Chest electrical impedance tomography measures in neonatology and paediatrics – a survey on clinical usefulness

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Abstract.
Objective: Chest electrical impedance tomography (EIT) is currently applied in neonatal and paediatric patients mainly within clinical studies. The findings of these studies imply that lung monitoring using EIT provides valuable information on regional lung ventilation and aeration at the bedside that might improve the therapy and care of this fragile patient population. In view of this postulated future use of EIT in neonatology and paediatrics we have conducted an international survey to assess the perceived usefulness of several measures derived from EIT examinations. *Approach*: A questionnaire validating the clinical usefulness of 14 previously described EIT measures was designed and sent to 36 clinicians with previous experience with EIT in neonatal and paediatric patients. A numerical rating scale was used to assess the usefulness of each measure. *Main results*: 34 clinicians from 12 countries responded to the invitation and 32 filled in the questionnaire. The mean clinical and EIT experience (±SD) of the respondents was 19.4±9.1 yr and 7.7±5.8 yr, respectively. The top-rated measures were the global inhomogeneity index, silent spaces, change in end-expiratory lung impedance and ventrodorsal centre of ventilation. The bottom-rated were the regional respiratory time constant, tidal volume normalised to ml, respiratory rate and heart rate on the last rank. *Significance*: The survey revealed that EIT measures characterizing the ventilation and aeration distribution and the degree of their heterogeneity were deemed particularly useful. Respiratory rate, heart rate and overall tidal volume were considered less useful probably because these parameters are already routinely assessed by other conventional methods.

Keywords: EIT, electrical bioimpedance, respiratory system, lung, lung imaging

1. Introduction

Electrical impedance tomography (EIT) seems to be predestined for the clinical use in neonates, infants and children for the following reasons: EIT not only provides novel information on regional lung ventilation and aeration directly at the bedside that is not accessible to any other already established medical method but it also exhibits several features that make it particularly suitable for the use in patients at a young age. These features are mainly its non-invasiveness, radiation-free imaging and lack of need of patient´s cooperation.

Nonetheless, the use of EIT in neonatal and paediatric patients is still limited to only a few centres in the world. EIT has been applied there in the delivery rooms, neonatal and paediatric intensive care units, operation theatres and pulmonary function labs with the aim of monitoring regional lung function and examining its disease- and treatment-related changes. EIT has been used in neonatal and paediatric patients typically within clinical studies and not during routine care. The results of the published clinical studies show the potential of EIT chest monitoring in this patient population, as summarised in the recent consensus article (Frerichs *et al.*, 2017) and specifically highlighted in one of its online supplements dedicated to the EIT use in neonates, infants and children. The core patient population that might benefit from chest EIT are critically ill patients treated in neonatal (Chatziioannidis *et al.*, 2013; Miedema *et al.*, 2013; Rossi *et al.*, 2013; Hough *et al.*, 2014; van der Burg *et al.*, 2016) and paediatric intensive care units (Steinmann *et al.*, 2013; Wilsterman *et al.*, 2016; Lupton-Smith *et al.*, 2017). Children suffering from chronic lung diseases like cystic fibrosis or asthma (Lehmann *et al.*, 2016; Mueller *et al.*, 2018; Ngo *et al.*, 2018; Vogt *et al.*, 2018; Roethlisberger *et al.*, 2018), especially those in the pre-school age that cannot reliably perform conventional forced spirometric pulmonary function tests, represent another large patient group where EIT might become clinically relevant.

One of the reasons why the numbers of clinical studies in neonatology and paediatrics are relatively small compared with those in adult patients and why EIT is not routinely used in this setting yet was the unavailability of EIT devices approved for the use in neonates and infants by notified bodies. The introduction of devices certified for this specific patient population to the medical market and the availability of dedicated EIT electrode interfaces even for preterm neonates (Sophocleous *et al.*, 2018) can be expected to increase the clinical use. Another reason that still might be hampering the general use of EIT in the clinical setting is the lack of a consensus on the most adequate EIT measures needed for clinical decision-making. Although the recent consensus article on EIT (Frerichs *et al.*, 2017) provided a thorough summary and categorisation of EIT measures developed and used so far, it did not specify which parameters might be of particular relevance for the EIT use in neonatal and paediatric patients.

