‘Big data’ approaches to trauma outcome prediction and autonomous resuscitation

Massive clinical digital data routinely collected by high throughput biomedical devices provide opportunities and challenges for optimal use. This article discusses how such data are used in learning prediction models at level 1 trauma centres to support decision making in trauma patients.

In 2011, the IBM Watson supercomputer beat two human contestants in the television game show *Jeopardy!*, empowered by 2880 processor cores (Ferrucci et al, 2013). After its impressive performance in the game show, IBM’s Watson has made conquering health care its next objective, and generated new ideas on how big data could be harnessed with supercomputing power to improve our health. The big data analysis phenomenon is about vast volumes of data analysed at high velocity from a variety of sources (Laney, 2001). The goal of such big data analysis efforts applied to health care is to use all the available health information and recognize patterns linked to outcomes to develop actionable therapeutic interventions.

In the clinical realm, the volume of real-time physiological patient data has proliferated with each advance in computer hardware and medical sensor technology. High fidelity data are streamed into physiological monitors for care planning, clinical decision support, quality improvement and remote patient monitoring. Processing and extracting useful and actionable knowledge from these patient data also requires consideration of the techniques used to store, manage and analyse such massive data. Those techniques are far beyond the capacity of traditional database and spreadsheet-based analysis in linking common medical knowledge and relationships to features of physiological signals and other patient data. Military medicine considers these techniques as the future way to develop combat casualty autonomous resuscitation (Palmer, 2010; DuBose et al, 2011) and enhance real-time field decision-making (Provost and Fawcett, 2013).

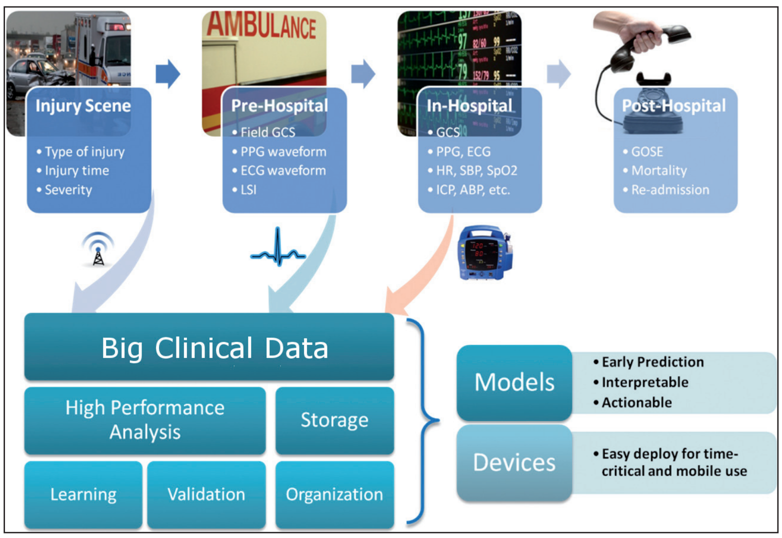
For the purposes of demonstrating a practical and beneficial application, this article describes how, in the next 2 years, we may achieve the unrealized goal of accurately predicting trauma patient outcomes related to actionable emergency therapeutic interventions and later be able to translate this into autonomous resuscitation.

Data sources and application of the raw big data

Clinicians are currently facing the challenge of collecting and organizing unprecedented quantities of data from multiple sources. These heterogeneous data are available and need to be collected with different formats and temporal resolutions, including ordinal or categorical data (e.g. Glasgow Coma Scale, age, sex), continuous (trend and waveforms), radiological images, text (medical records, clinical notes), and other important data (e.g. adverse events, treatments, response). In the current hospital environment, these data are in a loosely organized decentralized network. System failure or manual data entry errors can result in missing values, causing difficulty in application of decision-support algorithms, or such failures can lose data associated with rare events.

One approach to manage vital signs waveforms and trend data, used at a level 1 trauma centre that admits more than 8000 severely injured patients annually, is to design a triple redundant data collection server for high fault tolerance to maximize these data collection rates to nearly 100%. For an illustration, *Figure 1* shows the data streams of various stages in the care of a trauma patient including pre-hospital and in-hospital data and the components that manage and analyse the big data.

Figure 1. Data streams collected while a patient is transported, treated and discharged from a trauma centre. Critical components of the big data approach in handling those massive data are shown and the expected outputs.



