The Brain Monitoring with Information Technology (BrainIT) collaborative network: EC Feasibility Study Results

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Summary

Background: The BrainIT group works collaboratively on developing standards for collection and analyses of data from brain injured patients towards providing a more efficient infrastructure for assessing new health care technology. EC funding supported meetings over a year to discuss and define a core dataset to be collected with IT based methods from patients with traumatic brain injury. We now report on the results of a follow-up period of funding to test the feasibility for collection of the core dataset with IT based methods.

Methods: Over a three year period, data collection client and web-server based tools were developed and core data (grouped into 9 categories) were collected from 200 head-injured patients by local nursing staff. Data were uploaded by the BrainIT web and random samples of received data were selected automatically by computer for validation by data validation (DV) research nurse staff against gold standard sources held in the local centre. Validated data were compared with original data sent and percentage error rates calculated by data category. Feasibility was assessed in terms of the amount of missing data, accuracy of data collected and limitations reported by users of the IT methods.

Findings: Thirteen percent of data files required cleaning. Thirty "one-off" demographic and clinical data elements had significant amounts of missing data (> 15%). Validation nurses conducted 19,461 comparisons between uploaded database data with local data sources and error rates were generally less than or equal to 6%, the exception being the surgery data class where an unacceptably high error rate was found. Nearly 10,000 therapies were successfully recorded with start-times but approximately a third had inaccurate or missing end times which limits analyses assessing duration of therapy. Over 40,000 events and procedures were recorded but events with long durations (such as transfers) were more likely to have "end-times" missed.

Conclusions: The BrainIT core dataset is a rich dataset for hypothesis generation and post-hoc analyses provided studies avoid known limitations in the dataset. Limitations in the current IT based data collection tools have been identified and have been addressed. Future academic led multi-centre data collection projects must decrease validation costs and likely will require more direct electronic access to hospital based clinical data sources for both validation purposes and for reducing the research nurse time needed for double data entry. This type of infrastructure will foster remote monitoring of patient management and protocol adherence in future trials of patient management and monitoring.

KEY WORDS: ***clinical network, traumatic brain injury, Grid, Internet***

Background

Severe traumatic brain injury is a leading cause of death and survivors have serious and long term morbidity [1]. The loss of employment to the victim and the stress and increased burden of care to family members have significant social and economic effects.

The aetiology of the disease is complex often implicating multiple organ systems causing a high variation in the presentation of injury and, as a result, a large number of patients are required when assessing new health care technology. Recruiting patients from multiple centres will significantly reduce the time to assess new therapy and monitoring. However, despite the existence of guidelines for the management of severely head injured patients [2, 3] this group of patients is subject to considerable variability in care across centres [4-9]. To improve the monitoring and management standards in this population, the inter and intra-centre variability in the management, physiological monitoring and treatment of these patients needs to be assessed on a multi-national basis. To do so require a standardised, IT based, higher resolution methodology for acquiring multi-centre patient management and physiological monitoring information in a standardised way.

One consequence of the variability in management that exists across centres that manage patients with TBI (traumatic brain injury), is its confounding influence upon multi-centre trials of therapy. There have been in the last few years many multi-centre clinical trials of potential neuroprotective drugs targeted at patients with brain trauma. However despite promising pre-clinical results, most have failed to show efficacy in the head-injured population. A number of reasons have been proposed for these failures which include: poor study design, insufficient dose of drug penetrating the blood brain barrier and inter-species differences in brain injury mechanisms.

Another factor, not as yet systematically examined, is the occurrence of secondary insults which are missed through use of inappropriate monitoring methods. Recent estimates put the proportion of adverse events missed by using only end-hour recording compared with minute by minute computer based monitored to be in the region of 30%. Even in large scale randomised trials, an accurate sample size analysis cannot be made without a knowledge of the incidence of relevant confounding factors. Inaccurate sample size estimates will lead to trials that are under-powered.

Improving the standards and resolution for multi-centre data collection will also effect assessment of new medical technology which is of relevance to the medical device industry. The majority of

companies that develop or support devices used to monitor brain injured patients in intensive care are small to medium size enterprises. Unlike the pharmaceutical industry, these small device companies lack the resources to independently assess their devices in multi-centre clinical trials. This severely limits the provision of quality evidence demonstrating the clinical utility of their products.

What is required to address these issues is an open, collaborative network of centres interested in developing higher resolution and more standardised methods for collection of neuro-intensive care monitoring and management data from patients with traumatic brain injury. Such an infrastructure will provide a more efficient means for assessing new and developing health care technology, whether it is new drugs, management approaches or new monitoring devices.

To address these issues, the Brain Monitoring with Information Technology (BrainIT) group was formed (www.brainit.org) . The group has 3 main aims:

1) To develop and disseminate standards for the collection, analysis and reporting of intensive care monitoring and management data collected from brain injured patients.

2 To develop and use a standardised database as a tool for hypothesis generation and the development, testing and validation of new data analysis methodologies.

3 To provide an efficient multi-centre infrastructure for generating evidence on the utility of new invasive and non-invasive intensive care monitoring and management methods.

The BrainIT group have first defined a core dataset collected using PC based tools as part of a European Community (EC) funded study (QLGT-2000-00454). A series of meetings spread over one year enabled key stake holders to meet and the group to define a minimum set of data that should be collected from all patients with traumatic brain injury (TBI). The outcome of the study was to define a core dataset which would be useful in most research projects conducted in this population of patients [10].

This paper reports on the results of a subsequent three year EC funded study (QLGC-2002-00160) that enabled the group to develop IT methods to collect the core dataset and to assess the feasibility and accuracy for collection of this core-dataset from 22 neuro-intensive care centres across Europe. Feasibility was assessed in terms of missing data, accuracy of data collected and limitations reported by users of the IT data collection methods. To assess accuracy, data validation research nurse staff were hired on a country by country basis to check samples of the collected data against local gold standard clinical record sources in order to quantify the accuracy for collection of the BrainIT core-dataset using the group IT based data collection methods. This paper describes the results of analysis of 200 patient's data in which validation data was also acquired independently by data validation research nurses. The error rates classed by data category are presented and discussed. Known limitations of current IT data collection methods and proposed solutions to these limitations are also discussed.

