in the first place and then reanimation if they fail to adapt. Ventilatory, respiratory and hemodynamic transitions are linked, and in a matter of seconds positive pressure on airways is indicated, then delayed cord clamping to enhance cardiac precharge until the first breath. Clinical practices are being revised constantly and the timing and/or effect of new techniques, such as Minimal Invasive Surfactant Therapy (MIST), Less Invasive Surfactant Administration (LISA), Intubation-Surfactant-Extubation (INSURE) and Oro Pharyngeal Surfactant are, or should be, investigated using EIT [42][43][44].

MIST and LISA are proposed as new options to deliver surfactant to preterm babies with RDS, avoiding invasive ventilation and associated co-morbidities such as Broncho Pulmonary Dysplasia (BPD). These new clinical options consist of placing a semirigid or flexible catheter just below the vocal cords to administer surfactant during spontaneous breathing on noninvasive ventilatory support [45][46]. Evidence also supports the belief that these maneuvers diminish the need for intubation secondary to CPAP failure [47][48].

Using EIT, Van der Burg *et al.* found, measuring End of Expiratory Lung Volume (EELV) in lambs, that MIST and LISA improved the oxygenation in a very similar way as compared to conventional surfactant application techniques [49]. INSURE (intubation-surfactant injection and immediate extubation) is another protective technique for which no EIT evaluation study was found in the literature.

Oropharyngeal surfactant during the first neonate´s breath has also been suggested in order to treat RDS in premature infants. Oropharyngeal surfactant is very recent and scarcely described in the literature, which entails that there is no EIT evaluation of its effect. Only indirect clinical management characteristics (such as reduced need for delivery room intubation) are available and the real effect should be verified by anatomical and functional EIT measurements in order to continue its evidence-based use. Currently, oropharyngeal surfactant is being recommended in conjunction with SI and EIT evaluation is also being used to prove that there is no way to predict the appropriate time SI is to be continued? in order to avoid excessive insufflation [50].

6. Conclusion

Our description of EIT studies in neonatal medicine puts it in a privileged place among clinical methods to assess ventilation details and evolution. The introduction of EIT, with its current and potential uses in newborn babies, has unique characteristics that support non-invasive management of these special patients. As Friedrich *et al*. concluded, this is the priority of EIT research: to establish clinical practices that may help to understand the newborn infant.

IOP Conf. Series: Journal of Physics: Conf. Series **1272** (2019) 012008 doi:10.1088/1742-6596/1272/1/012008

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