Therefore, we have conducted a survey among neonatologists and paediatricians active in EIT research with the aim of obtaining their personal assessment of multiple parameters that can be derived from EIT recordings.

2. Methods

2.1. Survey

Thirty six clinicians with variable degrees of experience with EIT from 13 countries were contacted by email. All of them have previously published articles on EIT use in neonates and children in peer-reviewed medical journals and/or participate in the currently running large clinical study on critically ill patients treated in neonatal and paediatric intensive care units (http://cradlproject.org). The authors of this article did not participate in the survey.

The contacted clinicians were asked to complete a questionnaire for evaluation of different EIT measures. The following 14 established EIT parameters were assessed: relative tidal volume ($V_{T\,rel}$), absolute tidal volume normalised to ml ($V_{T\,abs}$), ventrodorsal centre of ventilation (CoV_{vd}) and ventilation ratio (v/d), right-to-left centre of ventilation (CoV_{rl}) and ventilation ratio (r/l), change in end-expiratory lung impedance (ΔEELI), respiratory rate (RR), heart rate (HR), low tidal variation regions, i.e. so-called silent spaces (SS), regional respiratory system compliance ($C_{rs\,reg}$), global inhomogeneity index (GI), coefficient of variation (CV) and regional respiratory time constants (τ_{reg}). The questionnaire included a brief description of each parameter, based on the definitions provided in the consensus article on chest EIT (Frerichs *et al.*, 2017), and its possible clinical applications. Clinicians were asked to evaluate the EIT parameters on a numerical rating scale ranging from 0 (not useful) to 7 (very useful).

The questionnaire additionally collected the information on the primary clinical specialty of the respondents (neonatology or paediatrics) and on the overall duration of both clinical and previous EIT experience in years. Subgroups of less (≤ 5 years) and more experienced (> 5 years) clinicians and EIT experts were then formed.

The participants in the survey were prompted to provide a short comment on each of the assessed EIT parameters in an allocated space below the ranking scale. At the end of the questionnaire, they were also asked whether there was any other EIT parameter they would wish to obtain from EIT examinations in neonates and children. Finally, an option for providing 'other' comments was given.

2.2. Data analysis

Data are shown as mean values ± standard deviations. Histograms of the counts of each score´s numerical values were generated and the percentages of positive and highly positive ratings of each EIT measure calculated. The ratings of all EIT parameters were compared with the repeated measures ANOVA with Bonferroni´s test for multiple comparisons. The effects of the primary clinical specialty and the length of EIT experience on the ratings of each EIT measure were assessed by the unpaired t test. (The possible effect of the length of clinical experience was not statistically tested because of a very low number of less experienced colleagues participating in the survey, see below.) All statistical analyses were performed using GraphPad Prism 5.01 (GraphPad Software Inc., San Diego, CA, USA).