Methods

Core dataset Definition

Through European Community (EC) funding (QLRI-2000-00454), a series of meetings over a year brought together neurosurgeons, intensivists, scientists and representatives from the medical device and pharmaceutical industries to define and discuss a "core-dataset definition" for data that will be collected from all patients with traumatic brain injury (TBI), irrespective of the underlying project aim. A core dataset was defined and published [10] which consisted of the following nine data categories:

i) **Demographic** and "one-off" clinical data (pre-neurosurgical hospital data, neurosurgical hospital admission data and the first and worst CT scan data). This is data that is collected only once per patient.

ii) **Daily management** data (eg: use of sedatives, analgesics, vasopressors, fluid input/output balance etc). This data is collected as an overview of the day to day intensive care management of the patient and is collected only once per day.

iii) **Laboratory** data (eg: blood gas, haematology, biochemistry data etc). This is "episodic" data which is data collected more than once but at unpredictable times.

iv) **Event** data (eg: nursing manoeuvres, physiotherapy, medical procedures (line insertion), calibrations etc – also episodic data).

v) **Surgical** procedures.

vi) **Monitoring** data summary (eg: type and placement location of ICP sensor, BP lines, etc). Typically this data is only collected once per patient and is an overview of the monitoring configuration for a patient.

vii) **Neuro Event** data (eg: GCS scores, pupil size and reactivity also episodic data).

viii) **Targeted Therapies** A set of therapy categories have been defined with some associated therapy type detail. For every therapy given and intended target must also be given (eg: mannitol for raised ICP).

ix) **Vital monitoring** data. This is bedside monitoring data which is collected at regular intervals with a minimum sampling rate of once per minute.

Network Structure

The BrainIT group network structure consists of a central coordinating and data centre (Glasgow) with individual centres clustered into language based regions where each language region contains a sub-coordinating centre. Each sub-coordinating centre is responsible for coordinating the training and validation activities across centres within their region and to meet this requirement hire a "data validation" nurse responsible for providing training on the data collection tools and web-services to all centres within their own language region. The data validation nurses also provide a data checking and validation service coordinated from Glasgow.

Data Collection Tools

Clinical data is entered by local bedside nursing staff either on hand held PDA's or on in-house designed JAVA based software running on a PC. In collaboration with Kelvin Connect Ltd [11] the BrainIT core dataset definition was implemented in a flexible and easy to use hand-held PDA based device. A training course was held for the data validation nursing staff in Glasgow on the optimal use of the data collection instruments which also provides data entry in six European languages. An anonymisation routine removed patient identification elements from the collected data and labelled the patient data file with a unique BrainIT study code generated from the BrainIT web-site. A local database held in each centre linked the anonymised data to local centre patient ID information which was needed during the data checking stage of the study. Anonymised data was uploaded via the BrainIT website. A server side data converter tool converts data from centre based format into BrainIT data format generating nine data category files which are imported into the BrainIT Microsoft SQL2005 database.

Data Validation Process

Figure 1 graphically represents the data validation process. Centre staff enter data using client side tools such as the hand held PDA. Data is uploaded via the BrainIT web-services and a server-side converter formats data into the series of common data format files which are input into the BrainIT SQL database. A validation request tool residing on the database server randomly samples 20% of the data uploaded for each data category and generates a validation request file for each local data validation nurse listing the timestamps and data items to be checked against local gold-standard data sources. Data validators move between their designated centres and enter into a *data validation tool* the requested data items from source documentation held in each local centre. The resulting validation data file is uploaded to the BrainIT data coordinating centre via the website and using data validation checking software tools, the validated data is checked against the data items originally sent from which percentage accuracy data was calculated.

As part of this validation process, and in addition to the categorical and numeric clinical data being checked for accuracy, we also assessed the minute by minute monitoring data. Random samples of monitoring data channels uploaded (eg: ICP, SaO2) were selected and validation staff asked to manually enter the hourly recorded values from the nurses chart (or local gold standard data source) for the first and last 24 hour periods of bedside monitoring for a given patient for a given channel. These "validation" values could then be compared with a range of summary measures (eg: mean, median) from the computer based monitoring data acquired from the patient.

Assessing Feasibility

To assess feasibility, we sought answers to specific questions including: a)what data cleaning was necessary prior to analysis? b) how much missing data was found in specific data categories? c) how accurate is the data that was collected? and d) what are the known limitations of the existing IT methods for collection of the data?

Results

Data Description

Over a two year period, core dataset data (grouped by nine categories) were collected from 200 head-injured patients by local nursing staff. One patient's data was discarded from the cohort as there was less than 4 hours of monitoring data which fell outside our inclusion criteria leaving 199 patients in the feasibility study dataset. Table 1 summarises the key demographic and clinical features of the study cohort. Mean age was 36 years with the usual predominance of male patients. Using the TCDB classification on worst CT, 100 patients were coded with diffuse injury and 60 with mass lesions. Using the extended Glasgow Outcome Scale (GOSe) there were 33 deaths (20%) with 47% good and 53 % poor outcome respectively. Table 2 summarises the quantity of data collected per patient classed by data category. There were 109 "one-off" demographic and clinical data items collected which included pre-neurosurgical (PHSH) and neurosurgical hospital (NSH) data. The majority of the data were "episodic" in nature in that they were collected more than once per patient but at un-predictable times. These data types included "*ICU monitoring*" categories describing, for example, the location and type of medical monitoring device placed (eg: right frontal ICP bolt), *neurological status* (ICU GCS scores/pupil size and reactivity) , *therapies delivered, surgeries performed* etc. The largest number of data items collected fell within the "*Other clinical events*" category which included annotations of blood samples, lab results, and other nursing and medical procedures. In this category there was on average greater than 230 recordings per patient. The next most common category of data collected were those of annotations of target driven therapies. In this category there were on average greater than 60 targeted therapies delivered per patient. By far the largest category of data collected was the "periodic" minute by minute physiological monitoring data with over 2 million records in the patient cohort. Table 3 lists the number of patients with specific types of monitoring.

Data Cleaning

On average three raw data files were uploaded per patient giving 600 patient data files uploaded to the central database using the BrainIT web-services. All data files were validated prior to inclusion into the study dataset and in a proportion of these errors were found with data values needing to be re-checked and corrected by local nursing staff. Seven raw data patient files required resolving mismatches between physiological data patient identifiers and other clinical data files (1.2 % of files uploaded). Ten raw data files required trimming of physiological data outside the range of clinical data (2% of files uploaded). Nineteen patient files required correction of one or more admission, surgery or discharge time stamps (3% of files uploaded).

Missing Data

One-Off Measurements

There was missing data across certain data fields. Figure 2 is a graph listing those "One-Off" demographic and clinical data fields with greater than 15% of missing data. Common patterns in the types of fields yielding the highest missing data rates could be identified: A) One third of the fields with significant amounts of missing data were "one off" laboratory data values (eg: glucose, Haematocrit, PaCO2) which should have been obtained from admission notes from either the pre-neurosurgical hospital (PNSH) or the receiving neurosurgical hospital (NSH). B) One third of the missing fields were explanatory variables associated with either the first or worst CT scan classification. These explanatory variables included "yes/no" categories as to whether or not specific pathologies were seen on CT such as SAH, pneumoencaphalopathy, hydrocephalus etc. C) Fifteen percent of the missing data fields were explanatory variables associated with the 6 month Glasgow Outcome Scale data. These included fields such as "who was the main respondent" to the questionnaire and what was deemed to be the "main cause of disability" (head injury or systemic injury).

