

Improvement of lung damage and lung recruitment monitoring in mechanically ventilated IC-patients using Electrical Impedance Tomography and pH-assessment in Exhaled Breath Condensate

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Abstract

Background: Ventilatory induced acute lung injury is a major problem in mechanically ventilated patients, which can result in permanent lung damage and even in death for patients who did not have respiratory problems before they were mechanically ventilated. To limit the amount of lung damage it is of critical importance to set ventilatory parameters at optimal settings. In today's healthcare the extent to which these settings can be optimised is limited because monitoring of the lungs is very difficult. Improvement in lung monitoring can therefore help to reduce the incidence of acute lung injury and improve health in patients.

Objective: The objective of this report is to determine a way of monitoring the lung damage and lung recruitment in mechanically ventilated IC-patients to optimize ventilation parameters.

Method: A review of the literature in the databases of Medline/Pubmed and Scopus was performed, looking for the background of ARDS and Lung monitoring devices.

Results: Exhaled breath condensate (EBC) and electrical impedance tomography (EIT) appeared to be very promising lung monitoring techniques. pH-assessment in the EBC is a technique which allows to determine the pH of alveolar lining fluid. Studies show that pH has a correlation with the severity of lung damage. pH-assessment in EBC is a promising technique because it is fast, cheap, non-invasive and can be done continuously. There are however some studies that suggest that assessment of pH in EBC is not a reliable indication for lung injury. Despite that most of these problems can be circumvented EBC has not been widely used in IC-patients. Electrical Impedance tomography is a promising technique, with practical downsides for use on the intensive care. Its high temporal resolution can provide very useful information about regional ventilation distribution. If spatial resolution can be increased, there is great potential for a ventilation-feedback system.

Conclusion: The combination of EIT and pH-assessment in EBC is believed to be a promising one and is worthwhile to be investigated, especially with the progress that both techniques are undergoing.

Monitoring atelectasis and hyperinflation during mechanical ventilation using an application of the adaptive slice method (ASM).

Group 2: Alette Koopman, Dorien van Blooijis, Mathilde Hermans, Sytse de Jong

Abstract

Artificial ventilation has proven to be a life-saving method of therapy in intensive care for patients with respiratory failure. However, mechanical ventilation might also contribute to the morbidity and mortality associated with respiratory failure by causing the so-called Ventilator Induced Lung Injuries

(VILI). Until now, it is a challenge to monitor VILI in a decent way, which makes it hard to adapt the ventilator settings on this specific patient in order to prevent VILI. However, with the development of the SLICE method it might actually be possible to display the presence and severity of stress due to atelectasis and hyperinflation using dynamic compliance. In the future, this method might therefore be used as a guideline for ventilator settings, resulting in a reduced impact of VILI.

Providing the best mechanical ventilator settings by detecting NF- κ B and AP-1 with the IC-kit

Group 3: T. Kappers, P.J. Porte, J. van Sluis

Adult respiratory distress syndrome (ARDS) is a lung disease which develops in response to lung injury. Patients with ARDS have to be mechanically ventilated. The best way to ventilate and oxygenate patients with acute lung injury is controversial. Low and high tidal volumes both cause systemic inflammation of the lungs, which makes it hard to choose between these two ways of ventilation. Which way is best probably differs between patients. We try to find the best way of how to adjust the mechanical ventilation to the specific situation.

The goal is to develop a device which can determine what the best mechanical ventilator settings are. Possible markers to measure collapse and overdistension in the lung are AP-1 and NF- κ B. It is unknown which marker provides us with the best reaction of the severity of the inflammatory process, so a device for both markers will be developed. The amount of AP-1 and NF- κ B will be measured in lung macrophages. Lung macrophages are obtained by means of bronchial toilet. In these macrophages the activation of AP-1 is measurable after half an hour, the activation of NF- κ B is measurable after approximately one hour.

We will measure the markers with the IC-kit which makes use of immunochromatographic techniques and has the advantage that it can be used at the patients bed-side. With some adjustments to the original IC-kit it is possible to detect AP-1 and NF- κ B. The levels of the markers should give an adequate indication to provide good settings of the mechanical ventilator.