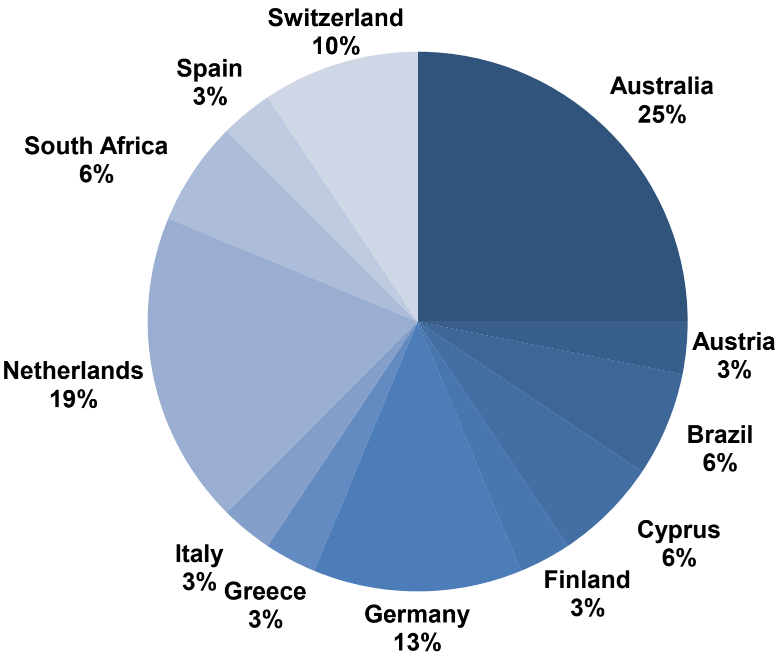

Figure 1. The countries of origin of 32 neonatologists and paediatricians who filled in the questionnaire on the clinical usefulness of EIT measures.

3. Results

3.1. Respondents

Thirty four clinicians responded to our initial invitation to fill in the questionnaires. Thirty two colleagues with a mean clinical experience of 19.4 ± 9.1 years and experience with EIT of 7.7 ± 5.8 years from 12 countries on four continents completed the questionnaire (figure 1). Twenty respondents came from Europe, 8 from Australia, 2 from Africa and 2 from South America. Two colleagues declined the invitation because of illness and cessation of working as a medical doctor. Two of the contacted colleagues did not react in spite of repeated invitations.

Sixty six percent of the colleagues who filled in the questionnaires specified neonatology as their primary clinical specialty, the rest were paediatricians (figure 2, left). The majority of the clinicians participating in the survey (91 %) had an overall clinical experience of more than 5 years (figure 2, middle). EIT experience of more than 5 years was documented by 56 % of the survey participants (figure 2, right).

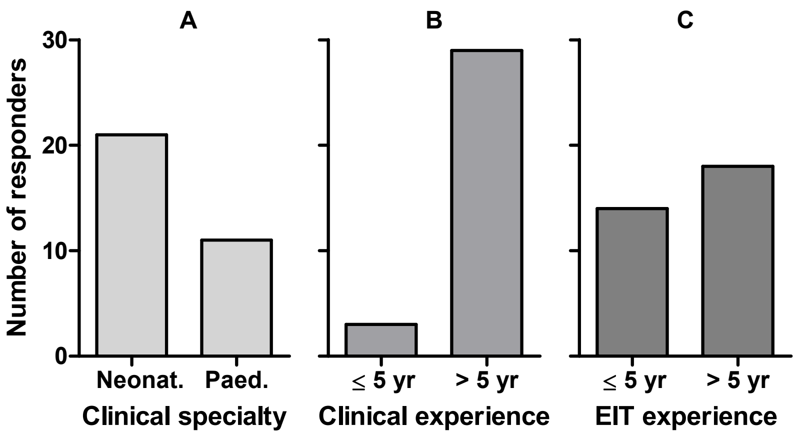

Figure 2. Numbers of respondents with the primary clinical specialty of neonatology (Neonat.) and paediatrics (Paed.) (A) with a short (≤ 5 yr) and a long (> 5 yr) clinical (B) and EIT experience (C).

3.2. Ratings

The ratings of the assessed EIT measures are summarised in figure 3. The scores differed significantly among the parameters ($p = 0.0001$) with the highest ones given to GI (6.28 ± 0.87), SS (6.16 ± 0.94), ΔEELI (6.16 ± 0.87) and CoV_{vd} (6.13 ± 1.45). The lowest rating was obtained for HR (4.19 ± 2.26, $p < 0.01$ vs. all rated parameters except for $V_{T\,abs}$). The other relatively low-rated EIT measures were RR (5.22 ± 1.93), $V_{T\,abs}$ (5.34 ± 1.81) and τ_{reg} (5.56 ± 1.56). There were no other statistically significant differences among the parameter ratings.