Episodic Measurements

These data types include therapies, laboratory values and nursing and medical procedures that were entered more than once at un-predictable times. For each episodic data measurement both a "start-time" and "end-time" should have been recorded for each measurement by local nursing staff. Nearly 10,000 therapies were successfully recorded with start-times but approximately a third had inaccurate or missing end times. Table 4 is a breakdown of the therapies delivered classed by type listing the proportion with missing "end-times". Clearly the quantity of missing end-times in this part of the dataset severely limits analyses assessing duration of therapy. Over 40,000 events and procedures were also recorded but events with long durations (such as transfers outside of the ITU for theatre or CT scan) were more than twice as likely to have "end-times" missed. These short-comings in the acquired episodic data has implications for the design of future data collection/validation tools as well as project training procedures.

Data Accuracy

In total, 19,461 comparisons were made between collected data elements and source documentation data by data validation research nurses. The number of comparisons made per data category were in proportion to the size of the data received for that category with the largest number checked in laboratory data (5,667) and the least in the surgery data (567) (Figure 3). Table 5 summarises error rates by data class. Error rates were generally less than or equal to 6%, the exception being the surgery data class where an unacceptably high error rate of 34% was found.

In the surgery data category, nursing staff had to choose surgical procedures from a fixed list of procedure types: *i) ICP placement, ii) Evacuation of Mass Lesion, iii) Elevation of depressed skull fracture, iv) Removal of foreign body, v) Anterior Fossa repair for CSF Leak, vi) Placement of Extra Ventricular Drain, vii) Active external decompression (with bone removal and duroplastia), viii) Other.* This classification system was used in an attempt at simplification and reducing the burden of data entry. However, through discussions with local nursing and data validation staff it was found that there was particular confusion over *when* to record ICP sensor placement and the presence of skull fractures as the primary surgical procedure. Typically, these procedures occur during the same operative procedure as for example during "evacuation of a mass lesion". Confusion over coding these two procedures between the original data entry nurse and the validation nurse accounted for the majority of errors in this data category.

We also checked the detection rate of acute events (eg: nursing management, physiotherapy, blood samples etc). It was found that short duration events were rarely missed but longer duration events such as transfer to CT or theatre were more likely to be not recorded. Through discussions with local nursing and data validation staff it is believed that the intense nursing activity just prior to and following a transfer is more likely to lead to omissions in recording these events on research systems.

Finally, we tested the accuracy of the minute by minute monitoring data that was collected. Table 6 shows the monitoring data validation results for the 6 data types with the most recorded nursing chart values. Data is expressed in terms of bias (+- 95% CL) between the nurses chart recorded values against the computer collected end hour averages. It can be seen from this data that the computer collected end hour data is an accurate reflection of the nurse's chart recorded data.
As an example, Figure 4 shows a **s**catter plot of computer monitored minute by minute ICP data averaged over 60 minutes (ICPavg) plotted against nurses chart end hour values (ICPvalid) collected by the data validation nurses. There is a good correlation between the two sets of data with a linear regression best fit R^2 value of 0.9773. Figure 5 is an Altman and Bland plot showing the average bias (-0.15 mmHg) and 95% confidence limits (0.12, -0.45) for the computer monitored end hour averaged data Vs the nurses chart end hourly recorded values collected by the validation nurses.

IT Tool Limitations

The PDA data entry tool and the website-upload tools did not incorporate sufficient validation mechanisms. Many fields with the PDA tool allowed export and upload of empty data fields. Although most IT technology nowadays can be configured to explicitly specify required fields and prevent upload of data with specific missing data, at the time this study was designed, such validation facilities were not available off the shelf. Also, the PDA tool allowed acceptance of new items not part of the drop down selection menu, which could generate multiple terms for the same data element. This caused added burden on the cleaning process to consolidate multiple text terms for the same data element. The most challenging limitation found with the IT technology used in this study was an inability to automatically track "continuous" (non-bolus) therapies which were started to ensure that a matching "end-time" was entered. This resulted in approximately 1/3rd of the therapies annotated to have missing end times.

Discussion

This project has studied the feasibility for collection of the BrainIT core dataset using our first generation IT based tools. Feasibility has been assessed in terms of amount of missing data, data accuracy for data that was collected and also in terms of identifying limitations in the IT technology used to collect the data.

Good clinical practice dictates that as part of clinical trial design, acquired data must be checked for accuracy against gold standard data sources. This is often implemented through either employing a contract research organisation or independent research nurse staff to perform this duty. In large multi-centre clinical trials, costs to hire research nurse data validation staff can become prohibitively expensive and feasible only if significant industry or research council funding support is provided. Now with the adoption of the new medical device standard ISO-14155, even small medical device studies are expected to provide some form of check on the accuracy of data collected even as part of a non-regulatory post-marketing study.

To our knowledge, this study conducted by the BrainIT group is one of only a few multi-centre projects to attempt to prospectively assess the data capture error rate within an academic environment [12].

Giuseppe – can you add some text here about your experiences with the NeuroLink Project?

Monitoring Data Validation

We have shown that computer collected minute by minute vital signs data, summarised as end hour averages, correlated well with nursing chart end hour recordings. This allows for the end hour averaged computer records to be used in database analyses that aim to assess nurses chart recorded detection of events with computer based sampling. Although, end-hour average data correlates well with the nurses hourly recorded value, this does not indicate that important features of the data are not being missed by employing only hourly recording. For example, Zanier and colleagues [13] conducted a study showing that although computer-monitored end-hour data is accurately reflected

by the nurses' chart value, more complex summary measures (such as the detection of an intracranial pressure (ICP) of more than 20 mmHg) are less accurate. Their finding that at least one-third of secondary insults for raised ICP are not identified from the nursing chart is similar to that reported by Corrie and colleagues [14], who also found a similar detection error rate for other signals such as blood pressure, particularly the events of shorter duration. Importantly, Zanier's paper has further shown that when data are categorised in terms of percentage of time spent with raised ICP, the patients exhibiting instability in ICP were most prone to under estimation of ICP insults. The data sampling rate may be pertinent here: Zanier's study sampled at 600 samples per minute, whereas other studies used 1 sample per minute [14] or as few as 4 samples per hour [15]. Our results here confirm those of other investigations showing that the end hour averaged computer values can be used as estimates of nurse's paper based end hour recordings and opens up the possibility for further studies assessing the clinical influence of missed short term adverse physiological events without requiring tedious recording of nursing chart values.

