Journal of clinical monitoring and computing 2014 end of year summary: respiration

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1 Monitoring: endotracheal intubation

Endotracheal intubation allows a clear airway for positive pressure ventilation and protects the respiratory tract from aspiration of gastric contents. However, placing the endotracheal tube is difficult in some patients with the risk of damaging the airways. In addition, placing the endotracheal tube in the esophagus can occur with potentially fatal consequences. Three papers were published in Journal of Clinical Monitoring and Computing during 2014 on visualization of the airways during endotracheal intubation and for verification of correct placement.

Saricicek et al. [1] reported that tracheal intubation was successful with the GlideScope video laryngoscope (Verathon Medical, Bothell, WA, USA) in four patients with ankylosing spondylitis. Ankylosing spondylitis is a chronic, progressive and autoimmune spondyloarthropathy. Stiffness in the cervical spine and of the atlantooccipital, temporomandibular and cricoarytenoid joints make these patients particularly difficult to intubate successfully. Saricicek et al. concluded that the GlideScope video

laryngoscope can be a good alternative for oral endotracheal intubation in patients with ankylosing spondylitis, but that their study size was too small to elicit general conclusions regarding the GlideScope and intubation in ankylosing spondylitis patients.

Karippacheril et al. [2] reported use of a custom made, and less costly (40\$) alternative to commercial video laryngoscopes in 24 patients, including three patients with anticipated difficult airways. Using the system, the glottis could be visualized and the authors could perform endotracheal intubation successfully in all cases, in 22 of the patients in the first attempt. Mean duration of laryngoscopy was 22.17 ± 12.78 (7–59)s, and mean time for intubation was 28.58 ± 21.01 (9–89)s. The authors concluded that the custom-made device was safe and reliable for clinical use.

Goethals et al. [3] presented a novel device for faster and easier verification of placement of the endotracheal tube. The device consisted of a tactile sensor connected to the airway occlusion cuff of an endotracheal tube. The authors evaluated the device in a plastic tracheal model with ridges shaped similarly to tracheal rings. With the visual output of the device, it was possible to detect the presence of the ridges in the plastic tracheal model immediately upon inflation of the airway occlusion cuff. With the concept verified, the authors would aim future research at evaluating the device in in vitro models and clinical studies.

This paper reviews 21 papers published in Journal of Clinical Monitoring and Computing within the field of respiration. With an overall focus on monitoring papers were published covering endotracheal intubation, gas exchange, capnography, breathing and lung mechanics. Furthermore, several papers were published on decision support systems and simulation for mechanical ventilation.

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2 Monitoring: gas exchange

The primary function of the lungs is to allow efficient gas exchange of O_2 and CO_2 between alveolar air and capillary blood. Impairment in gas exchange as due to disease or injury to the lungs is an important indication for mechanical ventilation, and monitoring of gas exchange status

is important for correct setting of the mechanical ventilator. The primary cause of impairment in gas exchange in respiratory disease has been shown to be poor matching of pulmonary ventilation and perfusion, with one extreme being pulmonary shunt, that is a fraction of the perfusion of the lungs not reaching ventilated alveoli, and the other being dead space, which is ventilated but not perfused lung regions [4, 5]. Dead space can be serial or alveolar, with serial being further subdivided into the anatomical dead space, which is the upper parts of the respiratory tract, and the apparatus dead space, the increased dead space due to the ventilator circuit and monitoring devices. Traditionally, measurement of shunt and ventilation/perfusion mismatch has required invasive measurements and complex experimental procedures, but technological solutions for noninvasive determination of the matching of ventilation and perfusion in the lungs simple enough for bedside application have been emerging during the last few decades. Five papers were published in *Journal of Clinical Monitoring and Computing* during 2014 on physiological monitoring of gas exchange, with focus on measuring ventilation/perfusion matching and reducing apparatus dead space.

Electrical impedance tomography (EIT) is an imaging technique, which measures the distribution of ventilation or perfusion by injecting alternating current and measuring impedance over several electrode sets. Algorithms are used to reconstruct images of distribution of ventilation or perfusion, which may be provided with up to 100 frames per second thus providing a noninvasive means for monitoring the dynamics of breathing and heart activity [6]. Available EIT systems are based on several electrodes mounted on a belt, which is fastened around the thorax of the patient.