The clinical usefulness of all EIT parameters was consistently assessed as positive or even highly positive. The percentages of positive score values ranged from 69 % (HR) to 100 % (ΔEELI and SS) (figure 3). The percentages of highly positive score values were in the range of 31 % (HR) to 88% (GI).

The primary clinical specialty exhibited no effect on the ratings of the majority of the assessed EIT parameters. Only τ_{reg} was rated significantly more useful by the paediatricians ($p = 0.0185$) and CV showed a trend for higher scores ($p = 0.0655$) in the same group of specialists. The ratings were similarly not affected by the duration of EIT experience, except for v/d that was rated less positive by the clinicians with less years of EIT experience ($p = 0.0283$) and $V_{T\,abs}$ with a trend for worse ratings by the survey participants with more than 5 years of EIT experience ($p = 0.0750$).

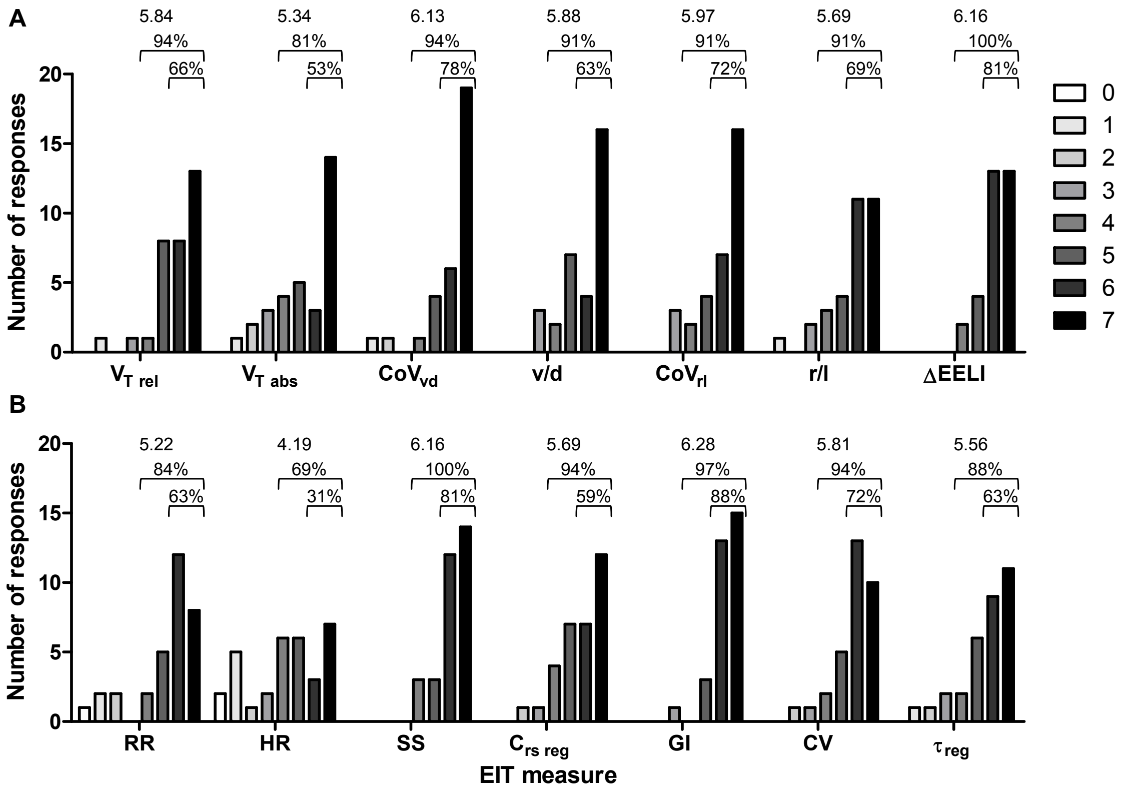

Figure 3. Assessment of clinical usefulness of EIT measures using a rating scale in the range of 0 (not useful, white columns) to 7 (very useful, black columns). The darker columns to the right of the ticks on the X axis imply clinical usefulness of the respective measure. The numbers above the columns in each panel show the average values of the ratings (top row) and the percentages of positive (middle row) and highly positive responses (bottom row). $V_{T\ rel}$, tidal volume determined by EIT in arbitrary units; $V_{T\ abs}$, tidal volume determined by EIT normalised to global tidal volume in ml; CoV_{vd}, centre of ventilation in the ventrodorsal direction; v/d, ratio of ventrodorsal ventilation distribution; CoV_{rl}, centre of ventilation in the right-to-left direction; r/l, ratio of right-to-left ventilation distribution; ΔEELI, change in end-expiratory lung impedance (A), RR, respiratory rate determined by EIT; HR, heart rate determined by EIT; SS, silent spaces, i.e. regions with low tidal impedance variation; $C_{rs\ reg}$, regional respiratory system compliance; GI, global inhomogeneity index; CV, coefficient of variation; τ_{reg}, regional respiratory time constant (B).

3.3. Comments

Thirteen out of the 32 participants in the survey provided additional hand-written or typed comments on the assessed EIT measures, specified which additional EIT parameters they would prefer to obtain and/or wrote some ‘other’ comments.

