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Book of Abstracts

Nautilus : a new compact E.C.G based guidance system dedicated to real-time correct positioning of the tip of central venous catheters

Şerban Bubenek, Ion Miclea

" Carol Davila" University of Medicine Bucharest. 1-st Cardiovascular Anaesthesia and Intensive Care Dept. of "C. C. Iliescu" Emergency Institute for Cardiovascular Diseases Bucharest – Romania

e-mail : bubenek@alsys.ro

Abstract

Background : Endo-cavitary electrocardiography (EC- ECG) is a well recognized method for controlled placement of central venous catheters (CVC).

The aim of this study was to assess the accuracy, feasibility and safety of a new and compact EC-E.C.G based guidance system (Nautilus®, S.C.Romedex International-Romania) dedicated to real-time correct positioning of the tip of CVCs.

Method : After obtaining institutional ethics committee approval and written informed consent, 30 consecutive adult patients who had malignant diseases and were scheduled for CVCs placement procedures (implantable ports) were included in this study.

Patients with P-wave abnormalities, arrhythmias, or pace-makers were excluded.

The Nautilus® system is a new device, build "al in one "(custom laptop with integrated ECG data acquisition module and its own software) which displays simultaneously both the surface ECG and the EC-ECG and allows freezing of the screen as well as printing and recording the data. Under local anaesthesia and using ultrasound guidance, thirty subclavian vein catheterizations were performed (26 left side and 4 right side).

Then, using the Nautilus system together with its dedicated saline (24 patients) or electric (6 patients) adapters, the CVCs were gradually advanced into the venous system during real time display of EC-ECG (lead II) and surface ECG (lead III), chasing the P wave changes on the EC-ECG, until a typical giant P wave (as high as the QRS) appeared. Because of the large consensus on the fact that the tip of a long-term CVC dedicated to chemotherapy should be positioned preferably inside the lower third of the superior vena cava or in the neighborhood of the cava-right atrium junction (CAJ), we left the tip of the CVCs at the supposed CAJ level, as shown on EC-E.C.G : the tallest positive P wave. At the end of the procedure, the tip position was verified by a chest x-ray and the equivalence between the EC-ECG method and radiology has been reviewed by a radiologist.

Results : The EC-ECG method was able to show typical giant P waves in all 30 patients. We found also that the CAJ position as determined on the EC-ECG was confirmed by the control chest x-ray in 100 % of cases. No adverse events or complications were noted.

Conclusions: In our study, the EC-ECG method provided by the Nautilus® system was easy to use, safe, feasible and accurate for real-time correct positioning -at the CAJ level- of the tip of subclavian vein introduced implantable ports.

Keywords : **:** endo-cavitary electrocardiography, real-time correct positioning of the tip of central venous catheters, new compact guidance system

Prognostic models in the ICU: From development to clinical practice

Lilian Minne, Dave Dongelmans, Saeid Eslami, Sophia de Rooij, Evert de Jonge, Ameen Abu-Hanna

Department of Medical Informatics, Academic Medical Center, Amsterdam, the Netherlands

Introduction

In the Intensive Care Unit (ICU) clinicians are faced with difficult decisions regarding provision of life support. End-of-life decision-making is perceived as a heavy burden and prognostication is the part of medical practice they feel most insecure about [1,2]. Survival predictions made by mathematical models may add to what clinicians already know and thereby have the potential to improve clinical decision-making. Clinicians do not always trust the models, however, due to lack of evidence about: their clinical credibility (e.g. the use of clinically relevant variables and refraining from adding unnecessary complexity); external validity (i.e. accuracy and generality) especially for their use in individual patients; and clinical effectiveness (i.e. their impact on patient outcomes) [3].

The aim of our work is to study optimal prognostication in the ICU and the role prognostic models can play in the care for (elderly) ICU patients. Specifically, we address: development and validation of prognostic models; acceptance and perceived needs of models by clinicians; comparison of predictive performance with clinicians; investigation of the models' fitness for clinical use; and their ability to alter individual patient decisions.

Methods

To get an overview of the field, we systematically reviewed literature on prognostic models of mortality and/or survival in the ICU and assessed their clinical credibility, validity and impact in clinical practice. To understand behaviour of predictive performance over time we used Statistical Process Control to monitor the discrimination, calibration and accuracy of two existing prognostic models: a recalibrated Simplified Acute Physiology Score-II (SAPS-II) model and a classification tree built for ICU patients aged >80 years.

To assist clinicians with making decisions about individual patients we built prognostic models that provide a prediction of mortality on each day of ICU stay. We first discover frequent temporal patterns in Sequential Organ Failure Assessment (SOFA) scores. SOFA scores were categorized as low (*L*) if SOFA $\in \{0, \ldots, 6\}$, medium (*M*) if SOFA $\in \{7, 8\}$ or high (*H*) if SOFA $\in \{9, \ldots, 24\}$. The pattern *M,H* means a medium score on day x followed by a high score on day $x+1$. Second these patterns were used as candidate predictors of hospital mortality along with the following candidates: day of prediction, SAPS-II, SOFA, type of admission, number of readmissions, and interactions of admission type and number of readmissions with the other variables. Predictive performance (discrimination, calibration and accuracy) was compared to that of physicians and a recalibrated SAPS-II model.

To understand how clinicians make end-of-life decisions and understand the possible role of objective models we observed daily clinical conferences in two hospitals; sent questionnaires to intensivists of three centres regarding their view on this process and their attitude towards objective prognostic models of mortality; and designed a study in which attending physicians of patients who died after deciding to stop treatment receive objective predictions of mortality of that patient. We will measure the effect of this additional information on how sure they feel about their decision and their perception of the survival chance by asking the same set of questions before and after they received this information.

Results

We found 7 studies describing 17 ICU models published between January 1966 and June 2010. We found that the use of these models in clinical practice is still very premature as their clinical credibility is moderate, the models are rarely cited or (externally) validated by others and their impact in clinical practice was not studied. The predictive performance of the classification tree and SAPS-II gradually decreased in a prospective validation set of 12,143 patients taken from the same centres for which the models were developed. The tree was less sensitive to changes in case-mix than SAPS-II, but both of them regained their original performance after repeated recalibration.

Temporal models achieved the same level of performance as physicians. For the last part of our work we built a prognostic model aimed at the individual patient level on a dataset of 5,935 patients with a total of 27,853 admission days. Model performance in terms of discrimination and calibration was comparable to that of physicians and better than SAPS-II.

We observed that end-of-life decision-making during clinical conferences is poorly structured and decision-making elements are mainly considered outside the conference. Physicians wish to receive additional objective information regarding their patients' chances of survival, but a minority does not trust this information.

Discussion

There is room for improvement of the end-of-life decision-making process and inter-collegial communication. Objective prognostic models may have the potential to improve the end-of-life decision-making process, but their use in clinical practice is still very premature. Future work should assess their possible role and their impact on clinical decisions and patient outcomes.

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Comparison or different statistical models for Intensive Care length of stay

I.W.M. Verburg MSc, N.F. de Keizer PhD, N. Peek PhD

Department of Medical Informatics, Academic Medical Center, University of Amsterdam, the Netherlands

Introduction Intensive Care Units (ICUs) are increasingly interested in assessing and improving their performance. Since ICU patients receive complex care, costs are high and hospitals face continuous pressure to both improve quality and reduce costs. Until now benchmarking has been used in the process of continuous quality improvement in ICUs, often using hospital mortality as an indicator for ICU quality. Benchmarking is less frequently used to compare efficiency among ICUs. Since Length of Stay of ICU patients (LoS) is related to ICU costs it can serve as a marker for efficiency. To compare LoS between different hospitals, one should adjust for differences in case mix. However, only few models exist to predict case mix adjusted LoS and no consensus exists which method should be used to model LoS for benchmarking purposes [1-3]. The aim of this study was to compare the performance of different statistical regression methods to predict LoS for unplanned ICU admissions.

Methods The Dutch National intensive Care evaluation (NICE) quality registry records data from intensive care patients in the Netherlands, including severity-of-illness data from the first 24h of ICU stay, and outcomes such as mortality and LoS. This study used data from admissions between January 1st, 2009, and December 31st, 2011 from 84 ICUs. All patients satisfying the APACHE IV inclusion criteria were included, excluding patients that underwent elective surgery. As the distribution of LoS and the association between patient variables and LoS differs between survivors and non-survivors, separate models were developed for these two groups of patients.

The distribution of LoS is highly skewed. Models which are available in literature often make use of Ordinary Least Squares (OLS) regression of LoS or OLS regression of log-transformed LoS. Theoretically, these are suboptimal choices. In this study we compared OLS regression of LoS and of log-transformed LoS with Generalised Linear Model (GLM) regression with Gaussian, Gamma, Poisson and negative binomial distribution families and a logarithmic link function, and with Cox proportional hazards (PH) regression. LoS was defined as the number of fractional days spent at ICU. Each model started with a set of variables known to be associated with LoS [1;4]. Subsequently, the models were simplified by stepwise backwards elimination of variables. Several performance measures were used to evaluate each model's ability to predict LoS, being the squared Pearson correlation coefficient (R^2), the root mean squared prediction error (RMSPE), the relative mean absolute prediction error (relative MAPE), and the relative bias (mean difference between predicted and observed LoS divided by mean observed LoS). In general, good predictions yield low values for the RMSPE, the relative MAPE and the relative bias, and high values for the R^2. All performance measures were calculated on the same dataset which was used to develop the models, and afterwards corrected for optimistic bias that was estimated from 100 bootstrap samples [5].