Dr Shiming Yang *is Data Analyst,* **Dr Mary Njoku** *is Associate Professor of Anesthesiology and* **Dr Colin F Mackenzie** *is Professor of Anesthesiology in the Shock Trauma Anesthesiology Research Center and Department of Anesthesiology, University of Maryland School of Medicine, Baltimore, Maryland 21201, USA*

Correspondence to: Dr CF Mackenzie (cmack003@umaryland.edu)

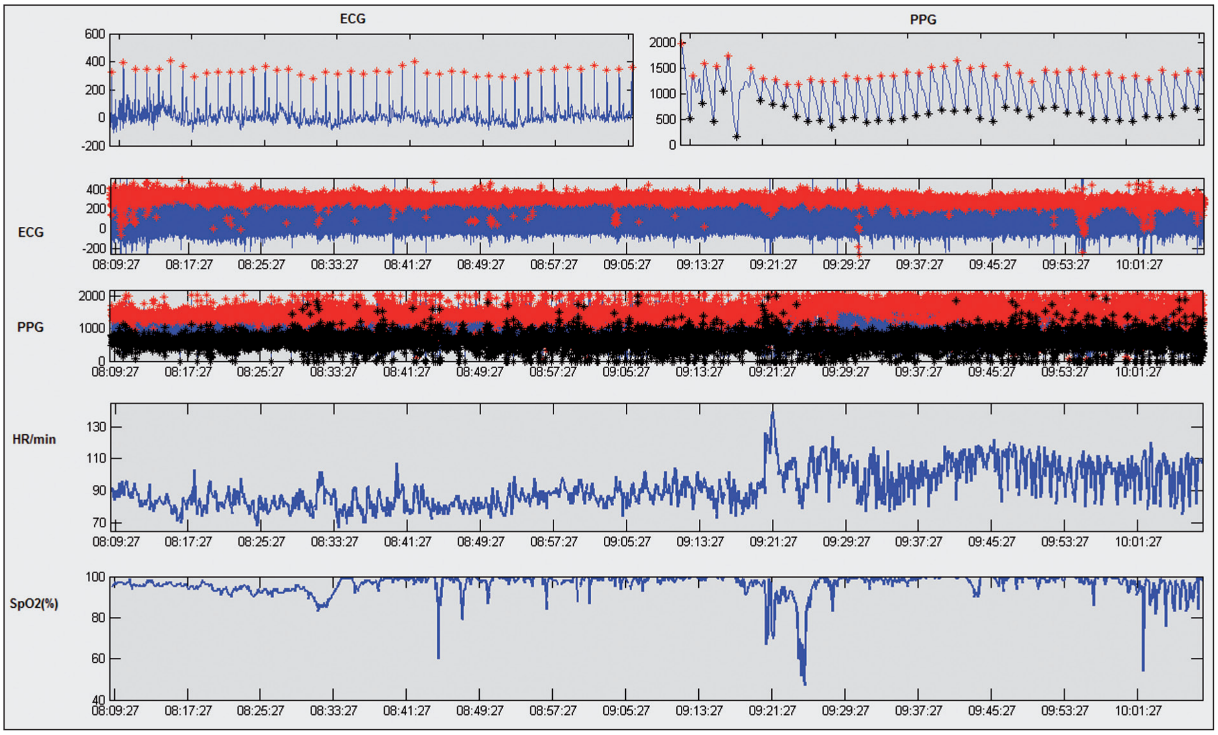
During pre-hospital transportation to trauma centres, vital signs signals including electrocardiogram, pulse oximetry photopletysmograph, end tidal carbon dioxide ($ETCO_2$) (collected at 240 Hz), non-invasive blood pressure (intermittent in mmHg), heart rate and respiratory rate (per minute collected at 0.5 Hz) are collected as the basic signals and contain more than 400 000 data points per minute (Mackenzie et al, 2008). Different groups of features (e.g. demographics, photopletysmograph derived, laboratory measurements, percutaneous haemoglobin oximetry) are identified based on thresholds with clinical meanings, such as pressure x time 'dose' of shock index (systolic blood pressure/heart rate) >0.9, percutaneous oxygen saturation (SpO_2) <90%, heart rate >120/minute (Kahraman et al, 2010; Stein et al, 2011). Low resolution temporal data, such as mechanism of injury, field Glasgow Coma Scale, and patient demographics such as age and sex, can also be collected through communication networks.