However, the key question remains unanswered as to whether missed adverse events using higher resolution sampling significantly influences clinical outcome. Work conducted by Chambers and colleagues may be relevant in this regard [16]. They found that in studies of children with TBI, the choice of summary measure is also important. They used an index termed the "Pressure Time Index (PTI)", which is a composite index taking into account both the duration of the adverse event and the degree of physiological impairment below a given threshold. They found, using ROC analysis of the influence of cerebral perfusion pressure adverse events (calculated using the PTI index) upon outcome, that models that included the PTI measure of CPP burden significantly improved the fit to clinical outcome compared with models that did not include measures of physiological instability. These results are in contrast to those published by Signorini et al who they found very little improvement in outcome prediction when "Insults" are added to the usual clinical features in prognostic models of patient outcome [17]. This approach, developed by Chambers and colleagues needs to be repeated in the adult TBI population and is one of the planned analyses on the BrainIT

dataset. If the result found in children can be replicated in adults, this will provide new evidence that using only the mean or median values are not optimal summary measures of the burden of physiological adverse events. (Iain – do you want to expand on this section?)

Validation Costs

These validation results calculated on a subset of patients provides an estimate of the data quality on a larger patient cohort of 350 patients collected using the same methodology but collected outside of the validation study. However future data collection projects will generate datasets under differing data collection conditions and will require a separate validation stage if we wish to maintain our confidence in the level of data collection accuracy. The approach used by the BrainIT group to validate data (using 20% sampling of uploaded data with some automation of generating data lists for validation) still requires significant research nurse time to track down and enter data for validation purposes. To maintain a full time data validation nurse across all participating countries costs in excess of 1 Million Euro's per year. Such large running costs for an academic network is prohibitively expensive and not sustainable in the long term and a more cost-effective solution for data validation must be found. One promising approach being assessed by the BrainIT group is developing collaborative research with experts in Grid based secure access technology. Grid technology covers more than just access to networks of high end servers in order to solve computationally intensive problems. There is a considerable amount of expertise and middleware software solutions now available that provide secure access to distributed medical datasets so that the right people see the correct data in the appropriate context [23]. Such an approach, once local and national IT policy staff are satisfied with the security, will enable remote data validation systems to directly query hospital based gold standard data sources for data checking. Most research datasets contain large portions of data elements that are collected for routine patient management purposes and the difficulty of accessing hospital based data sources often means that research nurses are employed to re-enter data extracted from local hospital sources into research data entry systems. This results in a high proportion of double data entry which is an inefficient use

of resources. Using Grid technology to interface directly with local hospital data sources will reduce the burden of double data entry. Clearly some data validation staff will still be required to support system queries but increased use of automatic data validation procedures and access to hospital based datasets should significantly reduce the cost burden to conduct multi-centre clinical trials. Towards this end, the BrainIT group as part of an EEC funded framework VII project plan to assess such an approach in a group of neuro-intensive care centres equipped with the latest Grid technology. This project – the AVERT-IT project [18] will install Grid services behind hospital firewalls in six BrainIT neuro-intensive care units. Grid services will interface to local hospital systems, extract data which maps to the BrainIT core dataset and integrate data from both hospital sources and local AVERT-IT data collection tools (for those elements not collected as part of routine management) into a local database. Once every six hours, data will be stripped of patient sensitive data, encrypted and "pushed" out of local hospital networks to an external secure server cluster hosted at the University of Glasgow National eScience Centre [19]. Local databases will be maintained which link local patient identifiers with an anonymous patient identifier. Systems running at the BrainIT coordinating centre in Glasgow will allow remote monitoring of the data acquired from all six participating BrainIT centres. Such a remote monitoring service in quasi real-time will allow more efficient collection and validation of hospital based data collected for research purposes. Requests to validate specific data elements can be generated by email and local staff re-enter data using the local data entry systems while the patient and their notes are still within the ITU. Also, such a network design supporting remote monitoring of data from multiple centres will allow monitoring of patient management for adverse events (such as treatments given for arterial hypotension) and will enable testing and tracking adherence to study protocols. Ideally, all project data should be recoverable from local hospital information systems, in reality, a finite amount of time and IT resources forces compromise between the ideal and the achievable. Nevertheless, this approach of enabling direct access to hospital based data for research purposes should in time significantly lower research nurse costs.

Lessons Learned

A number of lessons have been learned during this feasibility study.

Our surgery classification definition is ambiguous. Specifically our definition document did not make it clear how to decide which surgery is the "*Primary Reason for Surgery*". For example if a patient undergoes surgery for removal of a mass lesion and repair of depressed skull fracture, some approach must be used to provide a consistent classification response. We are proposing a modified surgery classification to include a "major surgery choice matrix" where individual surgery types are weighted and specific combinations that do occur can be resolved to a single surgical priority.

Not all staff favoured use of a PDA type data tool. By the end of the feasibility study, approximately half the centres collecting data preferred to use PC based systems rather than the hand-held PDA's. Increasingly, nursing and medical staff have good skills with using keyboards and mice and as a result now our new data collection tools are PC based. Also, our data tools (although state of the art at the time), did not provide sufficient local validation features in keeping with modern standards. For example, many fields with the PDA tool allowed export and upload of empty data fields. Most IT technology nowadays can be configured to explicitly specify required fields and prevent upload of missing data. Our current generation of data tools now almost entirely allow only specific choices to be made from drop-down "combo boxes" where the default choice is set to a text value of "not set". This makes it explicitly clear that a given field has not been entered. Our data schema will not allow mandatory fields to be left "not-set" before a patient is discharged from the system. For the entry of treatment information, every treatment must be assigned a specific target and again, the data schema will not accept treatments that have not been assigned a target. Furthermore, our next generation data collection tools, as implemented in the AVERT-IT project, allows annotation of any treatment or procedure with only two mouse clicks providing more rapid and efficient data entry for the bed side nurse. A single page display (see figure 6)

incorporates a data table where it can be readily seen if "continuous" treatments (eg: infusions) or events (eg: transfer to CT-scan) have missing "end times". The web-client software includes data validation routines which will prevent upload of missing data in any required fields. Patients cannot be discharged from the system until all required data is entered.

Future Direction

The BrainIT group aims and their implementation is a staged process. We have successfully defined a core dataset standard, developed standardised IT tools to collect the core dataset and tested the feasibility for collection of the dataset from 22 centres across Europe. Limitations in our methods have been found and attempts made to address those issues prior to starting future studies. Inevitably, with each new project, problems will arise and solutions will be found. This being a cyclical process. Our second aim "***To develop and use a standardised database as a tool for hypothesis generation and the development, testing and validation of new data analysis methodologies.***" has been achieved and a number of publications are now arising from access to this shared resource [20]. Currently on our 2nd database release with a third release planned for our BrainIT meeting being held in Vilnius 2009 [21], what is especially encouraging is that the existence of the database resource was directly responsible for generating the hypothesis about application of Bayesian neural network methods for prediction of hypotension adverse events – a project now funded under the VIIth EC information and communications technology framework [18].