Czaplik et al. [6] investigated if it was feasible to base EIT on electrodes attached to an esophageal feeding tube and a tracheal breathing tube, both tubes being used (without electrodes) in most mechanically ventilated patients and therefore representing convenient locations for EIT electrodes. Czaplik et al. compared time domain impedances and reconstructed lung shapes, and the separation of heart and respiration related signals in the frequency domain, measured by these internal electrodes with measurements using a standard electrode belt mounted on the thorax. The comparison was performed in seven mechanically ventilated pigs, with the pigs being randomized into one of four groups: acutely injured or healthy lungs with either a ventilator pattern with an end-inspiratory plateau or not. The authors found impedance values showing reasonable electrical contact was achievable but with increased standard deviations requiring improvement in the design. Results also showed that internal electrodes potentially leads to higher sensitivity in detecting cardiac-related signals. The authors concluded that use

of internal electrodes appeared to be reasonable and effective, and that future studies should address safety, feasibility and reliability of the approach.

Karsten et al. [7] evaluated two bedside technologies, EIT and exhaled nitric oxide (NO), for monitoring lung status in 24 patients with community-acquired pneumonia. The exhaled NO test consists of the patient inhaling NO free air to near total lung capacity followed by one or more exhalations at constant flow, with the measurement result being used for assessment of airway inflammation. Karsten et al. evaluated both single breath and multiple breath exhaled NO tests, and showed that both methods were significantly correlated and able to show a significant decrease in NO after beginning of antibiotic therapy. EIT was measured using an electrode belt fastened around the patient's thorax. EIT based detection of right-sided and left-sided ventilation disorders was in correspondence to chest X-ray at admission and 5–6 days following admission. The authors concluded that exhaled NO could be used as an individual trend parameter to describe local lung inflammation whereas EIT could be a useful tool to monitor functional lung status in patients with community acquired pneumonia.

It has previously been shown, that shunt and ventilation/perfusion mismatch can be estimated non-invasively at the bedside by mathematical model-based analysis of expired oxygen versus steady state arterial oxygen saturation following 3–5 variations in inspired oxygen fraction [8, 9]. These models have traditionally been two compartment [8] or three compartment models with perfusion distribution locked [9], with a compartment representing shunted blood and one or two compartments representing ventilated and perfused compartments with varying ventilation/perfusion matching. Lockwood et al. [10] analysed whether inclusion of three compartments in a model and variation of both ventilation and perfusion distribution were accurate in comparison to a two compartment model. The two models were compared for their description of 24 exact datasets of oxygen gas exchange generated by a separate mathematical model and three collections of data sets with added noise and removal of data points at the lower level of oxygen saturation. Analysis using the three compartment model was more accurate and less affected by removal of data points as compared to the two compartment model. Extreme values of cardiac output resulted in significant errors if assumed values of arterial to venous oxygen difference were inaccurate. The authors concluded that the resulting model parameters may have value as objective measures of gas exchange and for guiding oxygen therapy.

The achievement of steady state oxygen gas exchange after variations in inspired oxygen fraction, as necessary for existing methods for model based estimation of shunt and ventilation/perfusion methods normally requires a few

minutes for each variation in oxygen giving a total examination time of around 10–15 min [9]. Time to steady state may be prolonged in patients with chronic obstructive pulmonary disease (COPD) further extending the required examination time. Thomsen et al. [11] investigated if breath by breath changes in expired oxygen and pulse oximetry can be used as a more rapid alternative to measure gas exchange status. The authors compared the breath by breath method with the steady state method using data from 14 patients diagnosed with COPD. Estimated model parameters of shunt and ventilation/perfusion mismatch were similar for the two methods indicating that the breath by breath method may be used in COPD patients for more rapid assessment of shunt and ventilation/perfusion mismatch from variation in inspired oxygen.

The measurement of tidal volume to monitor lung mechanics in preterm infants is commonly performed using a flow sensor, which increases the apparatus dead space and may impair gas exchange [12]. Proquitté et al. [13] evaluated in 14 newborn piglets, how an endotracheal tube with reduced dead space but without the option of conventional volume monitoring, affected oxygen and carbon dioxide gas exchange. Improvement was seen in arterial partial pressures of CO₂ and O₂ in the smallest piglets (weight <900 g), however improvement was only modest and the authors concluded that it could not justify the waiving of volume monitoring.