After trauma patient admission, more than 50 types of automated and continuous vital signs are routinely collected in critically injured patients, from the resuscitation unit, operating theatre or intensive care unit. Like haemorrhage, traumatic brain injury is another common cause of emergency admission after injury (Eastridge et al, 2009; Stein et al, 2011). In trauma centres, vital signs collected in such traumatic brain injury patients include continuous intra-arterial blood pressure, pulse oximetry, $ETCO_2$, intracranial pressure and other waveforms. For a typical traumatic brain injury patient staying 7 days in a trauma centre, five 240 Hz waveforms are monitored and up to 700 million data points (equivalent to 8-gigabyte disk size, if data are stored in 12-bit format) would be collected.

Haemorrhage after injury has been shown in multiple studies to be the most common cause of preventable death in civilian trauma care and on the battlefield (Holcomb, 2010; Perkins and Beekley, 2012). Rapid identification of patients with life-threatening bleeding in the field and during pre-hospital care would allow pre-hospital providers to more accurately triage such patients to trauma centres. Patient outcomes can be obtained by a standardized query of the Trauma Registry database, including survival, hospital length of stay, therapeutic interventions, injuries, and laboratory and radiological results. As an example of application of big data analysis, these pre-hospital data can be used to discriminate bleeding from non-bleeding patients and predict resuscitation outcomes, such as those injured patients who are haemorrhaging enough to need blood transfusion. Such pre-hospital data could focus triage and the clinical management toward earlier haemorrhage control interventions, critical to saving life in exsanguinating patients.

The sequence of signal processing needed to process such pre-hospital vital signs signals in trauma patients includes artifact removal by applying a signal quality index. Features of these signals are identified and linked to outcomes; next, statistics are applied to see how well

Figure 2. An interface with display visualizing a 1-hour-long electrocardiography (ECG) and photoplethysmography (PPG) waveform measured from a pulse oximeter with corresponding each-minute heart rate and peripheral capillary oxygen saturation (SpO_2). The red and black dots indicate the peaks and valleys of the waveform. The PPG and SpO_2 feature selections can be entered along the right upper and lower boxes.



the features predict outcomes of interest. Features of the signals can include amplitude of a waveform, mean, median, inter-quartile range, or duration of signal values above or below physiological thresholds of normality. Twenty or 30 such features can be assessed for each single epoch of a waveform. *Figure 2* shows a typical view of the signals and the schema to select features of each signal during 30 seconds of photopletysmograph waveforms from the pulse oximeter. Three groups of features are illustrated from the one pulse oximeter signal: amplitude, SpO_2 features, and heart rate features obtained from this one device.

Massive learning and model verification

It is unwise to equate data with knowledge. From huge volumes of these data, interpretable and actionable knowledge needs to be derived. Traditionally, an experienced clinician distills concise and practical rules from years of observation and clinical practice. With massive data, such a process can be accelerated with automated machine learning algorithms. However, the algorithms may generate counterintuitive models, misled by outliers, missing values, biased data and incorrect assumptions (Bishop, 2006; Lantz, 2013). Therefore, a priori knowledge and cross-validation are essential in building and selecting models.

Expert clinical knowledge is of paramount importance in successful learning from data. In creating interpretable models to associate quantities derived from vital signs features with trauma outcomes (such as transfusion, mortality, length of stay, actionable therapeutic interventions), clinical guidelines are used to eliminate clinically irrelevant variables, to exclude unnecessary high-order functional relations and so simplify the process of learning from large datasets.

Learning from massive data and selecting models requires intensive calculation. In clinical datasets, the number of observations per subject could be an order of magnitude greater than the number of subjects that are observed. In identifying salient variables that best explain the outcomes, extra feature groups are gradually included and comparisons are made among models to evaluate the importance and contribution of each group of features. Advanced machine learning methods, such as stepwise logistic regression, lasso and random forest, can be used to select features from high-dimensional datasets (Bishop, 2006; Bühlmann and van de Geer, 2011).