Results From January 1st, 2009, until December 31st, 2011, 222,529 ICU admissions were recorded in the NICE database. After applying all exclusion criteria, 94,251 (42.4%) admissions remained. Of these, 81,190 (86.1%) survived ICU stay and 13,061 (13.9%) died.

Performance statistics for each of the models are shown in the table below. GLM models showed the best performance, while the Cox PH model had poorest performance. The model based on OLS regression of log-transformed LoS had a large relative bias. All models showed better results for survivors than for non-survivors, especially for R^2 and the relative bias.

	ICU survivors				ICU non-survivors			
	R^2	RMSPE	relative BIAS	relative MAPE	R^2	RMSPE	Relative BIAS	relative MAPE
OLS regression LoS	0.174	7.448	0.008	0.812	0.107	9.618	0.005	0.891
OLS regression log LoS	0.183	7.714	-0.400	0.674	0.107	10.213	-0.510	0.762
GLM-Gaussian	0.197	7.335	0.001	0.771	0.134	9.462	-0.009	0.868
GLM-Poisson	0.194	7.349	0.000	0.769	0.128	9.504	0.000	0.872
GLM-Negative binomial	0.186	7.388	0.005	0.773	0.120	9.545	-0.001	0.872
GLM-Gamma	0.184	7.407	0.005	0.773	0.112	9.602	-0.001	0.877
Cox PH regression*	0.097	9.002	-0.693	0.938	0.075	11.388	-0.808	0.906

*Performance estimates were not corrected for optimistic bias.

Discussion From our results we conclude that GLM-Gaussian and GLM-Poisson are the best choices to model LoS of unplanned ICU admissions, closely followed by plain OLS regression of untransformed LoS. Cox PH regression and OLS regression of log-transformed LoS are better avoided. A limitation of this study is that differences in performance were not statistically tested. Our study confirms the results by Austin et al. that was performed in a cohort of patients undergoing (elective) CABG surgery [6]. Future research will focus on developing a model which can be used for benchmarking purposes.

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Prognostic scales ISS-RTS-TRISS and APACHE II in Decision support of treatment children with trauma

Vasilieva I.V.[1,2] , Arseniev S.B Ph.D.[1,] Shvirev S.L. Ph.D.[2,] Zarubina T.V. M.D. [2]

[1] Cinical and Research Institute of Emergency Pediatric Surgery and Trauma, Moscow, Russia
[2] The Russian State Medical University, Moscow, Russia

Introduction

Prognostic scales ISS-RTS-TRISS [1,2] and APACHE II [3] are widely used in modern traumatology for evaluation of heaviness of state and probability of death outcome. However the application of these scales in children is not yet studied in sufficient.

Goal

Study the perspectives of using prognostic scales for decision support in treatment of trauma of children and integration the methodology in Hospital Information System.

Material and methods

The study included 399 patients (mean age 9 ± 5,0 years), 26 (6,5 %) patients died, The probability of death was determined using ISS-RTS-TRISS and APACHE II scales on the bases of anamnesis, initial examination, parameters of physiological and neurological status collected in the first day of admission. The used prognostic scales were integrated into HIS environment. For evaluation of the discrimination ability of prognostic scales the ROC-curve was used together with calculation of the threshold for optimal ratio for sensitivity and specificity.

Results

Probability distribution of death outcome did not follow the normal law. The main contribution for the probability of death outcome was between 0 and 30%. The study proved the high discrimination ability for ISS-RTS-TRISS scale (ROC area 0,908±0,029) and satisfactory prognostic properties of APACHE II (ROC area 0,875±0,038).

Conclusion

It was proved that ISS-RTS-TRISS and APACHE II scales are useful for assessment of outcome of children with trauma. The automation of calculation scales parameters in HIS provides quick and operative instrument for clinical decision support aimed at reducing children trauma death.

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Rex – to get

Hemodynamic Monitoring with the Transpulmonary Thermodilition Technique, The best is yet to come

Karim Bendjelid

Intensive Care Division Geneva University Hospitals, Switzerland

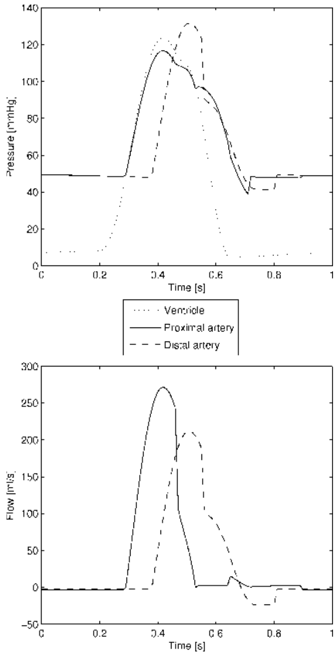
Over the last decade, the single transpulmonary thermodilution (TPTD) technique was implemented in clinical practice to measure cardiac output and preload parameters. The technique has started to supplant the Swan-Ganz catheter as many European surveys highlight the widespread use of this variety of hemodynamic monitoring tool. The technique was also the subject of many studies and scientific considerations as reflected in the number of publications in the index medicus. The cardiac output measured by this method (CO^{TPTD}) is determined using the Stewart-Hamilton equation applied to a thermodilution curve as it is the case when using a Swan-Ganz catheter. Except that in comparison to the right heart thermodilution curve, the TPTD curve is obtained by the injection of the thermal indicator into a central intra-thoracic vein instead to the right atrium and the thermal shift is collected via an arterial catheter placed in a large systemic arterial trunk (aorta, axillary or brachial artery) instead of the pulmonary artery. The result is that TPTD can be used to derive preload parameters like global end diastolic volume and intrathoracic blood volume Moreover, as a transpulmonary transit of the cold indicator occurs, after some calculation and subtraction, using the present technique, we may calculate pulmonary blood volume and extravascular lung water. The purpose of this tutorial is to review and assess the existing data related to the relevance of this technique as advanced hemodynamic monitoring.

A lumped parameter delay differential equation model of large arteries that captures reflection phenomena and integrates with modular models of the cardiovascular system.

Sven Zenker*, Gilles Clermont†, and Jonathan Rubin‡

*Dpt. of Anesthesiology and Intensive Care Medicine, University of Bonn Medical Center, Bonn, Germany ; † Dpt. Of Critical Care Medicine, University of Pittsburgh Medical Center (UPMC), Pittsburgh, PA , USA; ‡Dpt. of Mathematics, University of Pittsburgh, Pittsburgh, PA, USA; *Correspondence to: SZ, Email: zenker@uni-bonn.de*

Introduction. Mathematical models of physiology in general, and the cardiovascular system in particular, in combination with modern inference methodology, may enable a quantitative interpretation of monitoring data acquired in acute care settings[1]. In this context, lumped parameter models play an important role since they preserve direct physiological interpretability while at the same time minimizing the number of unknown parameters and states. Thus, they help to improve the conditioning of the inverse problem of state and parameter estimation that possibly presents the largest obstacle to practical bedside implementation of such approaches. Any model-based data interpretation approach is naturally restricted to accessing the information content in observed phenomena that the underlying mechanistic model can capture. An area where mechanistic models suitable for integration into a modular lumped parameter representation of the cardiovascular system are scarce is that of reflection phenomena within the arterial circulation, although these are important in generating the observed morphology of arterial pressure and flow curves. This is particularly important for peripheral measurement locations such as the radial artery, which are common in clinical practice. One class of previously described models uses partial differential equation formulations, which allow great flexibility and physical realism, at the expense of increased computational expense and parameter and state space dimensionality, with corresponding adverse effects on inverse problem conditioning. Others make, for the purposes of ab initio simulation, overly simplifying assumptions such as impedance matching at artery termination points and thus require realistic pressure or flow waveforms as input rather than being able to generate them (e.g., [2]). Finally, frequency domain formulations (e.g., [3]), while computationally advantageous, do not lend themselves to convenient interfacing with modular time domain models. Here, we present a time-domain mathematical model of the large arteries which is capable of ab initio simulation of arterial pressure and flow waveforms with realistic morphology using a minimal number of state variables and parameters. We then interface it to a simple model of the cardiovascular system to demonstrate its suitability for the applications described above. **Methods.** Initially following[2], we start from the d'Alembert form of the general solution of the Telegrapher's Equation. This decomposes the general solution of this one-dimensional partial differential equation describing a lossless transmission line used to represent a large artery as an elastic tube additively into forward and backwards propagating waves. We then impose boundary conditions representing influx and outflux against Ohmic resistances under general time varying input and output pressures. The resulting equations can equivalently be expressed in a form that further decomposes the current forward and backward propagating waves



additively into a function of known current and past state variables and parameters of the overall model and past values of the forward and backward propagating waves themselves. For comparable input resistance, output resistance, and characteristic impedance of the artery, it can be seen that the contribution of the latter term is small. Using this formulation, recursive substitution into this set of equations is therefore capable of generating time domain formulations of this model that come arbitrarily close to the true solution of the full partial differential equation and can be expressed as a system of delay differential equations. As proof of concept, we integrate an implementation of this model resulting from one iterative substitution with a simple monoventricular time-varying elastance model of the heart attached to an "aortic" (arterial side) valve and a "tricuspid" venous side valve implemented as pressure difference dependent resistances and linearly compliant representations of the distal arterial and venous components of the circulation. The model was implemented in MATLAB™ using the *dde23* delay differential equation solver. Numerical stability at non-smooth points where the pressure difference across the valves changes sign (i.e., the opening and closing times) is achieved using the *dde23* event detection mechanism, which is used to identify these points and restart integration appropriately. **Results.** Model behaviour proved to be numerically robust. The model quickly settles into quasi-steady state behaviour from reasonable but non-steady-state initial conditions and is capable of producing waveforms with many key morphological properties of real arterial pressure and flow waveforms. In spite of the low dimensional parametrization (essentially two parameters for the arterial tube + approx. a dozen to completely parametrize the entire cardiovascular system model for arbitrary heart rates, valvular resistances etc.), dependence of waveform morphology on the simulated location of measurement within the artery was captured in a physiologically plausible way (figure shows one cardiac cycle after initial equilibration). **Discussion.** The presented model is capable of capturing key morphological properties of the arterial pressure and flow waveforms utilizing a small number of parameters and states that retain direct physiological interpretability. Through its generic formulation which, at the interfaces, allows for arbitrary time varying pressures, it can seamlessly be integrated into modular lumped parameter models of the cardiovascular system, as illustrated by the simple example above. In addition to direct utilization in the application areas outlined above, future extensions will include systematic exploration of the possible benefits of utilizing higher order iterative substitutions and adaptation to more realistic physical representations of the arterial system, including branched vessel arrangements.