3 Monitoring:capnography

The Journal of Clinical Monitoring and Computing has featured several articles in 2014 focused on capnography including one paper on its use during high frequency oscillatory ventilation (HFOV) [14] two papers highlighting two clinical scenarios and the importance of interpreting capnograms in clinical context [15, 16] and a technically oriented paper that highlights some of issues and tradeoffs with the design and testing of a mainstream capnometer [17]. As these papers and others published in the past in this journal have illustrated, the application of capnography, time and volumetric, are varied [18] and the clinical use of capnography is growing being driven in part by recent changes expanding the use of capnography in the ASA basic monitoring during anesthesia standards [19] and AHA CPR guidelines [20].

Hartdorff et al. presented their bench study of the feasibility of using a commercially available mainstream capnometer placed in the expiratory limb of a breathing circuit for clinically relevant measurements of changes in carbon dioxide during HFOV (rates between 5 and 15 Hz) [21]. This is the latest publication to consider the feasibility of using capnography during HFOV. Due to the highly

dilutional nature of HFOV given the high rate and negligible tidal volumes, the measured level of carbon dioxide are very low relative to the normal values of end-tidal carbon dioxide (35–40 mm Hg) and tend to vary little between delivered oscillations. For example, an average carbon dioxide flow rate (or elimination) of 250 ml/min results in a carbon dioxide value (not end-tidal) of approximately 8 mm Hg. The application of mainstream capnography to HFOV is technology dependent and is related to the resolution, accuracy and linearity of the device at these lower carbon dioxide levels. Additionally, the ability to use capnography for this measurement is dependent on how much carbon dioxide is eliminated (i.e. patient size dependent) with 150 ml/min or approximately 30 kg estimated as the low end for HFOV in this study. Hopefully, this study and others will encourage the manufacturers of mainstream capnometers to considering adding this software functionality as perhaps a waveform averaging mode.

In a letter to the editor, Vinay et al. [15] present in the form of a case report a warning about an abrupt and apparently artifactual reduction in end-tidal carbon dioxide readings during neurosurgery when using low flow rate side-stream capnography. The abrupt change in carbon dioxide (28–9 mm Hg), it was reported, was not associated with changes in blood pressure, heart rate or amplitude of the photoplethymographic waveform. It appeared to be associated with condensate in the sampling tube leading to increased resistance and lower pump sampling rate. This was reported to be rectified by one or more of several actions including purging the sample tube, and recalibration/zeroing. This letter highlights the need as pointed out by the authors and associated with good practice to always interpret changes such as these in context with clinical observation.

In a case report, Singh et al. [16] report on one example of the difficulties associated with interpreting changes in waveform shape. In this case, a small dip during the expiratory phase of a capnogram was initially classified as a potential curare cleft. It was noted that increases in the IPPV rate caused the waveform to quickly appear “normal” while decreases, that is return to the earlier settings, cause the artefact to reappear. This change appear to be related to the particular clinical and equipment circumstances in this case and highlights the need for better and more quantitative criteria for assessing potential artefacts such as this, perhaps in the form of improved analysis capability embedded in the software of monitoring devices.

Yang et al. [17] describe some of the technical aspects associated with their design of mainstream capnometer and the human testing of the same capnometer design. This design of an infrared based capnometer using pyroelectric detectors measures, as most do, how much radiation is received after passing through the gas sample using a data

channel, sensitive to the presence of carbon dioxide (center wavelength typically 4.26 micron), and a reference channel, not sensitive to the presence of carbon dioxide (center wavelength in this case 3.95 micron). As an aside, such designs typically measure the received radiation with one of three detectors types, photoconductive, pyroelectric, or thermal (thermopile) detectors, each with its respective advantages and disadvantages including cost, response speed and signal to noise. As with any sensor-design choices influences overall performance. The authors describe tradeoffs in their design including (a) selecting a sampling frequency to optimize CO₂ concentration precision and waveform fidelity and (b) the application of linear and nonlinear digital filtering approaches including median filtering to improve the signal quality. Additionally, they report comparative waveform test data from measurements with small number of healthy volunteers and patients with COPD, which they repeated over the following 4 days latter to assess repeatability. Although more technical in nature and most readable to those versed in the physics of infrared spectroscopy, this paper highlights the nature of the tradeoffs that much be made and complexity in the design of such measurement devices that we all depend on in the clinical environment.