MONITORING TECHNIQUES TO ASSESS THE PATHOPHYSIOLOGICAL STATE OF THE LUNGS OF ARDS PATIENTS

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Keywords: EIT, Thermography, EVLW, ARDS, bedside, noninvasive

Introduction:

Acute respiratory distress syndrome (ARDS) is a severe problem in treatment of patients in the ICU due to the lack of possibility for individual treatment management and the fact that monitoring the relevant variables is still difficult for these patients. For this project knowledge of the clinical background, relevant clinical information and the mechanism behind ARDS is collected. To answer the clinical question "Is there a monitoring method, in current clinical practice or in the future, that

can help us determine the course of treatment for each acute respiratory distress syndrome patient individually?" several techniques will be reviewed.

Results:

The focus of this report was directed at several methods which could be applied at bedside, favourably non-invasive. In this report Electrical Impedance Tomography (EIT), extravascular lung water (EVLW) measurements and thermography are reviewed. EIT relies on the impedance properties which depend on the amount of fluid and ion concentration of the tissue. EIT measurements provide information on the ventilation of the lungs and could provide information about the EVLW. The gold standard for the measurement of EVLW is the double dilution indicator technique, however this is invasive. There are several thermographic monitoring techniques used in current clinical practice. The focus of this review is the possibility to locate the inflammation sites and atelectasis in the lungs due to the ARDS.

Conclusion and discussion:

Based on this report, it can be concluded that EVLW measurements can be implemented directly in the current clinical practice. The main disadvantage of this technique is that it is invasive, this can be avoided by using EIT to measure the EVLW, furthermore EIT also provides information about the ventilation of the lungs. However EIT is still experimental. Thermography is not yet applicable in current clinical practice due to several limitations. This might give possibilities for the future.

Ecmo as a solution for severe ARDS

Group 5: Jeffrey Benistant, Carmen van den Hoven, Dhabia Al Samarrai

Acute Respiratory Distress Syndrome (ARDS), a commonly found illness on the Intensive Care Unit (ICU), is often caused by mechanical ventilation. Positive pressure to keep the lungs open is accompanied by overloading of the lungs, causing extra damage and an increase of the severity of the ARDS.

In order to prevent further damaging of the lungs, an alternative to mechanical ventilation was researched: Extracorporeal Membrane Oxygenation (ECMO). ECMO is often used in infants, yet hardly ever in adults, because of the risks associated with its use. This study focuses on analysing these risks and potential preventive measures, to see if ECMO is a possible solution to the many patients encountering ARDS in the ICU.

Novel concepts for the quantification and localization of Ventilator-Induced Lung Injury in Acute Respiratory Distress Syndrome patients

Group 6: FC Bennis, BSc TM Fabius, BSc BJM Hermans, BSc F van Rosmalen, BSc

Abstract

Despite years of research, treating patients with acute respiratory distress syndrome (ARDS) is still difficult. Beside treating the underlying cause of ARDS, ARDS patients also need to be mechanically

ventilated which is challenging due to the heterogeneity of this disease. Mechanically ventilating ARDS patients can lead to ventilator-induced lung injury (VILI) which will damage the patients lungs even more. In this paper two novel techniques to quantify and localize VILI in ARDS patients will be discussed.

Quantification A technique for the quantification of the amount of VILI is to analyse exhaled nitric oxide (NO) at different tidal volumes (TV) and levels of positive end-expiratory pressure (PEEP). A component of NO is produced due to mechanical stress, which is interesting because it corresponds to the amount of VILI. Inhibition of iNOS is needed, as iNOS does not respond to mechanical stress. Some challenges for the development of this technique will be discussed. The most prominent problem with this is that two key factors, continuous exhaled breath condensate analysis and complete iNOS inhibition, are not available yet. A second problem is in which order PEEP and TV should be adjusted and whether one first increases or decreases the ventilator settings. Moreover, one could question the safety of the trial and error procedure for the patient. Another problem are the boundary values of the TV, PEEP and resulting oxygenation. The minimum and maximum acceptable values of these parameters have to be determined as the NO quantification will only take fast damaging processes into account. The final problem is to what extent eNOS and nNOS can produce more NO due to more mechanical stress or if the synthases have to be upregulated, which take longer.