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Cellular monitoring: A technological and creative challenge

Egbert G. Mik, MD PhD

Department of Anesthesiology, Laboratory of Experimental Anesthesiology, Erasmus MC – University Medical Center Rotterdam, Rotterdam, The Netherlands

In technological and preclinical laboratories more and more methods become available to measure biochemical and biophysical parameters in living cells and tissues. Especially advances in biomedical optics have led to a large number of techniques that would in principle allow for the development of methods for patient monitoring at the cellular and subcellular level. For example, an advanced optical technique like optical coherence tomography (OCT) allows structural imaging of tissues on the micron level. Another optical technique, Raman spectroscopy, is able to get an optical fingerprint of the constituents of a sample volume and can nowadays be applied on the level of a single cell.

Unfortunately a large discrepancy exists between the technical possibilities in a laboratory setting and the clinical availability and usability. On the one hand this might be due to the enormous technical challenges one faces in the transition to an uncontrolled in vivo setting. On the other hand the engineers might miss the insight in the potential use and clinical impact of a newly developed technique.

In my presentation I will discuss some of these technological and creative challenges by a number of examples. Furthermore, I will share some thoughts on the potential use of cellular monitoring in critical care medicine. This is meant as an introduction to the rest of the session in which techniques for monitoring of mitochondrial and metabolic function will be presented. One of these techniques, NADH fluorimetry, uses the fluorescent properties of reduced nicontinaminde adenine dinucleotide (NADH) to monitor mitochondrial redox state. Another technique that will be presented is a method to directly measure mitochondrial respiration by means of delayed fluorescence of aminolevulinic acid-induced protoporphyrin IX.

Conflict of interest statement – I am founder and shareholder of Photonics Healthcare B.V., a company aimed at making protoporpyrin IX delayed fluorescence lifetime technology commercially available. Photonics Healthcare B.V. holds the exclusive licenses to several patents regarding this technology, filed and owned by the Academic Medical Center in Amsterdam and the Erasmus Medical Center in Rotterdam, The Netherlands.

Shedding Light on Mitochondrial NADH in Vivo:

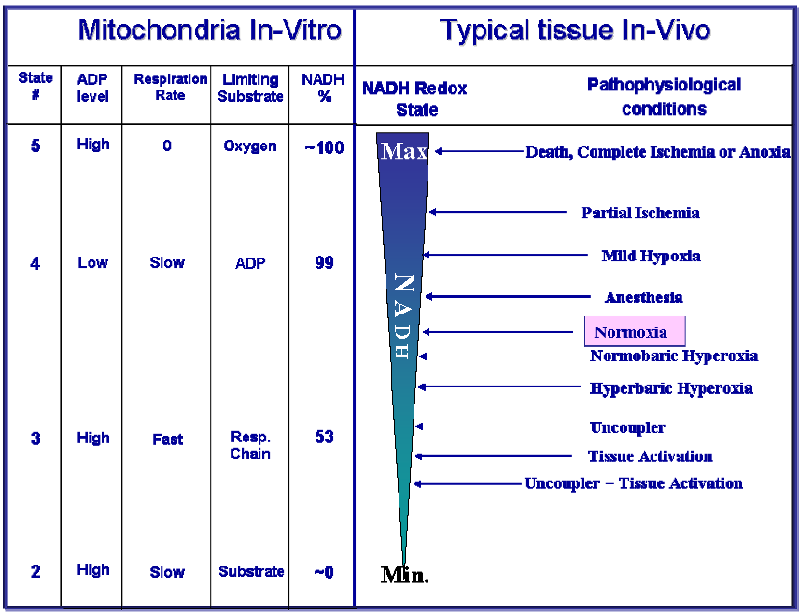
From experimental animals to clinical applications

Avraham Mayevsky

The Mina & Everard Goodman Faculty of Life-Sciences and The Leslie & Susan Gonda Multidisciplinary Brain Research Center, Bar-Ilan University, Ramat-Gan, 52900, Israel

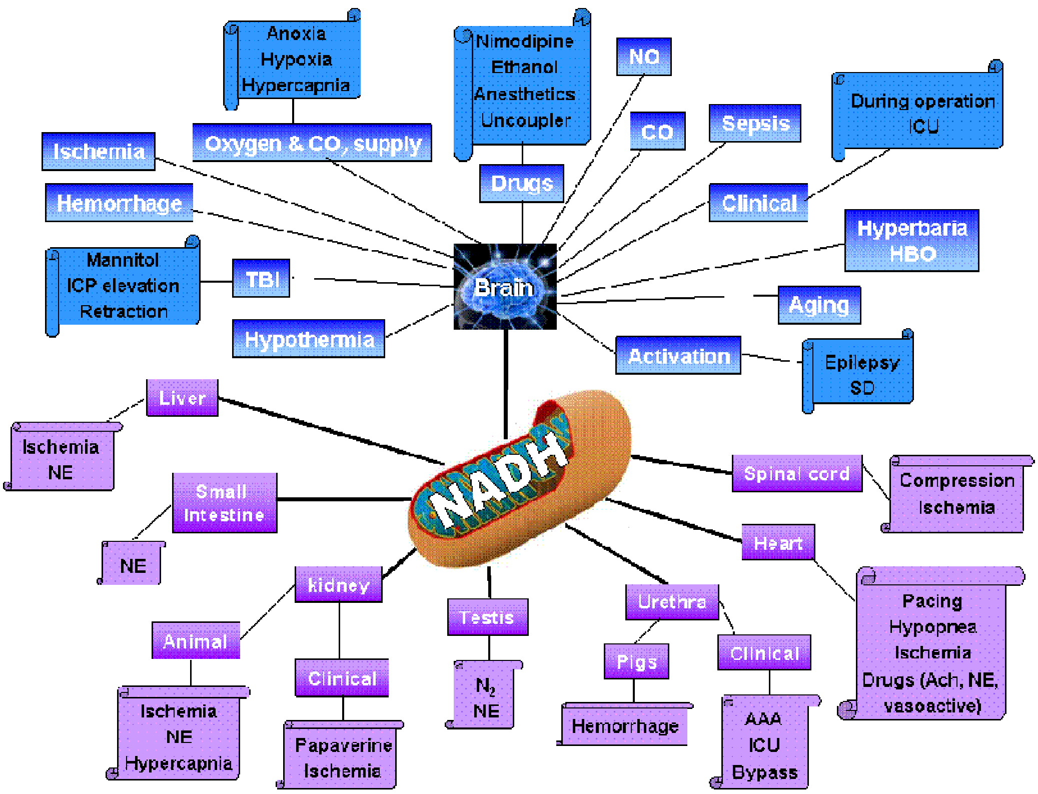
Email: mayevskya@gmail.com

Understanding the mitochondrial function has been a challenge for many investigators, since its discovery more than 120 years ago. The description of pyridine nucleotides (i.e. NADH) by Harden and Young 100 years ago led the complete understanding of their structure by Warburg and collaborators 30 years later. In 1955, the seminal work of Chance and Williams defined for the first time the metabolic states of isolated mitochondria *in vitro*, and correlated these states to the oxidation-reduction levels of respiratory enzymes including the NADH. The physiological significance of these metabolic states was elaborated, by Chance and collaborators, to the In Vivo monitoring of NADH fluorescence resulted in 1,000 relevant publications on NADH fluorescence monitored *in vitro* and *in vivo*. The comparison between the metabolic states under the 2 conditions is presented in the next Scheme.



More recently, this technique was adapted for clinical applications (in intra-operative and intensive care units). In this lecture I will summarize my almost 40 years of activities and contributions to the understanding of mitochondrial redox state and tissue functions In Vivo. Normal mitochondrial function is a critical factor in maintaining cellular homeostasis in various organs of the body. Due to the involvement of mitochondrial dysfunction in many pathological states, the real-time *in vivo* monitoring of the mitochondrial metabolic state is crucially important. This type of monitoring in animal models as well as in patients provides real-time data that can help interpret experimental results or optimize patient treatment. The monitoring of NADH levels in the tissue provides the most important information on the metabolic state of the mitochondria in terms of energy production and intracellular oxygen levels.

In addition to NADH, we measured, optically, the microcirculatory blood flow and volume, as well as HbO_2 oxygenation, from the same tissue area. The four detected parameters provide real time data on tissue viability, which is critical for patients monitoring.



Monitored organs and perturbations measured by Mayevsky et al in experimental animals as well as in patients during the last 40 years.

Porphyrin-based in vivo mitochondrial respirometry.

Floor A. Harms, Sander I.A. Bodmer**, Nicolaas J. H. Raat,** Egbert G. Mik

Department of Anesthesiology, Laboratory of Experimental Anesthesiology, Erasmus MC – University Medical Center Rotterdam, The Netherlands

Introduction

A reduction in mitochondrial respiration has been associated with a variety of human disorders, like cardiovascular diseases, sepsis and septic shock. Several methods have been developed and used over the years to estimate the respirometry *in vivo*. However, most of the available methods are based on semi-quantitative measurements. Recently we introduced the Protoporphyrin IX - Triplet State Lifetime Technique (PpIX-TSLT) (Mik et al., 2006) that enables to measure the mitochondrial oxygen tension (mitoPO_2) by means of the oxygen-dependent optical properties of 5-aminolevulinic acid (ALA)-induced endogenous protoporphyrin IX (PpIX) in the mitochondria. Further development of this technique can provide a new technique to monitor the oxygenation, oxygen consumption and oxygen affinity of the mitochondrial respiratory chain *in vivo*. In this presentation we present a novel approach that allows mitochondrial respirometry by dynamic measurements of mitoPO_2 during a local blockage of microvascular flow. We show the reproducibility of the measurement and the possibility to measure in difference spices like, rat, pig and man.

Methods

The measurements were performed in rats, pigs and healthy human volunteers. The princibles of the cuteneous mitoPO2 measurements were discribed in detail elswhere (Harms et al., 2011, Harms et al., 2012). In short, ALA cream was applied at the skin to induce PpIX in the mitochondria. Photo-excitation with pulsed green light was used to induce population of the PpIX triplet-state. The lifetime of the triplet state is related to mitoPO_2 and was measured by delayed fluorescence. Oxygen consumption was determined by repeated mitoPO_2 measurements while locally blocking oxygen supply. The latter was achieved by applying local pressure with the measurement probe. The mitoPO_2 was recorded before and during a period of 60 seconds compression and the mitochondrial respirometry was analysed with the aid of the decay from the slope of the mitoPO_2/ Δt.

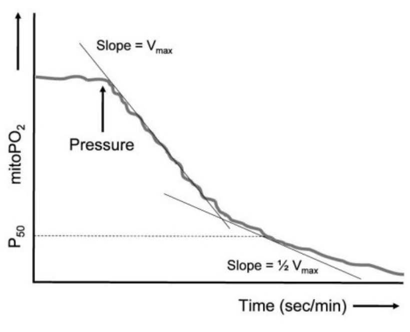
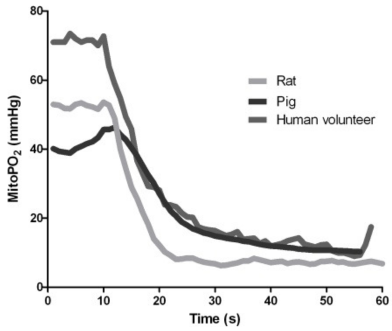


Figure 1. Principle of mitochondrial respiration by mitoPO_2 kinetics

Results

To test the inter- and intra-animal variability respirometry measurements, a total of 24 measurements were performed at for different regions on the abdominal skin of each rat. The mean PO_2 before stop-flow (P_0), the oxygen concumption (V_0) and the PO_2 at which cellular oxygen consumption is reduced to 1/2 V_{max} (P_{50}), were analysed by fitting the linear slope and were corrected for the the oxygen influx into the measurement volume. The P_0 59.4 ± 1.4 (SEM) mmHg, the mean V_0 was 4.99 ± 0.3 (SEM) mmHg/sec and the P_{50} was 3.95 ± 0.2 (SEM) mmH

The feasibility of the measurement in other spices was tested in a pilot experiment on the skin of a healthy volunteer and a pig (figure 3).



Conclusion

Our study shows the feasibility of cutaneous respirometry by a combination of PpIX-TSLT and local tissue compression. Enabling measurement of the mitochondrial parameters like, $mitoPO_2$, V_0 and P_{50}. We expect that clinical implementation of the method will greatly contribute to our understanding of mitochondrial function and oxygen metabolism in health and disease. For example, this technique could be useful for evaluation of dermal drugs, guiding of systemic mitochondrial therapy and monitoring of mitochondrial function in critically ill patients.

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Effect of partial brain ischemia on the metabolic and hemodynamic responses to hemorrhage hypotension measured in the brain and small intestine

Mira Mandelbaum-Livnat, Efrat Barbiro-Michaely and Avraham Mayevsky.

The Mina & Everard Goodman Faculty of Life-Sciences and The Gonda Multidisciplinary Brain Research Center, Bar-Ilan University, Ramat-Gan, Israel

Introduction: During hemorrhage blood is redistributed in favor of the vital organs and on the expense of the less vital organs. Bilateral carotid occlusion (BCO) is an animal model of arteriosclerosis, which is considered to be the leading cause of mortality due to reduced blood supply to the brain, in industrialized countries .

Objectives: The purpose of the present study was to investigate how BCO influences the responses of the brain (vital organ) and small intestine (less vital organ) to hemorrhagic hypotension.

Methods: Rats were bled until mean arterial pressure (MAP) of 40mmHg was achived, with or without the induction of BCO 24 hours prior to the bleeding session. MAP level was maintained for 15 minutes, after which the animals were resuscitated with the withdrawn blood. Metabolic and hemodynamic monitoring from both organs were carried out using the Multi-Site Multi-Parametric system, which simultaneously monitors tissue blood flow using laser Doppler flowmeter and mitochondrial NADH redox state using surface fluorometery.

Results: While hemorrhage under normoxic conditions caused a decrease in blood supply (30±7%, $p<0.01$) to the intestine, and mitochondrial dysfunction (132±10% ($p<0.01$), the brain preserved its normal function. However, under partial ischemic conditions hemorrhage caused deterioration in both organs. Blood supply to both brain and intestine rapidly decreased and remained low through the entire hemorrhage period (79.5±8% ($p<0.001$) and 56±10% ($p<0.001$), respectively). In addition, mitochondrial dysfunction was observed in both brain (137±9%, $p<0.01$) and intestine (145±12%, $p<0.01$). Furthermore, the responses of CBF to hypotension, exhibited an event called Ischemic-Depolarization (ID) revealed by a vasoconstriction of small vessels in the cortex.

Conclusions: The Impaired blood supply to the brain decreased cerebral autoregulation abilities and therefore decreased its protection during hemorrhage. The ID demonstrated the severity of the ischemic damage to normal mitochondrial function under combination of partial ischemia and hemorrhagic hypotension. These results emphasis the importance of adequate cerebral perfusion for the maintenance of body homeostasis.

Physiological Data Stream Analytics to Evaluate Noxious Stimuli in the Newborn Infant.

Nadja Bressan[1], Andrew James[3, 4], Carolyn McGregor[1,2]
1Faculties of Business & Information Technology, and 2Health Science, University of Ontario Institute of Technology, Oshawa, Ontario, Canada; 3The Hospital for Sick Children, Toronto, Canada; and 4Department of Paediatrics, University of Toronto, Toronto, Ontario, Canada;

INTRODUCTION

Research to understand pain perception, nociceptive stimulus and physiological stress response in an immature organism, such as the premature newborn infant, has taken place over the last 40 years. Lowery et al. 1 demonstrated that while a fetus develops in utero or a premature newborn develops after birth, they are not able to perceive pain, but perceive nociceptive stimuli to create a neurological path in response to pain. Furthermore, Brummelte et al.2 showed a direct association between pain and maturation of neurological structures. Beyond Brummelte's findings, Anand3 found a correlation between early pain experienced in a neurologically damage brain in animal studies. Our aim was to correlate non-invasive physiological variables that describe a pain response and based on the correlation deploy a neural network capable of identifying a pain pattern in the Neonatal Intensive Care Unit (NICU).

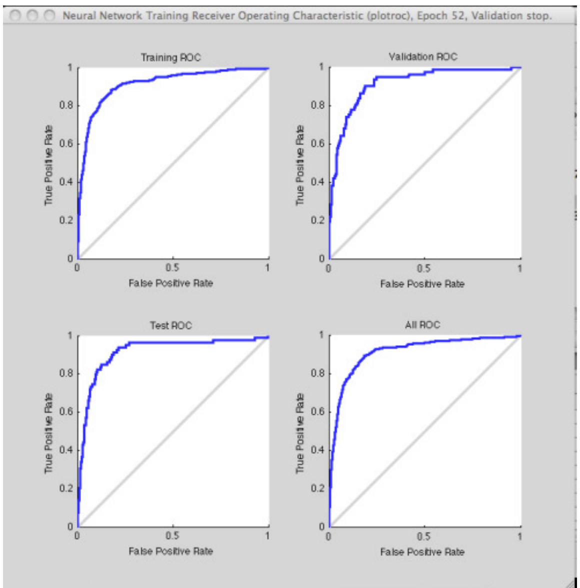
METHODS

The Neural Networks (NN) technique was considered appropriate to identify a behaviour pattern considering the complexity and non-linearity of the physiological data. The pattern recognition category of NN was used to learn from input-output relationships and use sequential training procedures to adapt to the data. In order to optimise the development of the NN to generate the intelligent alerts, a Radial Bias Function (RBF) was selected to implement the NN. Three male, preterm infants, gestational age 27.25±0.95 weeks, birth weight 941.25±189.31 grams, were randomly selected for this study from patients enrolled in the Artemis study. Artemis is a framework for concurrent multi-patient, multi-diagnosis and multi-stream temporal analysis in real-time for clinical management and research.4 Heart rate (HR), mean arterial pressure (MAP), Respiratory Rate (RR) and blood oxygen saturation (SpO_2) were considered for the NN Input Vector. Noxious stimuli were defined when the simultaneous occurrence of:

$$HR \geq 160\ AND\ MAP \geq 55\ AND\ RR \geq 40\ AND\ SpO_2 < 90$$

When this pattern was recognized by the NN the output vector should be otherwise.

RESULTS

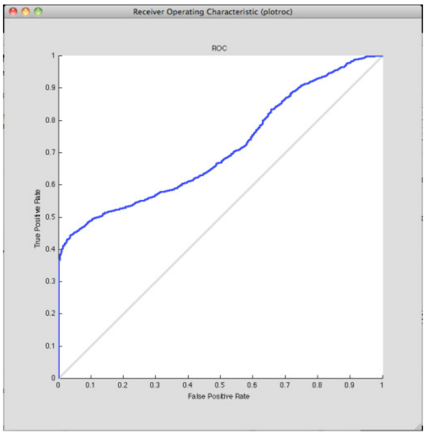


Data from different periods of the patient stay in the NICU were considered. The data training set comprised 7000 lines from patient 1 including physiological data in both normal and abnormal conditions. Figure 1 shows the result of the NN after testing:

Figure 1- ROC graph from NN tested with 7000 lines from patient 1.

Considering the good performance of the NN a second physiological data set from a different patient was inserted into the NN to test its performance. The NN performed fairly in the recognition of noxious pattern for patient 2 as shown in figure 2a. Data collected from a third patient, patient 3 was used in the NN presenting an excellent performance as shown in figure 2b.

a)



b)

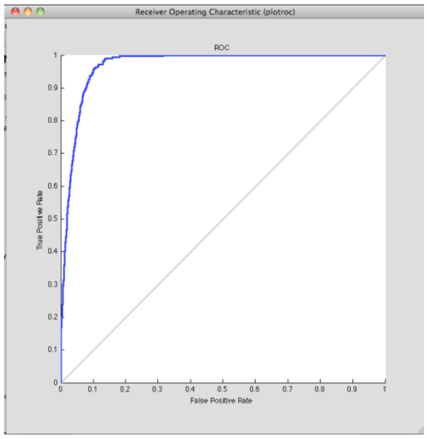


Figure 2 - NN tested with two different patients.

DISCUSSION

The Receiver Operating Characteristic Curve (ROC) from Figure 1 shown that training, testing and validation with the first patient's data set performed well, placing the NN as very good. When patient 2 was inserted to test the NN the result was a fair prediction of the noxious pattern, however patient 3 demonstrated a perfect prediction of the pattern resulting in an excellent NN. Although all three patients were preterm infants, patient 2 had experienced severe intrauterine growth restriction. The infant's small head circumference indicates that brain growth has been impaired and suggests that development and/or maturation of the brain is abnormal. Therefore, considering Anand and Brummelete findings and our own findings with a physiological data set to determine noxious stimuli, leads to the conclusion that brain development and damage are intrinsically correlative to pain stress response and is a deterministic factor to determine pain in preterm infants and their relation with pain later on in adult life.

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THE EFFECT OF CARVACROL IN OLEIC ACID INDUCED ACUTE LUNG INJURY IN RATS

Özkan Önal

ABSTRACT

This study was conducted to compare the effects of oleic acid on the antioxidant systems of lung muscle tissue and carvacrol which has been proven to have healing effects on tumors of the lung, liver, breat, and testis and is known to have antioxidant effects, with respect to their healing and protective properties.

28 male rats of the Wistar type (250-350 grams) were included in the study. They were divided to four groups. Group I: Group oleic acid (n:7, 50 µl of oleic acid were administered to the oleic acid group and 30 minutes later 73 mg/kg of saline solution was given intraperitoneal as the same volume as carvacrol) Group II: Group oleic acid+carvacrol (n:7, Fifty µl of oleic acid was administered to the oleic acid and thirty minutes after the injection 73 mg/kg of carvacrol was administered intraperitoneal.Group III: Group control(n:7, Fifty µl of saline solution (the same dose as the oleic acid group) was administered and thirty minutes after the injection 73 mg/kg of saline solution was administered intraperitoneal. Group IV: Group carvacrol: (n:7, Fifty µl of intravenous saline solution was administered and 30 minutes after the injection 73 mg/kg carvacrol was administered intraperitoneal). After being held in the oxygen room for 4 hours, blood and tissue samples were collected from the rats.Two histologists who were unaware of the group assignments assesed the acute lung injury via light microscopy;interstitial oedema ,alveolar haemorrhage, intraalveolar neutrophils, intraalveolar macrophages and intraalveolar pneumocytes and electron microscopy ;the integrity of the blood-gas barrier,the morfology of the type 1 and type 2 pneumocytes, and the presence of intraalveolar macrophages and granular material. The lung tissue was examined histopathologically and levels of protein carbonyl, malondialdehid tissue, catalase (CAT), glutathione peroxidase (GSH-Px) and superoxide dismutase (SOD) which are known as oxidant, anti-oxidant parameters were measured. Levels of antiinflammatory cytokines such as interleukin (IL)-6, IL-10, Tumor necrosis factor (TNF)-α and granulocyte colony stimulating factor (G-CSF) were measured in the blood samples. Oleic acid caused significant total lung injury compared to the control group and to the vehicle group and levels of protein carbonyl and malondialdehid were higher than the other groups. Total lung tissue damage score ,protein carbonyl, CAT, GSH-Px, SOD, levels were found to be similar in oleic acid and oleic acid+carvacrol groups. Levels of MDA tissue was lower in carvacrol and oleic acid+carvacrol groups than oleic acid group. Levels of proinflammatory and inflammatory cytokines IL-6, IL-10, TNF-α and G-CSF were found to be similar in both groups. As a result it has been shown that because of the antioxidant effects of carvacrol in lung tissue the increased use of carvacrol may be helpful in preventing and reversing lung tissue damage.

Key Words: Acute lung injury, oleic acid, carvacrol, antioxidant

Table 1. Histological scoring of acute lung injury at experimental groups,mean±standart deviation values and statistical differences betweeen groups

VARIABLE	GROUPS				p
	Group I (Oleic asid + Saline Solution)	Group II (Oleic asid + Carvacrol)	Group III (Saline Solution+ Saline Solution)	Gruou IV (Carvacrol + Saline Solution)	
Interstitial edema	2,46±0,87	2±0,6	1±0,8*	1,44±0,5	**0,034**
Alveolar hemorrhage	1,8±1,6	0,5±0,8	0±0	0±0	**0,028**
Intraalveolar neutrophil	1,6±1,5	0,5±1,2	0±0	0±0	0,085
Intraalveolar macrophage	2,4±0,9	1,6±0,8	1±0,8	1,2±0,4	0,055
Intraalveolar pneumocyte	1,8±1,6	0,5±1,2	0±0	0±0	0,058
Interstitial neutrophil	1,6±1,5	1,6±1,5	0,5±0,7	0,4±0,6	0,62
Total lung injury	11,66±7,87	6,7±6,1	2,5±2,3*	3,04±1,5*	**0,02**

*p<0,05 (when comparing with group 1)

Table 2. The mean±standart deviation values of oxidant and anti-oxidant parameters of acute lung injury at experimental groups and statistical differences between groups

VARIABLE	GROUPS				p
	Group I (Oleic acid + Saline Solution)	Group II (Oleic acid + Carvacrol)	Grup III (Saline Solution + Saline Solution)	Group IV (Carvacrol + Saline Solution)	
Protein carbonyl (nmol/mg prot)	5,3±0,8	3,4±1,1	3,2±0,8*	3,06±1,1*	**0,011**
MDA tissue (µmol/g wet tissue)	1,05±0,4	0,6±0,2*	0,47±0,09*	0,43±0,11*	**0,003**

CAT (k/g prot)	0,18 ±0,07	0,2±0,05	0,2±0,06	0,23±0,04	0,458
GSH-Px (U/g prot)	2,4±0,7	3,6±0,8$^{\#§}$	5,7±1,4*	6,15±1,1*	**0,00**
SOD (U/g prot)	0,32± 0,11	0,47±0,1	0,49±0,04	0,4±0,07*	**0,043**

*p<0,05 (when comparing with group 1)

$^{\#}$p<0,05 (when comparing with group 3)

§p<0,05 (when comparing with group 4)

Table 3. The distrubition of IL-6, IL-10, TNF-α, G-CSF levels between groups

Variable (pg/ml)	Oleic asid	Oleic asid + Carvacrol	Control	Carvacrol	p
IL-6	30,8±2,1	37,9±11,3	35,3±7,1	33±3,1	0,43
IL-10	26±14,5	89,4±111,1	13,5±5,2	76,1±104,4	0,4
TNF-α	48,7±1,2	55,1±10,6	50,8±0,96	56,4 ±6,7	0,28
GCSF	41,9 ±7,7	45,9±20,1	38,2±3,7	44,4±7,5	0,8

Anesthesia for Intraoperative MRI

Keith J Ruskin, MD

Yale University School of Medicine, New Haven, Connecticut, USA

Intraoperative magnetic resonance imaging (IMRI) provides substantial benefits for patients undergoing surgical management of intracranial pathology. IMRI is most commonly used to locate a target for a brain biopsy or to guide resection of brain tumors. It allows the surgeon to accurately determine whether additional resection is needed while the patient is still in the operating room, or to determine whether the surgical approach will imping upon a critical area of the brain. One study found that 96% of patients with a glioma in whom IMRI was used to guide the surgery had a complete tumor resection as opposed to 68% of the controls.[1] In several studies, gross total resection is significantly related with the patient survival.[2] In a recent study, survival was increased from 60 weeks to 88 weeks ($p = 0.07$) if IMRI was used to guide surgery.[3] Although this technique improves surgical outcome, it does expose the patient and surgical personnel to significant hazards.

The MR operating room (MROR) is a hybrid environment in which the MRI coexists with ferromagnetic surgical instruments and anesthesia equipment. Although magnet safety underlies all aspects of patient care, the MROR presents unique hazards that fundamentally affect anesthesia care. The anesthesiologist is confronted with unfamiliar equipment and limited to access to the patient during much of the procedure. Bringing the scanner into the room presents multiple distractions, and problems (e.g., hypotension or a disconnected endotracheal tube) may go unrecognized. During the scan, the room is dark and noisy, which makes it difficult to hear alarms, communicate with other personnel, or troubleshoot problems.

A comprehensive training program includes a tutorial on how to use the MRI safe monitors and infusion pumps. Anesthesia personnel who will work in the room are taught about the changes in workflow imposed by the equipment and safety procedures. Lastly, all personnel are given a demonstration of the magnet's strength using small, ferromagnetic objects. Team training is essential to maintain communication and ensure that all team members are empowered to intervene when the scanner is brought into the OR. The MROR impacts all aspects of anesthesia care, but following safety procedures, constant training, and an understanding of the physics and physiology of strong magnetic fields can mitigate the hazards of working in this unique environment.

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Anaesthesia and Critical Care in a Helicopter

Giulio Trillò MD, Paola Perazzolo RN, Elio Carchietti MD

Helicopter Emergency Medical Service, Udine University Hospital, 33100 Udine – Italy

Introduction

Despite the title, this paper will not focus solely on Anaesthesia and Critical Care (CC) *inside*, a helicopter. It must be noted, in fact, that the vast majority of civilian helicopter used in Helicopter Emergency Medical Service (HEMS) duties are of the 3-4,5 ton of Maximum Takeoff Mass (MTM), and therefore the inside space is quite limited and does not allow to perform most of the procedure that we deem associated with anaesthesia and CC.

In fact, the HEMS systems view the Helicopter as a mean for *transporting* a highly skilled professional medical team (1) to the site where their competence is needed, being the landing spot, its surroundings. Sometimes the patient may be reached using another vehicle, or, thanks to the so called HEMS-Helicopter Hoist Operation (HEMS-HHO) where no other vehicle may ever arrive, like a mountain, a ship and so on.

So, I will deal with the Procedures that are performed, the Equipment needed to perform this procedures, and discuss them against the logistics nightmares where this will be used. I will also briefly discuss the Drugs that are used, but avoid any in-depth analysis, due to the target of this congress.

I must also state immediately that very few Authors published works in this field, and from my Medline peregrinations the majority of those were coming from the military community. So I will more often than not discuss my personal experiences and views.

Procedures

If we look closely at what happens in the pre-hospital emergency arena, we may point out that the procedures that are performed are usually conducted according to a predetermined sequence based on the clinical priorities. This sequence is usually made easier to remember to the rescue personnel using some kind of acronyms, like A.B.C.D.E.

The most common procedures performed in the pre-hospital arena are:

A-Airways

Securing the patient airways with the positioning of an endotracheal or nasotracheal tube, as well as using different kind supraglottic devices or performing a percutaneous or surgical tracheostomy (2).

B-Breathe

Evaluation and support of patient's ventilation, with the use of bag-valve devices or mechanical ventilation.

In this step may be also included the treatment of a pneumothorax, since this is an absolute emergency that may be dealt immediately.

C-Circulation

This step comprise the control of haemorrhages and if needed the infusion of fluids to compensate for blood losses or other clinical needs. This step imply the need to gain access to peripheral, but sometimes also central, venous lines. Sometimes infusion pumps are used, but this is mostly for precise drug infusion, and not for volume replacement.

D-Defibrillation
This step is self explanatory.

E-Exposure
In this step the rescuers will examine head-to-foot the patient but also install all the needed tools to perform a complete monitoring of the vital signs of the patient.

Equipment
To achieve these goals we may use different equipment and devices, but all of them should specially chosen to work inside a helicopter or worse in the field, that may be a street, the mountain, a shore... And these are quite different logistic conditions compared to what is usually encountered in an Operation Room or an Intensive Care Department or a ground based ambulance (3).

Basically, everything is against the machines: temperature, ranging to extremely hot to freezing low, humidity easily reaching the 100%, rain, dust, vibrations. But very few devices are especially constructed to operate in these conditions, and if the HEMS organization is so skilled as to identify such few machines, their cost is obviously higher compared to the ones normally used inside an OR.

There are a series of problems that should be reminded.

One is the need of electrical power for most of the devices. In fact, many of these equipments may be able to operate under normal main power (220V AC), but also on the power of ambulances (12V DC), or on board of a helicopter (where anything between 12 and 28V DC may be available). Obviously using self contained batteries, these machines are able to guarantee a reasonable autonomous operation so as to complete the rescue operations if all else fails.

Any electrical device used on board of a helicopter, moreover, should be certified for this specific task. This is due to the possible interference of the device with the extensive electronic systems of the helicopter. It is obvious that any interference with these systems may pose a severe risk to the safety of flight, more or less to what happens on board of any commercial flight we may have boarded in our business or leisure travels.

The problem is that this kind of certification is machine specific, i.e. the single device should be tested on board of any single helicopter. These is needed since basically any helicopter is different form any other, although similar, machine. Therefore, the costs rise sky-high.

Looking into detail of some specific device used in the pre-hospital field we may appreciate some peculiarities.

Airway control
The devices used to secure an airway range from the long known traditional laryngoscope, to some alternative devices that may be used especially in difficult airways patients, like the McCoy blade or an assortment of different intubating stylets. A very successful difficult airway tool introduced some time ago is the Airtraq, defined as an "optical laryngoscope" by the producer. Recently a more sophisticated device was made commercially available from Pentax, the ASW, that combines the disposable plastic blades on which

the endotracheal tube is mounted and made slide into the patient's trachea like in the Airtraq, with a more effective fibre-optic monitor that allow a direct high quality visualization of the vocal cords (4)(5).

Ventilation

In the pre-hospital setting the de-facto standard for ventilating a patient is the self-expandable bag valve device, since it needs no power to operate and, in conjunction with an oxygen (O_2) source and a reservoir bag may deliver O_2 concentrations up to 100%.

For a higher quality ventilation many different portable mechanical ventilation devices are commercially available, with a range that goes from basic devices powered only by the O_2 pressure, but usally not extremely friendly to the patient's lungs, to very high end machines, with several ventilation modes, able to perform the most sophisticated breathing assistance.

Circulation

Access to the venous system is still recommended with traditional peripheral large bore catheters. There are some circumstances in which these may not be available, i.e. severely burned or shocked patients, and therefore some equipment for gaining access to a central venous line should be available.

In the pre-hospital settings fluids are usually not administered through infusion pumps, but with a free flow, or if needed with pressure bags to assure a quick delivery.

On board of helicopters there are usually some syringe infusion pumps, that may be used for drug delivery. These are subject to the same logistic problems that were described before, although the vast majority works on internal batteries.

Defibrillation

Cardiac arrest recognizes in a prompt defibrillation the only factor influencing the Return Of Spontaneous Circulation (ROSC). It is well known that defibrillation implies delivering a short burst of energy through the patient's chest, and therefore it should not come as a surprise that the pilots did not like much such a procedure being carried on in a flying helicopter.

It is well known to any physician that defibrillation implies the administration of a very short but very powerful burst of electrical energy through the patient's body. This high energy is one of the main dangers for the helicopter's electrical systems, but also to the whole flying team, since it is difficult to ensure total complete isolation of the patient from the helicopter body, due to the cramped spaces and extensive use of metal conductive parts.

Monitoring

One of the mainstay of anaesthesia is keeping a tough monitoring of the patients vital signs. This ensure that any sudden change is promptly recognized and dealt (6).

The need is therefore for sturdy, lightweight, self powered monitoring devices, able to offer at least the most useful parameters: ECG, peripheral Oxygen saturation (SpO2) (7), Non Invasive Blood Pressure (NIBP), End Tidal CO2 (EtCO2) (8).

Several other parameters may be useful, but they may add complexity, weight and power consumption to the device. Their usefulness must be well weighted therefore.

Conclusions

The pre-hospital arena is a complex scenario, and to the Authors knowledge there are few scientific evidences and honestly we see a very limited interest from the industries, at least compared to the in-hospital setting.

For achieving the best results we hope that more articulate research on this field will be performed from the HEMS services, as well as more cooperation with the Industries in the design process of the devices used in the pre-hospital arena.

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Fighting the robot.

René Hagenouw, MD, Department of Anesthesiology,

Erasmus MC, P.O. Box 2040
3000 CA Rotterdam, The Netherlands
r.hagenouw@erasmusmc.nl

Introduction
At first blush it would seem that robot-assisted operations should be similar to laparoscopic surgery in its anesthetic requirements. Partly, that is true, for instance with robot-assisted nephrectomies. However, during the most common robot-assisted operations, in the lower abdomen and pelvic cavity (i.e. robot-assisted prostatectomy) circumstances can get quite severe, due to a complete lack of access during the case and positioning in extreme Trendelenburg. This talk will deal specifically with these types of operations.

Access
Because of the size and shape of the robot, the arms of the patient have to be alongside the patient. There is no room for an armboard. The Da Vinci robot has arms in the abdomen from all angles which basically turns the whole patient surface into the sterile field, including the area above the head. This mandates that the possibility to correct all likely and not so likely eventualities must be present before draping and the start of surgery. Any lack of preparedness may well come back to haunt you during the case.

Extreme Trendelenburg
A head down position of 45º or more is standard for these procedures and is maintained throughout the case, quite often for 4 or more hours. This means that 70% or more of the patient's weight pulls the patient cranially. If the head and shoulders are not immovably supported relative movement between them may result in great strain and brachial plexus lesions. The same goes for the leg supports. They are not designed to be used in extreme Trendelenburg and can cause thrombosis and necrosis of muscles. Furthermore, any cranial shift of the body, with the skin stuck in place, wil put strain on the bloodvessels to the skin, leading to sores and ulcers.

Respiratory problems are similar to laparoscopuic surgery, only more so.
Maintaining proper circulatory physiology can become difficult, not in the least because we really don't know what appropriate physiology is when you stand on your head. We also lack data on what is safe and for how long. Measuring invasive pressures is tricky as it is nearly impossible to calibrate the height of the pressure sensors.

It is clear that the elevated venous pressure in the head leads to visible edema of the head. If this extends to brain edema, whether that has deleterious effects and what a safe period might be is unknown. Several cases of permanent blindness have been reported. The precise mechanism of this has not been elucidated, nor do we know if and how it can be prevented.

Conclusion
Robot-assisted operations may be minimally invasive as counted by the number of holes in the abdomen. They are however major in regard to the stress imposed on the body. What is safe and what isn't is currently poorly defined.

Education technology

Keith J Ruskin, MD

Yale University School of Medicine, New Haven, Connecticut, USA

Situation Awareness in Anaesthesia and Intensive Care – Implications for the Design of Monitoring Devices.

Schulz CM, Heuser F, Wagner KJ

Department of Anaesthesiology, Klinikum rechts der Isar, Technische Universität München, Munich, Germany

Background:

According to Endsley's definition, Situation Awareness (SA) is "the *perception* of elements of the environment within a volume of time and space, the *comprehension* of their meaning and the *projection* of their status in the near future"[1]. In medicine, SA describes the health care provider's ability to perceive and understand patient related information and the ability of foreseeing patient's future development[2]. Accurate SA is crucial for effective team work, task management and decision making and therefore, it is an indispensable part of high performance. Developing SA requires integration of perceived information with experience and knowledge. This knowledge includes mental models about (patho-)physiology, therapy goals, guidelines and medical knowledge in general[2].

In anaesthesia, patient monitors provide basic as well as extended information about the patient's state. Actual patient monitors offer increasing numbers of parameters that almost exclusively base on the single-sensor-single-indicator (SSSI) design[3]. To comprehend and to integrate these parameters can be a time-consuming task, especially during dynamic phases of anaesthesia, e.g. during anaesthesia induction or the management of critical incidents[4]. An overload of the anaesthetist's working memory with impaired patient safety is a possible consequence. For accurate development of SA, improvements of monitor designs for optimal presentation of information are rare but favourable. Therefore, the ability of the present generation of patient monitors to increase SA optimally remains questionable.

Evaluating designs of patient monitors

Since patient monitors provide information about the patient's state, the physicians' SA or their performance (being a result of accurate SA) are potential objects of assessment and evaluation. Performance and SA-related behaviour are considered to be indirect indicators of SA. For evaluation of performance, time markers (e.g. time to detect a problem, time until correct diagnosis, time until clinical decision) and checklists evaluating key tasks have been used. In contrast, direct measures of SA use standardized queries like "The Situation Awareness Global Assessment Technique (SAGAT)" which is applied during random scenario freezes in simulation environments[5]. The queries have to be adapted to scenario contents and evaluate SA on the *perception*, *comprehension* and *projection* level providing more detailed knowledge about the processes how information is acquired.

For example, one study[6] used SAGAT to compare a traditional SSSI display with an object display providing information about functional cardiovascular physiology through the integration of hemodynamic variables. The object display was not found to be superior with respect to SA and performance and the authors concluded that the unfamiliarity with the new display stated a major problem even after training. Therefore, for unbiased testing of new displays, several month of training have been recommended[3].

A promising tool to evaluate patient monitors is eye-tracking[4]. This technique records anaesthetists' gaze targets with a high timely and spatial resolution and can be applied in the real work place as well as in simulation environments. In combination with SAGAT, it simultaneously determines what information had been *seen* and to what degree this information has been *perceived* and *understood* by the individual.

Implications

New monitor displays are a promising tool to reduce cognitive workload and errors[3]. In anaesthesia, the integration of basic data from multiple SSSI variables by means of physiologic models is suitable to present information graphically and in a single display field. Another important option is the development of an "intelligent" patient monitor: given a certain constellation of basic data (low blood pressure, tachycardia, increased airway pressures), such a monitor might offer several differential diagnoses (e.g. anaphylaxia, tension pneumothorax) and suggest additional diagnostic and therapeutic tasks. Progress in display design was initiated and realized in other domains to obtain information on the *comprehension* and *projection* level of SA which reduces both workload and errors[7]. However, it has been recommended that traditional display information should remain available along with the integrated information because it may be necessary to understand individual parameters for an in-depth analysis of a complex situation.

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Electrical Impedance Tomography

Michael Czaplik[1,2], Steffen Leonhardt[1].

1. Chair for Medical Information Technology, Helmholtz Institute for Biomedical Engineering, RWTH Aachen University, Aachen, Germany.
2. Department of Anaesthesiology, RWTH Aachen University, Aachen, Germany.

Introduction

Employment of technical equipment and devices increased intensely in anaesthesiology and intensive care medicine respectively during the last decades. Regarding mechanical ventilation, which is of outstanding clinical value up to date, lots of modes, parameters and features have been developed and technically implemented in modern respirators [1]. Although the ARDS network encouraged scientific projects concerning concepts of protective artificial respiration during the past ten years, there is still a major deficiency regarding monitoring of ventilation [2]. Up to date, there are just global and very imprecise modalities to monitor injurious impacts of ventilation to lung tissue at bedside. Since CT and MRI scans are associated with high resource consumption, the central method for controlling ventilatory settings and further treatment still is blood gas analysis and predefined algorithms (e.g. according to the ARDS network protocol).

Methods

Electrical Impedance tomography (EIT) is a rather new monitoring modality which has been around for some time. It allows to derive real-time images and video streams of regional ventilation at the bedside. Basis for EIT is the typically circular attachment of electrodes around the human thorax. Predefined changing pairs of electrodes are used to inject alternating current and voltage measurement respectively in order to gain electrical impedance [3]. For impedance distribution reconstruction of the concerned lung cutting, diverse algorithms exist that have various advantages and disadvantages. Dependent on used hardware, number of electrodes and current frequency, up to 40 frames per second can be achieved by repetitive measurements.

Results

Most studies published so far focused on illustrating and measuring (regional) tidal ventilation. That regard, various animal trials have shown that EIT is able to visualize quantitatively variation of tidal volume during respiration. Furthermore, regional tidal volume distribution can be displayed and estimated very precisely [4]. In diverse clinical trials potentialities but also challenges of EIT have been pointed out. Nonetheless, further clinical applications have already been addressed in other studies like perfusion imaging, generating ventilation-perfusion matches, estimating intra-cerebral masses, performing tumour diagnostics and other fields [5,6,7].

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PULMONARY MONITORING: END EXPIRATORY LUNG VOLUME (EELV)

Giacomo Bellani, Valeria Meroni, Antonio Pesenti

Department of Experimental Medicine, University of Milano-Bicocca; Department of Perioperative Medicine and Intensive Care, San Gerardo Hospital, Monza, Italy.

1. METHODS FOR EELV MEASUREMENT DURING MECHANICAL VENTILATION (MV)

Functional Residual Capacity (FRC) is the volume of gas that remains in the lungs at the end of expiration, while EELV corresponds to FRC in the presence of positive end expiration pressure (PEEP). In classical physiology, the measurement of EELV can be performed through techniques based on imaging, body plethysmography or dilution of a gas tracer. Mostly due to technical reasons, EELV measurement has not become a routine monitoring tool in intensive care, but several techniques for use in patients undergoing MV have been recently described and tested, while computed tomography (CT) scan is probably the most solid standard reference for EELV measurements during MV. Wash-in or wash-out of a tracer gas (as nitrogen or oxygen) in a multiple breath maneuver seems to be well applicable at bedside, and promising techniques have been presented with acceptable accuracy and repeatability. The simple instrumentation required might increase the diffusion of EELV measurements in the clinical practice.

In 2005 Olegard et al [Anesth Analg. 2005;101(1):206-12] described a modified nitrogen wash-in/wash-out technique after a change in inspiratory oxygen fraction (FiO_2) to measure EELV in patients undergoing MV. It is based on standard monitors and nitrogen concentration is estimated from inspiratory and end-tidal plateau gas concentration values of O_2 and CO_2. This technique has recently been implemented in a commercially available mechanical ventilator. Three years later Chiumello et al [Crit Care 2008;12(6):R150] showed that this technique has a good agreement with reference methods such as CT and helium dilution.

In 2006 Weismann et al [J Clin Monit Comput. 2006;20(4):251-60] developed a new system for EELV measurements called LUFU (acronym for Lung Function). It is based on oxygen wash-in/wash-out after a change in FiO_2. This method is non-invasive and does not require modifications to the ventilator or interruption of the care process. Its reliability has been demonstrated in healthy subjects and volunteers with pulmonary disease [Intensive Care Med. 2007;33(5):912-6] and during control and assisted MV in intensive care units [Intensive Care Med. 2008;34(12):2235-40].