4 Monitoring:breathing and respiratory mechanics

Monitoring of respiratory mechanics is necessary during mechanical ventilation as positive pressure ventilation, although live-saving, can be deleterious to the lung tissue if high volumes or pressures are applied [21]. Monitoring of the patient's breathing effort is important for maintaining respiratory muscle activity and preventing hypoventilation and apnea during supported modes of mechanical ventilation, even more so when the patient is sedated as is common during surgical procedures. Four papers were published in Journal of Clinical Monitoring and Computing during 2014 on physiological monitoring of breathing and respiratory mechanics.

Tanaka et al. [22] compared the accuracy of acoustic monitoring, capnography and clinical observation for detection of respiratory pauses during sedation. Acoustic monitoring was performed using an adhesive acoustic respiration sensor placed on the patient's neck and connected to a Pulse CO-Oximeter with Rainbow Acoustic Monitoring (Rad-87, software v. 7805, Masimo Corp., Irvine CA, USA). The data set contained measurements from 20 patients undergoing surgical procedures with 51 respiratory pauses verified by retrospective analysis by a clinician. Sensitivity, specificity, and likelihood ratio positive for detection were 16, 96 %, and 3.5 for clinician observation; 88, 7 %, and 1.0 for capnography; and 55, 87 %, and 4.1 for acoustic monitoring. The authors found no correlation between respiratory pause events and the patient state index, a brain function index for assessment of depth of sedation. Based on the

likelihood ratios, the authors concluded that acoustic monitoring was the best method for respiration monitoring during the observed procedures.

In a letter to the editor, Ramsay stretched, in reference to the work of Tanaka et al. [22], the importance of finding a robust and friendly technology for detecting apnea [23]. Currently, breathing is mainly monitored by pulse oximetry and capnography, which each have known limitations. Pulse oximetry must be monitored continuously for timely detection, and its ability to detect apnea is affected by administration of supplemental oxygen. Capnography is often measured using a nasal cannula, which many patients do not tolerate well, and the value of end-tidal CO₂ depends on adequate mixing of expired and alveolar air which may not occur during hypoventilation [23].

In a letter to the editor, Ganigara and Ramavakoda proposed that the endotracheal tube cuff pressure waveform might have potential in airway pressure monitoring, although little description can be found in the literature of this measurement [24]. In their institute, the authors use traditional pressure transducers to provide measurement of the cuff pressure in the operating theater, and report the waveform to have a sine wave appearance at lower cuff pressures and to closely follow the capnograph. Ganigara and Ramavakoda argued that further studies are needed to investigate the possible utility of this waveform.

Buehler et al. [25] presented a graphical user interface (GUI) for visualizing within breath (intratidal) lung mechanics and supporting titration of positive end-expiratory pressure (PEEP). The intratidal lung compliance-volume curve was calculated using the gliding slice method [26], which is based on piecewise solution of the equation of motion on collected flow and airway pressure. The gliding-SLICE method and earlier versions of the technique has been analysed in several previous studies. The GUI shows an automatic classification of the compliance-curve to identify if the curve represents under distended, over distended or well distended lungs. The identification of the appropriate shape category, if valid, can be considered decision support for PEEP, as the PEEP associated with the appropriate degree of distention should be least damaging to the lung tissue. The authors presented a proof of concept, with two patient examples showing intra-tidal compliance-volume curves and their shape categories for various PEEP levels. The authors intend to use the GUI for use in an intensive care unit and in animal studies.

5 Decision support systems and simulation for mechanical ventilation

The ARDSNet trial of 2000 highlighted the critical role of correct management of mechanical ventilation showing

that mechanical ventilation with low tidal volumes was associated with significantly lower mortality compared to high tidal volumes in patients with acute respiratory distress syndrome [27]. However, studies have shown that clinical practice is slow to implement the findings of clinical studies [28], and large variations in care exist between experienced clinicians [29] indicating need for tools for supporting the attending clinician in making decisions at the bedside and also for optimizing the training of clinicians for mechanical ventilation. Five papers were published in *Journal of Clinical Monitoring and Computing* during 2014 on decision support systems and simulation for mechanical ventilation.

Banner et al. [30] evaluated an open-loop, rule-based, decision support system for its advice in comparison to the settings selected by attending clinicians in 117 patients in pressure support ventilation. The system collected measured inspired oxygen, PEEP, pulse oximetry oxygen saturation, plateau pressure, and mean arterial pressure and propose advice automatically on decreasing, maintaining or increasing inspired oxygen and PEEP to keep measured values within predetermined ranges. For each advice from the system, attending clinicians were asked to evaluate inspired oxygen and PEEP according to clinical practice, blind to the advice of the system. A total of 326 recommendations were made by the system. The system was able to detect occasions of unsafe levels of plateau pressure and mean arterial pressure. Agreement rate was 92 % between the system advice on direction of change in settings and decisions by attending clinicians. Assuming that magnitude of change following system recommendation would have been 10 % for inspired oxygen and 2 cm H₂O for PEEP, system recommendations were significantly correlated to values selected by attending clinicians.

Wysocki et al. [31] gave in their review a short overview of closed loop mechanical ventilation, which in contrast to open loop decision support systems execute the advice without an attending clinician first reviewing the advice. Wysocki et al. present three levels of sophistication of closed loop systems. Simple closed loop represents standard mechanical ventilation modes, i.e. pressure and volume regulated modes. More sophisticated systems are based on physiological signals, these being Proportional Assist Ventilation (Puritan Bennett ventilators), Neutrally Adjusted Ventilatory Assistance (Maquet ventilators) and Adaptive Support Ventilation (Hamilton ventilators), which all require decisions of the clinician such as degree of support. Yet more sophisticated are explicit computerized protocols, which have built in decisions based on measured values often in the form of rules. Examples of commercial explicit computerized protocols are SmartCare (Dräger ventilators) and IntelliVent (Hamilton Ventilators). The focus of SmartCare is weaning, and the system has been

shown to reduce weaning time significantly compared to usual care. IntelliVent adjusts minute ventilation, PEEP and inspired oxygen based on user adjustable targets, and have been evaluated successfully in pediatric and adult patients. The authors conclude, that further studies are necessary to assess the impact of closed loop mechanical ventilation on clinical outcomes and cost-utility.

Schädler et al. [32] evaluated a novel combined open and closed loop decision support system for automated weaning from mechanical ventilation. The system includes models of gas exchange and lung mechanics to simulate effect of changes in settings on physiological target values. The physiological targets are defined by rule tables or by the attending clinician. The system automatically adjusts pressure and respiratory rate and gives open loop decision support for inspired oxygen. The system was prospectively evaluated in 19 postoperative patients, where the system automatically adjusted the ventilator settings until patients were extubated or the system provided no significant changes to settings. The majority of patients were ventilated without violating the safety limits of the system. A comparison of system suggestions at the start of the protocol to settings selected by attending clinicians showed that the system in general ventilated patients at higher respiratory rates and lower tidal volumes. Overall, authors concluded that the system was stable, and able to safely ventilate patients by decreasing the respiratory load of mechanical ventilation.

Application of physiological models at the bedside present certain challenges, as the models should be accurate but identifiable from clinically available measurements whilst being computationally feasible. Kretschmer et al. [33] presented a proof of concept for using a simplified cardiovascular model in a framework of models of gas exchange, respiratory mechanics and cardiovascular dynamics for use in decision support of mechanical ventilation. The simple beat-to-beat model was compared to two compartmental models based on differential equations with 3 and 19 compartments, respectively. The beat-to-beat model and the 3 compartment model were parameterized to simulate the behavior of the 19 compartment model. Computing time improved by a factor of 186 for the beat-to-beat model compared to the 19 compartment model. Blood pressures were calculated with a maximum deviation of 1.8 % in systolic pressure and 3.5 % in diastolic pressure, leading to a simulation error of 0.3 % in cardiac output for the beat-to-beat in comparison to the 19 compartment model. The gas exchange submodel of the framework showed deviations in simulated output of less than 0.1 % indicating that the error in simulated cardiac output had little effect. The authors therefore concluded that the proposed beat-to-beat simple cardiovascular model was usable in combinations where cardiovascular simulation does not have to be detailed.

As opposed to bedside application of models, use of mathematical or mechanical models for simulation in medical training has the purpose of producing signals that closely mimics the dynamical signals at the bedside, requiring and allowing use of models of high complexity. Baldoli et al. [34] presented a novel high fidelity simulation system for medical training in neonatal mechanical ventilation. The system consists of five chambers with variable volumes connected to a mechanical ventilator with individual sensor and individually controlled pistons to simulate different compliances and resistances of pulmonary lobes. In addition, the system comprises a laptop with a dedicated user interface for controlling the system and presenting simulation scenarios. In the paper, Baldoli et al. presented as proof of concept a single chamber implementation of the system, with which they performed three clinical simulation scenarios: spontaneous breathing, controlled mechanical ventilation and assisted mechanical ventilation.

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