To test and validate these models' performance on new data and to prevent potential over-fitting, a scheme of 10-fold cross-validation repeated 10 times is commonly adopted. A balanced training and testing model prediction is used to see if the model can be generalized to new previously unused data. For example, with multiple combinations of five outcomes, six feature groups, 10-fold repeated 10 time cross-validation, about 1500–3000 multiples of model calculations and 100–300 model comparisons and statistical tests are required. To handle such data-intensive and computation-intensive learning tasks, the steps of data preparation, feature selection, model comparison and output are automated to allow efficient near 'real-time' (within seconds) implementation of predictions.

Ideal pre-hospital trauma patient outcome prediction tool

An ideal tool for pre-hospital data collection would be fully automated and require no user input to produce updated predictions in near real-time, and would include a simple display format (e.g. red, yellow, green warnings). This approach would allow any pre-hospital care provider to simultaneously provide patient care and hands-free documentation, while automatically enabling early detection of the need for intervention. For example, a useful prediction in trauma patients would be the need for emergency blood transfusion, as this is an indication of injury sufficient to cause life-threatening haemorrhage. The benefits of such early identification of haemorrhage are associated with increased survival.

Big data analysis application to pulse oximetry signal processing

Can features of the pulse oximeter signal including heart rate, photopletysmograph waveform and SpO_2 rapidly identify patients with life-threatening haemorrhage in the field and during pre-hospital care? To discriminate bleeding from non-bleeding trauma patients, clinicians want answers to questions such as can automated analysis of these pulse oximeter signal features from a single monitoring device do this as well or better than conventional indices based on manual collection of vital signs or as well or better than clinical experts.

To predict transfusion in a recent study, 12 amplitude-related photopletysmograph features, nine features of the percutaneous SpO_2 signal and nine features from the pulse oximeter heart rate signal were selected by stepwise logistic regression (Mackenzie et al, 2014). Area under the receiver operating characteristic (AUROC) curves were used to compare transfusion outcomes in 556 enrolled patients, 37 of whom received blood within 24 hours. The first 15 minutes of vital signs signals, including pre-hospital heart rate plus continuous pulse oximeter signal analysis, predicted 1–3-hour transfusion better than all 24-hour-interval blood use predictions using conventional transfusion predictions (Sasser et al, 2009; Fitzgerald et al, 2011; Vandromme et al, 2011; Mitra et al, 2014) based on heart rate or shock index alone (AUROC 0.84, $P<0.03$) or heart rate and photopletysmograph features predicting 1–12-hour and 1–24-hour blood use ($P<0.04$). Predictions of transfusion <6 hours based on the first 15 minutes of data were no different using 30–60 minutes of data collection. Shock index plus photopletysmograph and SpO_2 signal analysis (AUROC 0.82) predicted 1–3-hour transfusion no differently than pulse oximeter signals alone.

To see if these analyses may be enhanced with the use of continuous non-invasive pulse oximetry-derived haemoglobin, percutaneous haemoglobin oximetry was collected in trauma patients to test this hypothesis. The addition of continuous percutaneous haemoglobin oximetry data to the conventional pulse oximetry features selected in the study above did not improve predictions of early blood transfusion. Percutaneous haemoglobin oximetry is insufficiently accurate (percutaneous haemoglobin oximetry bias 0.6 ± standard deviation 1.96 g/dl) in detecting changes in total haemoglobin in unstable trauma patients during resuscitation (Mackenzie et al, 2012; Moore et al, 2013).

Prospective survey of clinicians' clinical judgment

To further evaluate transfusion prediction models, a survey of clinicians' judgment was conducted and compared with the models. Pre-hospital providers, nurses and consultant-level physicians predicted emergency transfusion with AUROC 0.74–0.84 and transfusion within 1–3 hours with AUROC 0.67–0.77, essentially no different from the automated predictions derived from the pulse oximeter waveform analyses. Pulse oximeter features collected in the first 15 minutes of this trauma patient resuscitation cohort therefore predicted transfusion in the critical first hours of care using only a single device with no user input as well as experts.

Implications of such automated predictions of transfusion

Given the 20–30-minute en route transit time for typical helicopter emergency medical services, these findings suggest that pre-hospital collection of data is sufficient to warn the trauma receiving team and, through them, the blood bank of impending need for increased blood product support with >95% accuracy. Such analytic software could have important potential as a platform for field-ready algorithms that could be integrated into patient monitoring systems. This work also supports the efforts of trauma care and emergency medical services to forward-deploy instrumentation capable of automated collection of continuous, high-quality vital signs data for future generations of clinical decision-support instrumentation.