Four to six comments were provided for each EIT parameter. The comments regarding $V_{T\ rel}$ and $V_{T\ abs}$ pointed out that conventional V_T measurements in neonates ventilated invasively through uncuffed tubes were unreliable and that EIT might become a reliable alternative. One respondent considered $V_{T\ rel}$ to be “one of the most important EIT measures” whereas another one wrote that “$V_{T\ rel}$ change might be interesting as a trend but absolute reliable values are more interesting for real time titration”. One participant in the survey wrote that “$V_{T\ abs}$ would be most helpful for clinicians” but that he would be “extremely cautious to use it in clinical practice”. He continued that “one had to be careful to ’calibrate’ a chest slice as a representation of the whole lung” and that movement of a baby or changed body position would change the impedance characteristics and impact the value of $V_{T\ abs}$. This is in harmony with the comment of another respondent who mentioned that “$V_{T\ abs}$ would only be useful if there was sufficient data to confirm accuracy over a period of time (e.g. 4-6 hours)”. One participant in the survey raised the point of “reliability of both $V_{T\ rel}$ and $V_{T\ abs}$ assessment obtained from EIT examinations with electrodes placed in only one plane”. The clinical application of $V_{T\ abs}$ was considered “doubtful” by one respondent “because (transcutaneous) blood gases, like arterial partial pressure of CO_2, were more useful to monitor under/over-ventilation”.

The measures of ventrodorsal (CoV_{vd}, v/d) and right-to-left ventilation distribution (CoV_{rl}, r/l) received overall positive comments. CoV_{vd} and v/d were considered valuable mainly for the assessment of atelectasis, recruitment and positive end-expiratory pressure (PEEP) titration. One respondent mentioned that these measures were “easily understood by clinicians” and that both CoV measures “were critical for commercial EIT as they provided a simple trend measure of regional V_T distribution and also allowed for identification of adverse events (e.g. endotracheal tube malposition and airleak)”. The ability of CoV_{rl} and r/l to confirm suspected pneumothorax was described as “extremely useful” by another participant in the survey. One clinician added that more harmful chest X-ray was presently used to establish the pneumothorax diagnosis. Three colleagues commented that CoV_{vd} and v/d were similar parameters describing one phenomenon. Consequently, they recommended that only one of the two would be needed in the future. (CoV_{rl} and r/l received the same comment.) One participant in our survey wrote that “the larger the child, the more added value these parameters might deliver”.