One of the papers arising from the work of the BrainIT group was a report on its own internal survey of patient management which indicated that, according to the survey, international management guidelines are for the most part adhered with [9]. However, there is a risk with surveys that there may be differences in results between what users "think" management is applied in their centre and studies which measure it directly. In this regard, a recent paper published by one of our collaborators on analyses of the BrainIT dataset was to assess, subsequent to the BrainIT

survey, whether the use of hyperventilation therapy for the management of raised ICP was indeed conducted according to international guidelines. Interestingly they found that despite what was suggested by the earlier survey results, and in conflict with current management guidelines, there was significant over use of early prophylactic hyperventilation [22]. This result highlights the importance of directly monitoring the applied management, and if it can be achieved in near real-time, will enable future management trials to monitor protocol adherence and better select when patients data can be recruited to a study.

The third and most challenging aim of the BrainIT group is to use its improved infrastructure to generate new evidence on the utility of monitoring and management methods for patients with TBI. The AVERT-IT project now underway, will put in place in six BrainIT centres, Grid middleware systems enabling direct access to hospital data and remote monitoring of patient management. We believe that this type of remote monitoring facility is a pre-requisite for the conduct of a future multi-centre management trial by the BrainIT group. Discussions of a management trial design are planned for the next BrainIT group meeting (Vilnius, September 2009) and the AVERT-IT project will pilot the feasibility of the remote monitoring infrastructure required for the conduct of such a trial.

Conclusions

In this study we have shown that it is feasible to collect the BrainIT dataset from multiple centres in an international setting with our IT based methods and the accuracy of the data collected is greater than or equal to 94%, with the exception of the surgery data definition which is being revised. Lessons learned have been met with advances in client/server tools providing improved validation support. We anticipate that the second generation of BrainIT data collection tools (being used as part of the current AVERT-IT project will improve missing data and validation accuracy rates. A future BrainIT management trial will rely on a Grid based infrastructure capable of remotely

monitoring patient management and protocol conformance now being piloted in six BrainIT centres. Academic led multi-centre data collection projects must decrease validation costs and likely will require more direct electronic access to hospital based clinical data sources for both validation purposes and for reducing the research nurse time needed for double data entry of data currently not accessible from hospital based systems for research purposes.

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Table 1

Demographic and Clinical Features of Feasibility Study Data set (n = 199)

Sex			**TCDB (Worst)**		
	Male	162		*Diffuse1*	9
	Female	37		*Diffuse2*	51
Age				*Diffuse3*	34
	Mean	36.1		*Diffuse4*	12
	Range	4-83		*Mass*	60
	<14yo	7		*Missing*	33
Trauma Type			**GOSe**		
	RTA	84		*1 (Dead)*	31
	Pedestrian	16		*2*	3
	Fall	55		*3*	35
	Assault	18		*4*	8
	Sport	6		*5*	30
	Work	5		*6*	17
	Missing	14		*7*	30
				8	24
				Missing	21

Table 2 – Summary of Data Collected

Data Type	No. of Fields	Avg No. of Rows per Patient
Demographic *(eg: PNSH/NSH)*	109	1
ICU_Monitoring *(eg: Types of Device/Location…)*	12	15.0
Neurological Status *(eg: GCS/Pupils)*	10	42.3
Other_Clinical_Events *(eg: Blood Samples, Suction…)*	20	230.9
Surgery	11	1.4
Target_Therapies	59	69.6
Daily_Observations *(eg: Daily Summaries of Management)*	11	8.4
Total	**232**	

Table 3 – Monitoring Data Distribution

Channel	Number of Patients
BP (blood pressure: mmHg;systolic, diastolic, mean)	199
ICP (intracranial pressure: mmHg;mean)	195
CPP (cerebral perfusion pressure: mmHg;mean)	195
HRT (Heart Rate: bpm)	165
SaO2 (arterial Oxygen saturation: %;pulse oximetry)	164
Tc (core temperature: degrees C)	149
CVP (central venous pressure: mmHg; mean)	105
ETCO2 (end tidal CO2: mmHg)	79
NIBP (blood pressure: mmHg;systolic, diastolic, mean)	50
Tp (peripheral temperature: degrees C)	17
PtiO2 (brain tissue oxygen partial pressure: mmHg)	11
SjO2 (jugular venous oxygen saturation: %)	10
CO (cardiac output: ml/hour)	7
brTemp (brain temperature: degrees C)	3
PrX (bp-icp reactivity:dimensionless)	1

Table 4 – Therapy Type Vs Missing "End Times"

Therapy	**Start Entries**	**End Entries**	**Missing End Entries**
Sedation	1108	499	55%
Analgesia	1032	574	44%
Paralysis	741	460	38%
Volume Expansion	1674	1308	12%
Inotropes	614	199	68%
Anti-Hypertensives	63	22	65%
Anti-Pyretics	788	505	36%
Hypothermia	22	10	55%
Steroids	51	6	88%
Cerebral Vasoconstr.	0	0	---
Osmotics (Mannitol)	807	538	33%
Barbiturates	90	45	50%
Other	2576	2026	21%
Totals	**9566**	**6192**	**35%**

Table 5

Percentage Error Rate by Data Type Class with Description of Common Error Types.

Data Class	Error Rate (%)	Common Fields with Errors
Laboratory	2	pCO2, FiO2 value wrong
Demographic	4	Monitoring time on arrival at neurosurgery, intubation present on arrival at neurosurgery wrong
Neuro Observations	5	Pupil Size, GCSv (code 1 Vs Unknown code error)
Monitoring Summary	5	ICP type, ICP Location wrong
Daily Management Summary	5	Infusion type (bolus Vs infusion or both), drug number (1 or > 1)
Targeted Therapy	6	Non-standard target, no Target specified
Surgeries	34	ICP placement, Skull #, mass lesion wrong

Table 6

Monitoring Data Validation Results – Bias (+- 95% CL) Between Nurses Chart Recorded Values Vs Computer Collected End Hour Averages

Data Type					
Value	*ICP (mmHg)*	*BP (mmHg)*	*CPP (mmHg)*	*SaO2 (%)*	*Tc (C)*
Bias	-0.15	0.16	0.46	0.46	-0.29
+95%	0.32	1.57	1.81	1.23	0.09
-95%	-0.62	-1.25	-0.88	-0.31	-0.67
n	749	558	457	499	223

Figures Legends

Figure 1. Graphical representation of the data validation process. Centre staff enter data using client side tools such as the hand held PDA. Data is uploaded via the BrainIT web-services and a server-side convertor converts data into the series of common data format files which are input into the BrainIT SQL database. A validation request tool residing on the database server randomly samples 20% of the data uploaded for each data category and generates a validation request file listing the timestamps and data items to be checked by local data validators. Data validators move between their designated centres and enter into a *data validation tool* the requested data items from source documentation held in each local centre. The resulting validation data file is uploaded to the BrainIT data coordinating centre via the website and using data validation checking software tools, the validated data is checked against the data items originally sent from which percentage accuracy data is calculated.