If point-of-care testing and other vital signs devices are added, potentially simple software upgrades to existing pre-hospital monitors could 'call' ahead to warn the blood bank, advise the trauma team and operating team to start preparations for these interventions, activate blood product processing to reduce the coagulopathy of trauma, and coordinate other logistics for trauma patient reception and resuscitation. For transfusion prediction, parsimonious models (five to nine features derived from photopletysmograph waveform) can be built into small single-board computers or smartphone apps for use in time-critical and mobile situations. Since the models provide probabilistic scores to measure the possibility of transfusion, numeric scores with three simple colours (red, yellow, and green) can be displayed so that the predictions can be easily grasped by busy pre-hospital clinicians. This way, new knowledge can be decoded from continuous photopletysmograph data for practical use.

Autonomous resuscitation

Autonomous resuscitation of trauma patients takes all these ideas to create a futuristic vision of decision support (Darrah, 2013) driving closed-loop controllers of vital functions (Palmer, 2010). In the battlefield 5 years hence, remote operations will occur in hostile areas far from access to fixed medical facilities. Casualties may be transported back for definitive medical care by unmanned or remotely piloted vehicles with duplex audio video communications but no co-located medical care providers. A highly mobile unmanned system mounted under a stretcher will provide fully autonomous patient resuscitation and stabilization through closed-loop control of fluid infusion, pain medications, ventilation/oxygenation, chest decompression, and tourniquets for haemorrhage control, or could function in an advisory status for control through telecommunication links with a remotely situated medical care provider. The end objective would be to autonomously respond to changes in casualty physiology during up to 6 hours transport in a pilotless vehicle.

Total prototype device weight is approximately 7 kg (including fluids), and the device attaches underneath a standard NATO litter. Remote interfacing with the system can be done via any linked computer platform or smartphone while on the battlefield. The predictive algorithm models are run on a quad redundant computer system built into the device. Before boarding an autonomous transport vehicle, the predictions of transfusion would ensure that patients with ongoing haemorrhage were triaged by co-located clinicians to immediate interventions to control bleeding. While this may seem very advanced, autonomous, pilotless, full-sized helicopters have been flying for more than 8 years. The predictions obtained from photopletysmograph and other vital signs signal processing can drive the autonomous resuscitation with remote oversight through audio-video and interface with other patient status devices through telecommunication links.

How do these advances impact the future of health care in general?

Clinicians are embracing more non-invasive sensor technology and techniques to better understand patients' physiological changes and trends, and it is anticipated that the volume of health-care data will increase exponentially. New architectures for massive data processing, such as MapReduce, Hadoop (O'Reilly Radar Team, 2011), and secure storage for data sharing in multicentre studies can run on current affordable mainstream multi-core desktops and workstations. Large volumes of data alone do not make big data (Needham, 2013); rather, the distillation of knowledge from enormous and heterogeneous data sources makes these analyses 'big'.

With the increasing power of high throughput data stream processing capability and massive data storage capacity, clinical observations of high integrity can be efficiently analysed for their association with patient outcomes of interest. These, in turn, can be summarized into parsimonious models to enable rapid validation. In the very near future (12–24 months) new big data-derived linkages will prompt timely updates of patient triage, diagnostic assistance and clinical guidelines to allow more precise and personalized treatment to improve clinical outcome for patients.

Conclusions

Hospital and emergency health interventions provide rich sources of high fidelity data. Storing, managing and analysing those data are beyond traditional means and call for 'big data' approaches. With ambient non-invasive data sensors and reliable collecting techniques, fractional information from heterogeneous data sources can be assembled in a real-time fashion and applied for specific studies and can incorporate expert knowledge of clinicians into the automated learning process. The analysis of photopletysmograph waveform-derived features is an illustration of the benefits of using massive data for early trauma outcome prediction and autonomous resuscitation. Future study and analysis will establish a framework to accommodate large-scale data and allow these to be analysed in real-time for insight and practical use, a framework that calls for multidisciplinary collaboration of clinicians, statisticians, technologists and computer scientists. BJHM

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KEY POINTS

- Massive clinic data analysis is an interdisciplinary enterprise.
- The pulse oximeter is a source of continuous electronic data suitable for automated real-time prediction analysis.
- Interpretable and actionable models can be learned from large-scale clinic data.
- Through machine learning, we can convert 'big' data into 'small' models running on 'small' devices.