Four comments were given on ΔEELI. Two respondents were convinced of the clinical relevance of this measure describing it as “very useful” and important for “guidance of recruitment manoeuvres at the bedside.” However, one participant in the survey wrote that he could “not figure out how much this index would help during ventilation” and another wrote that “intrathoracic fluid volume changes might make it impossible to quantify end-expiratory lung volumes” using this measure.

Regarding HR and RR it was stated that “ECG monitoring is standard” and that “other techniques like respiratory inductive plethysmography, electromyography and measurement of electrical chest trans-impedance through ECG electrodes are competitive to EIT”. Another participant in the survey pointed out that “whilst respiratory rate was measured accurately already in neonatal intensive care unit (NICU) using other systems, the ability to have less monitoring attached to a patient´s skin was desirable (and increased commercial viability of EIT systems)”. Two of the participants highlighted the importance of RR for the classification and therapy of apnoea, another one for the monitoring of spontaneously breathing or non-invasively ventilated patients. One colleague wrote that it would be desirable to have “reliable RR and HR data in the first couple of minutes after birth”.

SS received comments from five participants in our survey. One of them wrote that he expected SS to “guide clinicians during mechanical ventilation“ and show “if certain lung areas needed to be recruited or if a pneumothorax or chylothorax were present and if new air or fluid was accumulating”. Another noted that SS “might be useful since most other techniques were unable to detect these ‘silent zones’ of ventilation” although EIT might not cover the whole lung. One clinician considered SS to be useful “to confirm if the aims of used lung protective ventilation were fulfilled”. Although SS obtained only high scores, one comment implied that this parameter might need further refinement. This participant in the survey wrote that “from his experience, the clinicians understood this measure and found it very simple to visualize”. But he continued that "from his experimental and clinical observations he was not sure it was actually showing the clinically relevant information of whether a part of the lung was truly not engaging in much tidal change". The comment further implied that the availability of specific neonatal/paediatric reconstruction models might improve the value of SS.

The comments on $C_{rs\ reg}$ were interesting in the way that they all gave a positive feedback at the beginning but afterwards all of them mentioned potential limitations. For instance one respondent wrote that $C_{rs\ reg}$ "would surely revolutionise the way ventilation was optimised" but he warned of "possible pitfalls related to real time information and measurement accuracy". Another participant wrote that $C_{rs\ reg}$ was an excellent measure for research but "less important for clinicians since most neonatologists did not even know what to do with this value". The next respondent´s standpoint was that $C_{rs\ reg}$ would "provide a true point of difference over other monitoring systems. It would be useful even if just relative (e.g. one region-of-interest vs. another)". Finally one respondent correctly wrote that changes in $C_{rs\ reg}$ reflected changes in regional V_T if the pressure swings were identical in the EIT plane.

The two global measures of ventilation heterogeneity (GI and CV) received very similar comments. One representative comment stated that "these single-number measures were what clinicians really wanted at this stage for simple understanding of temporal changes in ventilation distribution. Whether this was GI or CoV did not really matter." One respondent commented that "these parameters were interesting but that there was some redundancy between them and the other rated measures". He continued that "having too many parameters might 'pollute' the interpretation of findings".

τ_{reg} was described as an "interesting measure for patient care and research" and even as "one of the most useful parameters". However, one respondent wrote that although he personally valued this measure "in reality, it was an 'expert' user parameter as most clinicians did not understand simple time constants". One participant in our survey wrote that τ_{reg} might be a useful parameter for avoiding intrinsic PEEP during mechanical ventilation.

The prompt to provide a comment on the need of any additional EIT parameters was followed by three participants in the survey, all of them paediatricians. (None of them provided any other comment on the other 14 EIT measures specified in the questionnaire.) They requested EIT measures allowing 1) the assessment of overdistension and collapse after each change in ventilator settings, 2) the early detection of pneumothorax and pulmonary interstitial emphysema and 3) the estimation of pulmonary perfusion and cardiac output.

The possibility to add 'other' comments at the end of the questionnaire was taken by four respondents. One paediatrician reported her positive experience with CoV and GI in ARDS patients and another one wrote down his wish to obtain EIT measures at various chest levels, i.e. also from apical and basal lung regions. One neonatologist commented that "she would have probably had more comments if her experience with EIT had been longer". Finally, one neonatologist pointed out that "clinicians would ideally need guidance on how to interpret all the EIT parameters". He gave an example of an alarm warning of a possible wrong location of the endotracheal tube.

4. Discussion

Our survey focused exclusively on the clinical use of EIT in neonatal and paediatric patients. The first clinical chest EIT studies in neonates and children were initiated in the mid-1990s, much later than those in adults. These were initially mainly case reports documenting the feasibility and safety of EIT examinations in neonatal and paediatric patients with the first unique findings in specific diseases and clinical situations (Taktak *et al.*, 1996; Frerichs *et al.*, 1999; Frerichs *et al.*, 2001). The latest studies have already been performed on larger groups of patients with more sophisticated study protocols and EIT data analyses (van der Burg *et al.*, 2015; Hough *et al.*, 2016; Lehmann *et al.*, 2016; van der Burg *et al.*, 2016; Bhatia *et al.*, 2017; Lupton-Smith *et al.*, 2017; Vogt *et al.*, 2018). These research activities are driven by the presumed benefit of EIT monitoring in neonates and children with potentially high clinical relevance. This was also documented by several reviews describing the EIT use in these patients (Pillow *et al.*, 2006; Frerichs *et al.*, 2008; Riedel and Frerichs, 2010; Reiterer *et al.*, 2015; Smallwood and Walsh, 2017; Frerichs *et al.*, 2017).

Several commercial and non-commercial EIT devices have been used in neonates and children up to now. EIT examinations were performed at different scan rates and with dissimilar electrode interfaces (single electrodes and electrode belts). The acquired data was analysed using the built-in graphical user interfaces and/or dedicated, study-specific software. The analyses were often carried out offline. A variety of EIT measures was calculated from the EIT recordings. However, as the EIT technology advances and its use in a true clinical setting beyond the clinical studies becomes more probable, there is a need to define which EIT measures are relevant for clinical decision-making. The first step in defining these essential measures is the feedback from the current users of EIT regarding the clinical usefulness of the measures used so far. To obtain these perceptions on EIT measures and their use in neonates and children with ratings, was the primary motivation for our survey.

The users of EIT in neonatology and paediatrics are a relatively small group of researchers/clinicians but they are a very active and dedicated group within the EIT community. This was also confirmed by the high response rate to our invitation to participate in the survey of 94.4%. The analysis of the filled-in questionnaires revealed that the participants valued mainly those EIT measures that assessed the distribution of ventilation and aeration and its heterogeneity. Therefore, the top ranked measures were GI, SS, ΔEELI and CoV_{vd}. The rankings of measures like HR, RR and $V_{T\ abs}$ that are already routinely derived from conventional monitoring were the lowest. However, as pointed out by one of the participants, if these measures were reliably provided by EIT then duplicate assessments by other techniques might become unnecessary. This might reduce the numbers of electrodes and other interfaces applied on the skin which is a relevant issue in preterm neonates and at birth.

The value and utility of the measures of regional respiratory system mechanics ($C_{rs\ reg}$ and τ_{reg}) was acknowledged but many respondents were concerned that these parameters might be too 'complicated' for the future clinical users without a research background. However, such supposedly 'difficult' measures need not be explicitly shown and communicated to the clinical personnel in the later routine EIT monitoring. For example, one of the participants in the survey commented that the knowledge of regional overdistension and collapse would be valuable feedback information for assessing the effects of changed ventilator settings. To determine the degree of relative overdistension and collapse during a PEEP trial, changes in $C_{rs\ reg}$ are typically calculated from the EIT recordings (Costa *et al.*, 2009) but the underlying calculations are not necessarily presented to the users.