Figure 2. Graph showing "One-Off" demographic and clinical data fields with greater than 15% of missing data.

Figure 3. Pie chart showing the distribution of the 19,461 data validation comparisons which were made in proportion to the size of the data received with the largest number checked in laboratory data (5,667) and the least in the surgery data (567).

Figure 4) Scatter plot of computer monitored minute by minute ICP data from an example patient showing the data averaged over 60 minutes (ICPavg) plotted against nurses chart end hour values (ICPvalid). Linear regression best fit R^2 value = 0.9773.

Figure 5) Altman and Bland plot from an example patient showing the average bias (-0.15 mmHg) and 95% confidence limits (0.12, -0.45) for the computer monitored end hour averaged data Vs the nurses chart end hourly recorded values collected by the validation nurses.

Figure 6) A screen shot of the AVERT-IT data collection tool which will support collection of hypotension treatment information during the clinical trial phase of this project. Any treatment can be recorded by just 2 mouse clicks by the bedside nurse. A single page display incorporating a treatment/event entry table makes it easier to identify missing "end-times".

Figure 1

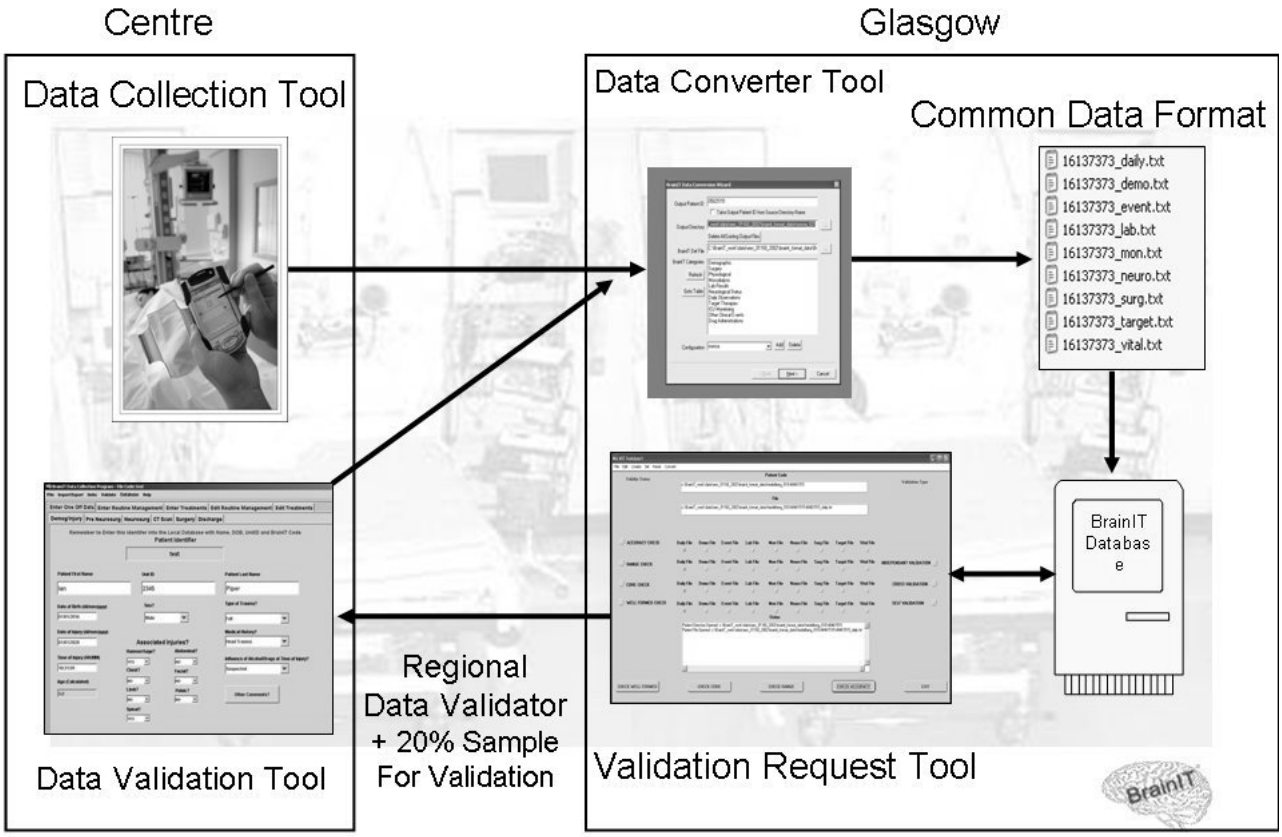
Centre
Glasgow
Data Collection Tool
Data Converter Tool
Common Data Format
16137373_daily.txt
16137373_demo.txt
16137373_event.txt
16137373_lab.txt
16137373_mon.txt
16137373_neuro.txt
16137373_surg.txt
16137373_target.txt
16137373_vital.txt
BrainIT Database
Regional Data Validator + 20% Sample For Validation
Data Validation Tool
Validation Request Tool
BrainIT