Localization To determine optimal mechanical ventilation settings, a technique to estimate and localize the occurrence of overinflation and atelectasis can be useful. The most useful imaging tool in ARDS patients is computed tomography (CT). Daily CT examination however is not advisable, among others, due to high radiation levels. Electrical impedance tomography (EIT) is a new promising real-time continuous monitoring technique which might be helpful in treating ARDS patients. A major disadvantage of EIT is its poor spatial resolution. We will discuss a concept of a new imaging technique which combines ultrasound imaging and tomography in ICU patients. This concept might improve spatial resolution and so reduce EIT's limitations while maintaining EIT's major advantages. Overall sono-tomography may be a useful non-invasive monitoring technique to localize overinflation and atelectasis in ARDS patients. Until now however it is not entirely clear if it is technically possible. Furthermore the development and purchase costs of this technique will be high. There will be a future for sono-tomography only if the clinical relevance will compensate these costs.

Recommendations Both techniques might be useful in monitoring VILI in ARDS patients. However, both techniques are still in an early stage of development and more research has to be done. Our general recommendation is to do (animal) experiments to investigate the feasibility of both techniques.

Imaging ARDS with ultrasound joule heat tomography based on the acousto-electric effect

Group 7: X.L.R. Hoppenbrouwer, J.C. van Os, E.J. Vinke

Introduction Acute Respiratory Distress Syndrome (ARDS) is a syndrome due to injury or infection of the lungs and is characterized by inflammation. Mechanical ventilation is an important part of the treatment by recruiting the collapsed alveoli. Recent studies have shown that mechanical ventilation

can overdistend alveoli, resulting in a secondary lung injury known as Ventilator Induced Lung Injury (VILI). Ideally the regions and extent of atelectasis and overdistention are known to determine the optimal treatment. A promising technique to achieve this goal is Ultrasound Joule Heat Tomography (UJHT) based on the acoustoelectric (AE) effect.

Method UJHT is a technique based on a pressure-induced change in resistivity known as the AE effect. Additionally, UJHT encloses the inhomogeneity of the conductivity in the human body by using Joule Heat mapping. We examined the possible clinical applications for patients with ARDS in the intensive care .

Conclusion UJHT is a promising technique for body imaging, which should increase the spatial resolution in comparison with Electrical Impedance Tomography (EIT). In the future we see the application of UJHT similar to EIT combined with ultrasound. More studies are necessary, in particular to determine the differences in the AE effect in different tissues especially lung tissue.

Master track Medical Imaging and Intervention

Improving Time Efficiency of MRI- Guided Cryoablation of the Prostate by Reducing the Needle Placement Error

Group 8: R.F.M. van Doremalen, D. Lobeek and L.B. van den Oever

Cryoablation is one of the possible focal therapy treatments for prostate cancer. Focal therapy helps to preserve uninvolved prostatic tissue with the aim of preserving genito-urinary function. During cryoablation the needles are pushed into the prostate. Due to the elastic properties of the prostate, this results in needle deflection and prostate motion. Using multiple needles can result in relocation of the preceding inserted needles. This results in long procedure time before the actual ablation of the tumour tissue can occur. In this article, several methods are evaluated to improve time efficiency by reducing the needle placement error. One method discussed is anchoring the needle tip that can be used to minimize the relocation of the inserted needles. In addition, a controlled loop feedback model and a needle guidance device are suggested to minimize the needle misplacement. They can be used to calculate the error, correct the path of insertion and map the location of the needle tip. As a short-term solution, cryoanchoring can be used to reduce the relocation of the needles. As a long-term solution, the controlled loop feedback model could help to insert the needles efficiently. More research is required to implement these methods for a time efficient cryoablation procedure.

The application of nanoparticles to improve the outcome of cryoablation of prostate tumors

Group 7: Roy van den Ende, Esmée van Geffen and Thijs ter Mors

The very promising cryoablation treatment of prostate tumors is still in development. In our research the use of nanoparticles is investigated, the abilities to influence the shape of the ice ball and to reduce the damage to healthy tissue make it a very promising product. Two types of nanoparticles are discussed and compared. Microencapsulated phase change nanoparticles can be inserted into the healthy tissue to insulate this tissue from the freezing heat of the cryoablation. Also, conductive nanoparticles can be inserted into the tumor, by varying the concentration of these particles the freezing heat can be conducted in the desired direction to realize an ice ball that follows the shape of the tumor. In this way the chance of recurrence decreases and the damage to the healthy tissue is reduced.

A concept design of a closed loop MRI-feedback system for management of the ice ball in prostate cryoablation procedures.

Group 5: R. Poel, E.L. Leemans, I. Slouwerhof and T. van den Broek

Since cryoablation is a relatively new technique, there is not a lot of standardization in the procedure. The objective of this project is to formulate a concept for a novel closed loop MRI-feedback system for ice ball formation in combination with a planning modality. This feedback system eventually will improve the reproducibility and accuracy of the minimal invasive cryoablation procedure. The outline of the closed loop, the optimal MRI sequence, computerized comparison with the planning and the possible feedback mechanisms will all be addressed. Furthermore the influence of ice ball dynamics and essential safety issues will be discussed.

Combining cryoablation and laser ablation; the next step in focal prostate treatment

Group 4: S. Brinkhof, L.P. Karbaat, W.B.G. Sanderink, A. Zada

Introduction: Prostate cancer has a large prevalence (21%) in the Netherlands. Shortcomings in the existing techniques ask for a new option. In this article the combination of laser ablation and cryoablation is discussed.

Existing techniques: Current techniques are radical prostatectomy, cryoablation and laser ablation.

New possibilities: The combination of cryoablation and laser ablation are stated and problems arising when combining these two techniques are discussed.

Conclusion: The problems with combining cryoablation and laser ablation are almost solved, but a combination of all the solutions in one technique has to be subject of further research.

Simulation cryoablation during intervention

Group 3: Bruce Boti, Kay van der Hoogt, Arico Verhulst, Carrie Wismans

Keywords: Prostate Cryoablation, Simulation model, MRI, Intra-operative, Delineation tissue

Cryoablation has been an innovative technique to treat prostate cancer for the past decade. However cryoablation is still struggling with problems like unwanted tissue damage and incomplete tumor cryosurgery. Therefore a step forward would be a new type of protocol that would increase the understanding of the ice ball formation by an prediction during the operation. This could help the interventional radiologist to improve the procedure insight, leading to better clinical results. To reach this goal a proposal is made to combine the marking of tumor tissue within the prostate with a simulation of the ice ball formation during intervention in MRI. The result of this article is a description of a bioheat transfer simulation with an algorithm called Bubble Backing and a logistic regression model to delineate the tumor tissue in the prostate. At last, a proposal is made to combine these techniques to achieve clinical relevance.

MR-thermometry during cryoablation of a prostate tumor

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Key words: Prostate cancer , Cryoablation , UTE , MR-thermometry , Half pulse excitation , MRI

In the 2010, 2.593 males deceased in the Netherlands as result of prostate cancer as primary cause of death. Several ways of treatment exist of which one is a minimally invasive intervention, namely cryoablation. Excellent monitoring of the freezing process is an important criterion in order to perform successful cryoablation, so unnecessary damage is avoided and merely malignant tissue is ablated. MRI might be suitable for monitoring the freezing process, however currently available methods do not perform well in temperatures below zero degrees Celsius. This is mainly due to free proton spins being taken up into the ice crystals resulting in an extremely weak signal and an abnormal short T2. By applying a method that utilizes half-pulse excitations, ultra-short echo times (UTES) can be achieved and the drawback of the short T2 is accounted for. Assuming a linear dependency of $R2^*$, the inverse value of $T2^*$, on the temperature a real-time temperature map can be created. Furthermore, the technical hurdles, for example eddy current compensation which occur in the application of UTES will be addressed to and finally a personal opinion on the clinical feasibility of UTES for subzero thermometry will be given.

TARGETED DELIVERY OF TNF WITH CONJUGATED NANOPARTICLES: A WAY TO ENHANCE CRYOABLATION

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Keywords: cryoablation, PCa, TNF, targeted delivery, nanoparticles, mAb, CYT-6091, J591

Abstract Cryosurgery, frequently used as a treatment for PCa, creates an ice ball, which will destroy the tumor cells by direct cell injury. Although, for the PCa cells in the transition zone of the ice ball, cell death is unsure and therefore enhancement of cryosurgery is preferable. A new method will be discussed in this article, which will extend the kill zone up to the ice ball edge and simultaneously, cryoinjuries to surrounding critical structures can be avoided. Enhancement of the cryosurgery can be achieved when the cytokine TNF is present in the cancerous tissue. Three types of nanoparticles, as a deliver system for TNF, are discussed and four different mAbs as a target agent are investigated. CYT-6091 seems very suitable for delivery due to its promising properties and successful results of research *in vivo*. The same applies for the mAb J591, which consequently seems the most promising target agent for delivery into the PCa.