Interestingly, τ_{reg} received higher ratings by the paediatricians. This might be related to the fact that older children are often treated for obstructive lung diseases where the utility of this measure of respiratory system mechanics might be more intuitive. In adult patients, the use of τ_{reg} for visualising the spatial heterogeneity of regional expiration in chronic obstructive lung disease has recently been documented (Karagiannidis *et al.*, 2018). CV as an overall measure of ventilation heterogeneity also trended to get higher scores by paediatricians which probably reflected the higher usage of this parameter in studies on regional lung function outside the NICU setting. Another difference between the perceptions of neonatologists and paediatricians was that only the participants with the latter specialty expressed their concern about EIT findings not being representative for the whole lung. This seems to be not the case in neonatal patients (van der Burg *et al.*, 2014). Therefore, only the paediatricians articulated their need of obtaining EIT information at several chest levels.

We have no clear explanation why the respondents with a short EIT experience rated v/d worse than those with a long one. CoV_{vd}, a measure with similar information content, was not assessed differently by the experienced and less experienced users of EIT. The trend to give higher scores to $V_{T\,abs}$ by the less experienced users seems to be easier to explain. These users prefer units (millilitre or litre) they are familiar with. They start to perceive the potential pitfalls of calibrating the EIT signal with the global volumetric measurements only with increasing expertise in EIT. This assessment is supported by some of the rather cautious comments regarding this measure requesting that the long-term reliability of $V_{T\,abs}$ needed to be proved.

Several comments of the respondents emphasised that the usefulness and clinical acceptance of EIT measures would decisively depend on whether the users of EIT technology were provided with adequate guidance how to interpret the findings. Thus, the essential issue is the generation of interpretation schemes for different EIT parameters and their combinations. Ideally, they should also take other clinical findings into account. As stressed by one of the participants in the survey, the clinicians need to be alarmed and trained that a highly asymmetric ventilation distribution might be indicative of a pneumothorax. Whether the alarm is triggered by CoV_{rl} or r/l or by a combination with other measures (e.g. ΔEELI) will depend on the underlying interpretation algorithm.

The comments of the participants in the survey also draw attention to the potential utility of some measures derived from the EIT recordings in detecting adverse events like endotracheal tube malposition and pneumothorax or other pathological findings with high ventilation asymmetry. Several published case reports seem to confirm the validity of this assessment (Frerichs *et al.*, 2005; Miedema *et al.*, 2011; Tingay *et al.*, 2018). The use of EIT in these situations might lead to faster finding of the proper diagnosis, treatment initiation and/or adjustment.

Our study has a few limitations that we wish to acknowledge. Although we successfully reached almost all clinical users of EIT in neonatology and paediatrics, the overall number of participants was still rather low. The individual assessment of the measures and the comments may have been influenced by the personal experience of the users with specific EIT technology. The users normally use the EIT devices of just one brand and are not familiar with other devices. This may have induced a possible bias toward measures offered by the device available in their department. Finally, to establish a set of clinically relevant EIT measures undeniably not only subjective clinicians´ assessments but also evidence-based data will be needed in the future.

5. Conclusion

A group of neonatologists and paediatricians with various degrees of experience with EIT have rated the clinical usefulness of a selected set of 14 EIT measures using a questionnaire. The ratings revealed that the parameters characterising ventilation and aeration distribution (GI, SS, ΔEELI and CoV_{vd}) were considered particularly useful for neonatal and paediatric patients. The free-text comments written by the participants in this survey provided additional valuable information on the advantages, drawbacks and possible future directions in neonatal and paediatric EIT research, clinical implementation and use.

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