Figure 2

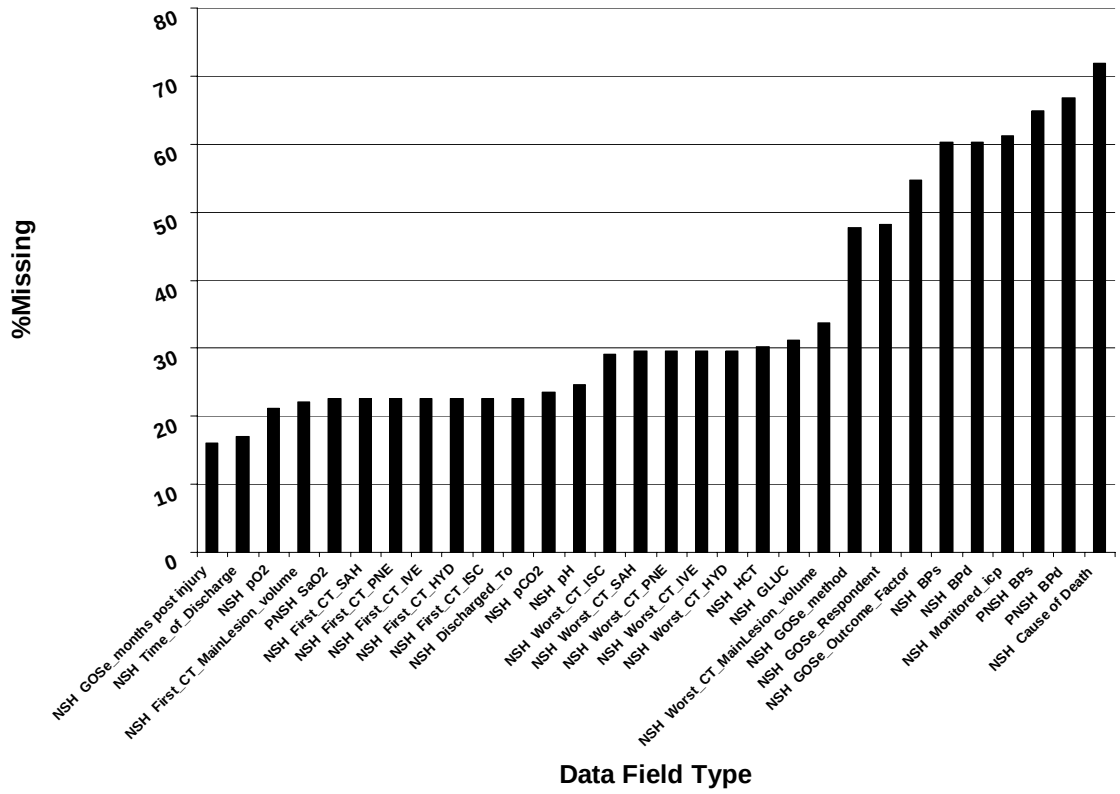
%Missing
0
10
20
30
40
50
60
70
80
NSH_GOSe_months post injury
NSH_Time_of_Discharge
NSH_pO2
NSH_First_CT_MainLesion_volume
PNSH_SaO2
NSH_First_CT_SAH
NSH_First_CT_PNE
NSH_First_CT_IVE
NSH_First_CT_HYD
NSH_First_CT_ISC
NSH_Discharged_To
NSH_pCO2
NSH_pH
NSH_Worst_CT_ISC
NSH_Worst_CT_SAH
NSH_Worst_CT_PNE
NSH_Worst_CT_IVE
NSH_Worst_CT_HYD
NSH_HCT
NSH_GLUC
NSH_Worst_CT_MainLesion_volume
NSH_GOSe_method
NSH_GOSe_Respondent
NSH_GOSe_Outcome_Factor
NSH_BPs
NSH_BPd
NSH_Monitored_icp
PNSH_BPs
PNSH_BPd
NSH_Cause of Death
Data Field Type

Figure 3

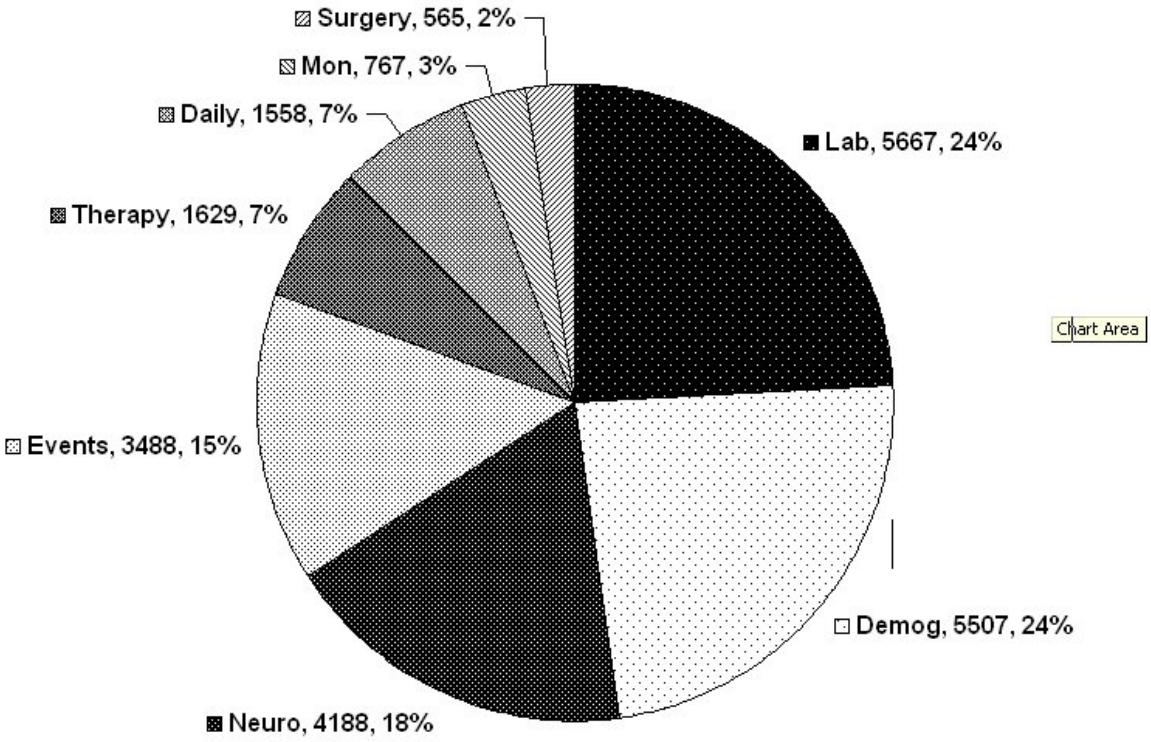
Surgery, 565, 2%
Mon, 767, 3%
Daily, 1558, 7%
Therapy, 1629, 7%
Events, 3488, 15%
Neuro, 4188, 18%
Demog, 5507, 24%
Lab, 5667, 24%
Chart Area