2. POTENTIAL CLINICAL APPLICATIONS OF EELV

EELV for assessment of alveolar recruitment

PEEP promotes recruitment of non aerated lung volume and therefore it increases EELV, although recruitment of previously non-aerated lung units must be distinguished from the distension of lung units that were already ventilated. As the benefits of PEEP are more significant in patients with high recruitability, a method to assess the quantity of recruited lung might improve the management of patients in MV tailoring PEEP to the individual patient needs. In clinical research PEEP-induced volume recruitment is usually assessed as the volume difference between multiple pressure-volume (PV) curves at different levels of PEEP: this approach is rather complex and seldom used in everyday practice. Using this approach, measurement of EELV might be used to reference the starting point of the curves on the volume axis [Crit Care Med. 2010;38(5):1300-7]. In this context EELV appears to be a very promising tool for evaluating alveolar recruitment.

In 2011 Dellamonica et al [Intensive Care Med. 2011;37(10):1595-604] described a method derived from bedside EELV measurements to assess PEEP-induced lung recruitment. The authors estimated recruitment as the difference between the change in EELV at different levels of PEEP (measured with nitrogen wash-in/wash-out technique) and the minimum predicted volume gain. This one is the smallest possible increase in lung volume due to the application of a PEEP and it is computed as the product of respiratory system compliance and the increase in PEEP. Estimated recruitment is well correlated with the recruited volume measured on PV curves, as a reference technique.

EELV and ventilator induced lung injury (VILI)

Strain is the lung distortion caused by tidal inflation and PEEP and it is defined as the ratio between the end expiratory inflated volume and the lung resting volume (FRC or EELV). Lung strain has been proposed as the determinant of VILI and its role in ARDS was shown by a few studies.

In 2011 Protti et al [Am J Respir Crit Care Med. 2011;183(10):1354-62] showed that in healthy pigs VILI occurs when strain exceeded a critical threshold which corresponds to an interval ranging from 1.5 to 2. In 2011 our group studied lung tissue inflammatory response to tidal deformation. Its intensity can be measured by positron emission tomography (PET) imaging of [^{18}F]fluoro-2-deoxy-D-glucose. We found a tight relationship between metabolic activity and glucose uptake of normally aerated tissue and regional tidal volume (V_T) normalized by EELV [Am J Respir Crit Care. 2011;183:1193-1199]. In keeping with these findings Gonzàles-Lòpez et al [Intensive Care Med. 2012;38:240-247] showed that patients with ALI undergoing MV and with high levels of V_T/EELV (measured at bedside with an oxygen wash-in/wash-out technique) exhibit an increased alveolar inflammatory response in terms of matrix remodelling and inflammation markers.

These findings have potential clinical relevance because they support the evidence that during MV EELV should be taken into account to set the appropriate tidal volume and so a lung-protective ventilation.

Bed-side measurement of pulmonary gas exchenge

Stephen E. Rees

Respiratory and Critical Care Group (rcare). Center for Model Based Medical Decision Support Systems, Aalborg University, Fredrik Bajers Vej 7, DK

Pulmonary gas exchange abnormalities are common in the ICU and place the patient at risk of developing hypoxaemia and hypercapnia. The underlying cause of the impaired gas exchange is due to mismatch between ventilation and perfusion ranging from pulmonary shunt, to infinitely high V/Q i.e. alveolar dead space. The Automatic Lung Parameter Estimator (ALPE) is designed for bedside measurement of pulmonary gas exchange [1]. In 2012 a commercial version of this system has been released for use in the ICU.

This presentation reviews the development of the ALPE system resulting in the 2012 commercial version. The technological components are described including a) the general principle of using changes in FIO2 to identify gas exchange abnormalities and b) the current state of mathematical models included in ALPE [2], which allow estimation of pulmonary shunt and parameters describing regions of the lung with low ventilation perfusion (V/Q) ratio and high V/Q ratio.

In addition, potential clinical application of the system will be presented, including clinical examples with special reference to a) Appropriate selection of inspired oxygen fraction [3] and appropriate selection of positive end expiratory pressure (PEEP).

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Improving medical data collection and processing using Web technology.

F. O’Connor.

Amphia ziekenhuis Breda – Oosterhout, The Netherlands.

Introduction

Attention is drawn here to the growing gap between access to contemporary and medical information. Paper based medical documentation and it's processing are rapidly becoming obsolete. Hospitals are investing in Medical Information Technology which though useful for administration, falls far short of the degree of sophistication required for adequate medical care. This contrasts starkly with the achievements in computing hardware and programming that are part of daily life. This difference is steadily increasing but little is being done to address it. Medical personnel are essential for developing such sophisticated systems. Through lack of interest, time, motivation, or ignorance, even through denial of the necessity, only tiny minority of them have become involved or have much knowledge or experience.

Methods

Financial constraints are not a limiting factor for learning software development. This is specially the case with Open Source(OS) software which can be used free of charge by all. OS offers educational opportunities, operating systems, programming languages, and applications and that are mature and universal, and, excellently maintained and developed.

Learning

There is vast Internet community support with tutorials, forums, and documentation for OpenSource. Advanced educational material, such as audiovisual aids (web casts and Pod casts) and interactive tutors help to popularize them.

Development

For programming with OS applications, a wide variety of technology is available. The many databases include Mysql, Postgres, and Sqlite. Scripting Languages (Ruby, JavaScript, Perl) offer simpler programming for the less experienced. Programming aids allow earlier completion of applications. Dedicated text editors (TextMate, Sublime) assist the writing of code. Frameworks such as Rails guide this learning. Using conventions they simplify program writing and shorten the time to completion of an application. Using Test Driven Development, software is examined during in its primary stages to speed secure correct completion. Web software repositories (Github), for public and private use, facilitate software access and team contribution.Web presentation and design are also catered for. Account must be taken of how the information is being displayed on the viewing port (browser, telephone). Integrated Development Environments (IDE) allow application production coordinated collections of programming tools (NetBeans, Eclipse).

Deployment, staging, and use.

Deployment (making the application available on a web server) and staging, are the following steps in making a Web application available. Finally, public can access information deployed on a dedicated computer, a leased computer (hosting) or even on a computer in the home of the programmer. Web Hosting is at present inexpensive, and flexible (Heroku, Webbynode, Amazon). Besides the Web application itself, copies of the complete operating system on which it runs can be hosted. With the Cloud Computing of Amazon (S3 storage, Elastic Cloud), infrastructure use is billed on data storage and transfer. Storage can be rapidly acquired or released, making it ideal for low budget projects. Amazon Cloud Computing use is simple rapid and Web browser based. Statistical information on the performance of the project can be made available through services such as New Relic.

Results Discussion

Inexpensive technology is available for developing sophisticated software. It has as yet been sparsely applied in medical practice. It remains to be seen if and when the medical professionals realize this short-coming.

BI solution for Data Mining Hospital Information Systems

Sergei B. Arseniev, Ph.D.

Department of New Medical Technologies, Clinical and Research Institute of emergency pediatric surgery and trauma, Moscow, Russia

Introduction

Typical HIS provides automation of information processes accompanying daily clinical activities. Usually HIS is capable to produce only a set of routine reports, however the constantly growing HIS data potentially contains valuable information important for improving hospital clinical and economic results. The solution is to use Data mining techniques according with multidimensional analysis and interactive reporting.

Data mining cycle

1. Data level. Conversion of the operation data in historical data and building up the data warehouse. This stage includes performing certain queries to HIS DB, data cleansing and aggregation.
2. Analytical level. Building and testing Data Mining models and multidimensional cubes.
3. Report level. Design screen and printable reports.
4. Control level. Assignment of user rights and setting up the schedule for executing various processes of analysis.

Software realization

Our Hospital Information System covers more then 200 computerized work places and is integrated with PACS, LIS and with Accounting and Finance modules. The Data mining solution we used is a client/server platform. The server part includes analytical instruments: data access and manipulation tools, Data Mining and text mining tools, multidimensional analysis modules, all over more then 80 instruments. The client part consists of several applications: analytical client (visual script editor), report designer, dashboard for viewing reports, WEB publisher for report visualization using thin clients.

First results

At the first stage of implementation of BI solution we have built the data warehouse for analysis of completed clinical cases. The basic questions (but not limited to) were: the amount of completed cases in slices of clinical departments, time, results of treatment, days spent in the hospital, distribution by sex and age, diagnosis, personal involvement of a doctor or nurse in treatment of a patient etc. From the available variety of analytical tools at this stage we used descriptive statistics, multidimensional link analysis and OLAP technique. Report generation was scheduled for a day, week, quarter and year periods. Each report is interactive and incorporates a drill down-feature which is a powerful easy-to-use data detailing mechanism.

Conclusion

Our first experience in using BI solutions for mining HIS data was positive. Ones the necessary procedure for building data warehouse, data mining models, multidimensional cubes, report designs and other initial settings are performed the system works practically automatically providing the end users with scheduled interactive drill-down reports.

Programmability of an Anesthesia Information Management System

Nico van Schagen, Vrije Universiteit Medical Center,
Amsterdam, Netherlands

For the OR's in our university hospital we have developed a home grown AIMS that consists of a web-based modular system. An AIMS, in our opinion, can be seen as a number of loosely coupled components: a GUI, forms, typesetting (anesthesia record), storage (database), the recorder that talks to the hardware and import and export modules that talk to the HIS, LIS etc. All components working together represent an AIMS 'suite'. In the ideal situation such a system should be open, not only to allow data to be processed, but also for supplementing and modifying components itself. This is fascilitated by using open standards where possible and setting up an open architecture. Still a lot of data extraction and extensions require programming skills. This is usually non-trivial and requires the investment of a substantial amount of time and expertise.
Is it feasible to move a step ahead and look beyond traditional programming languages, make programming easier and maybe even support non-programmers to contribute to the AIMS system? This will also be a good way to test and improve the openness of the architecture and interfaces.

The presentation will show a setup of how to create support for programming in an open environment.