Figure 4

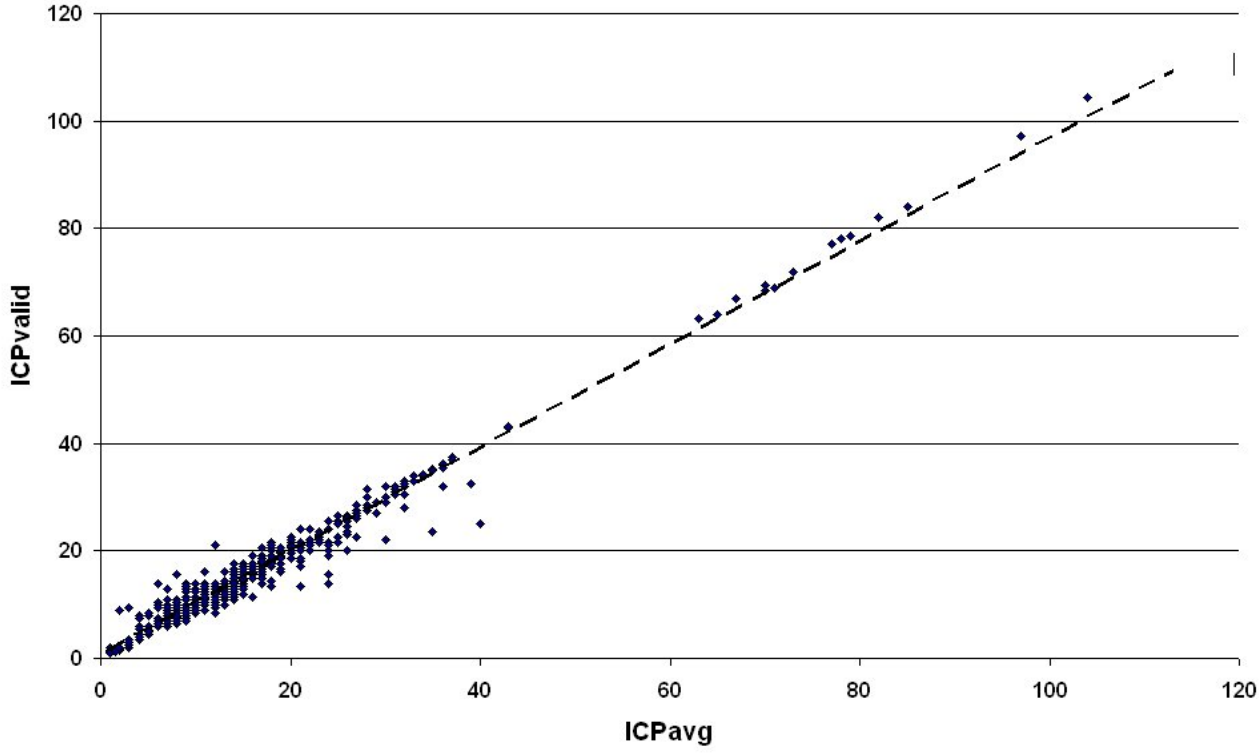

Figure 5

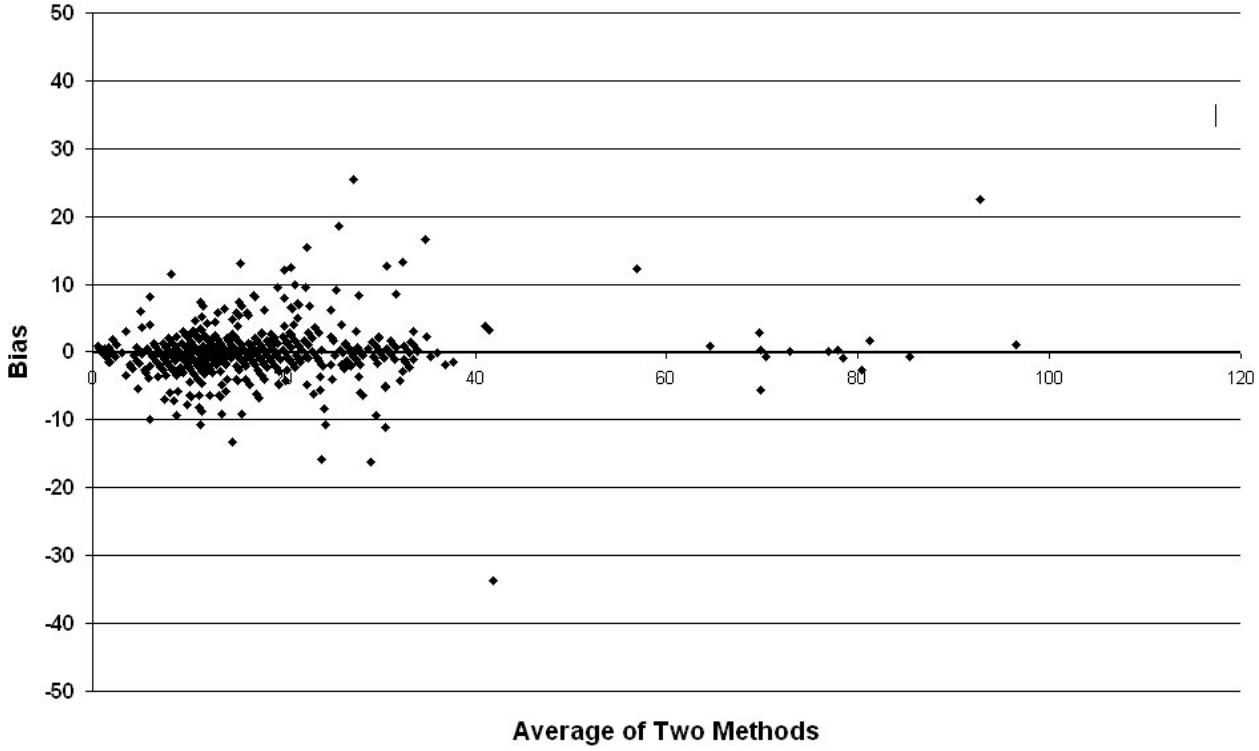
50
40
30
20
10
0
-10
-20
-30
-40
-50
Bias
0
40
60
80
100
120
Average of Two Methods

Figure 6


Avert IT
Logout : nurse
Home > ICU Patient List > Patient Treatment
Surname:
Hospital Coc
First Name: Ian
Age: 43
Treatment
ICU Notes
GCS...
Lab Data
Daily Obs
ICU Monitoring
PNSH
NSH
Surgery
CT
Targets
ICP
CPP
Neuro Drop
Fever
Hyponatraemia
Hypoxia
Hypercapnia
Hypotension
SjO2/PbrO2
Hyperglycemia
Seizures
Not Set
Mild Hyperventilation (4-4.5 kPa)
Severe Hyperventilation (< 4.0kPa)
Analgesia
Hypothermia
Paralysis
Sedation
Steroid
Crystalloids
Colloids (including Plasma)
Hypertonic Saline
Erythrocytes
Catecholamines
B-Blockers
Alpha2 Agonists
Paracetamol
Cooling
Dihydroergotamine
Indomethacin
Mannitol
Single
Continuous
Recent Patient Treatments Log
Started
Ended
Therapy
Type
Target
12/09/2009 22:22
12/09/2009 22:22
Cerebral
Indomethacin
Hyperglycemia
08/07/2009 12:12
08/07/2009 12:12
Volume Expansion
Crystalloids
ICP
21/06/2009 12:12
05/07/2009 12:12
Anti Hypertensive
B-Blockers
ICP
20/06/2009 12:12
20/06/2009 12:12
Volume Expansion
Crystalloids
CPP
13/06/2009 22:22
13/06/2009 22:22
Volume Expansion
Crystalloids
ICP
13/06/2009 22:22
13/06/2009 22:22
Volume Expansion
Crystalloids
ICP
13/06/2009 22:22
13/06/2009 22:22
Inotropes
Catecholamines
ICP
View Full Treatment Log
Avert IT: Research and development project funded by the European Commission under Framework Programme 7 - ICT-2007.5.2: