

# The brain monitoring with Information Technology (BrainIT) collaborative network: EC feasibility study results and future direction

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## Abstract

**Background** The BrainIT group works collaboratively on developing standards for collection and analyses of data from brain-injured patients and to facilitate a more efficient infrastructure for assessing new health care technology with the primary objective of improving patient care. European Community (EC) funding supported meetings over a year to discuss and define a core dataset to be collected from patients with traumatic brain injury using IT-based methods. We now present the results of a subsequent EC-funded study with the aim of testing the feasibility of collecting this core dataset across a number of European sites and discuss the future direction of this research network.

**Methods** Over a 3-year period, data collection client- and web-server-based tools were developed and core data (grouped into nine categories) were collected from 200

head-injured patients by local nursing staff in 22 European neuro-intensive care centres. Data were uploaded through the BrainIT website and random samples of received data were selected automatically by computer for validation by data validation staff against primary sources held in each local centre. Validated data were compared with originally transmitted data and percentage error rates calculated by data category. Feasibility was assessed in terms of the proportion 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 staff conducted 19,461 comparisons between uploaded database data with local data sources and error rates were commonly less than or equal to 6%, the exception being the

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surgery data class where an unacceptably high error rate of 34% was found. Nearly 10,000 therapies were successfully recorded with start-times but approximately a third had inaccurate or missing “end-times” which limits the analysis of 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 that studies avoid known limitations in the dataset. Limitations in the current IT-based data collection tools have been identified and have been addressed. In order for multi-centre data collection projects to be viable, the resource intensive validation procedures will require a more automated process and this may include direct electronic access to hospital-based clinical data sources for both validation purposes and for minimising the duplication of data entry. This type of infrastructure may foster and facilitate the remote monitoring of patient management and protocol adherence in future trials of patient management and monitoring.

**Keywords** Clinical network · Traumatic brain injury · Grid · Internet

## Background

Severe traumatic brain injury (TBI) is a leading cause of death and survivors invariably have serious and long-term morbidity [12]. There are significant social and economic effects including loss of employment and an increased burden of care to the victim, their families and society as a whole.

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 therapies and monitoring devices. However, despite the existence of guidelines for the management of severely head-injured patients [1, 8] this group of patients is subject to considerable variability in care across centres [6, 7, 9, 10, 15]. To improve the monitoring and management standards in this population, the inter- and intra-centre variability in the intensive care management, physiological monitoring and treatment of these patients needs to be assessed on a multi-national basis. To do so requires a standardised, IT-based, higher resolution methodology for acquiring multi-centre patient management and physiological monitoring information.

One consequence of the variability in the clinical management across centres that take care of patients with

traumatic brain injury is the confounding influence that this may have in multi-centre trials of therapy. Despite promising pre-clinical results of several potential neuroprotective drugs, 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, may be 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% [17]. Even in large-scale randomised trials, an accurate sample-size analysis cannot be made without the knowledge of the incidence of the true variability of relevant confounding factors. Inaccurate sample-size estimates will lead to trials that are not correctly powered.

Improving the standards and resolution for multi-centre data collection will also affect 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 (SME). Unlike the pharmaceutical industry, SMEs lack the resources to independently assess their devices in multi-centre clinical trials and this severely limits the ability to provide an evidence base demonstrating the clinical utility of their products.

In order to address these issues, it is essential to develop an open, collaborative network of centres interested in the realisation of higher resolution and standardised methods for the collection of neuro-intensive care monitoring and management data from patients with TBI. Such an infrastructure will provide a more efficient means for assessing new and developing health care technology which may be new pharmaceutical compounds, management approaches or monitoring devices.

To address these issues, the Brain Monitoring with Information Technology (BrainIT) group was formed ([www.brainit.org](http://www.brainit.org)). The group has three 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.

This paper reports on the results of a 3-year EC-funded study (QLGC-2002-00160) that enabled the group to develop IT methods to collect a 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 amount of missing data, accuracy of data collected and limitations reported by users of the IT data collection methods. To assess accuracy, data validation staff (usually research nurses) were hired on a regional basis (normally country by country) to check samples of the collected data against the local primary clinical record in order to quantify the accuracy of the IT-based data collection methods. This paper describes an analysis of the comparison of the data from 200 patients with that obtained independently by data validation staff. The error rates classed by data category are described and the known limitations of current IT data collection methods are considered along with some proposed solutions.

## Methods

### Ethics

Local and multi-centre research ethics committee approval was obtained in each participating centre. As patients were in coma and unable to consent themselves, relatives' assent was sought. We asked for and received permission to collect intensive care data normally collected as part of the routine patient management, and in addition to follow-up patients at 6-month post injury to assess clinical outcome using the extended Glasgow Outcome Scale (GOSe). Only anonymised data left the centres for storage in the central database in Glasgow. Research nurses were tasked to ensure data sent had any patient identifiers removed.

### Core dataset definition

Through European Community (EC) funding (QLRI-2000-00454), a series of meetings over a 1-year period 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 should be collected from all patients with TBI, irrespective of the underlying project aim. A core dataset was defined and published [13] that consisted of the following nine data categories:

1. Demographic and “one-off” clinical data (pre-neurosurgical hospital data, neurosurgical hospital admission data and the first and worst CT scan data). These data are collected only once per patient.
2. Daily management data (e.g. use of sedatives, analgesics, vasopressors, fluid input/output balance etc). These data are collected as an overview of the day to day intensive care management of the patient and are collected only once per day.
3. Laboratory data (e.g. blood gas, haematology, biochemistry data etc). These are “episodic” data which are data collected more than once but at unpredictable times.
4. Event data (e.g. nursing manoeuvres, physiotherapy, medical procedures (line insertion), calibrations, etc.—also episodic data).
5. Surgical procedures.
6. Monitoring data summary (e.g. type and placement location of ICP sensor, BP lines, etc). Typically these data are only collected once per patient and are an overview of the monitoring configuration for a patient.
7. Neuro event data (e.g. Glasgow Coma Score, pupil size and reactivity also episodic data).
8. Targeted therapies. A set of therapy categories have been defined with some associated therapy type detail. For every therapy given an intended target must also be given (e.g. mannitol for raised ICP).
9. Vital monitoring data. These are bedside monitoring data which are 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. To meet this requirement a “data validation” nurse was hired and was 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 PDAs or on in-house designed JAVA-based software running on a PC. In collaboration with Kelvin Connect Ltd [<http://www.kelvinconnect.com/>], 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

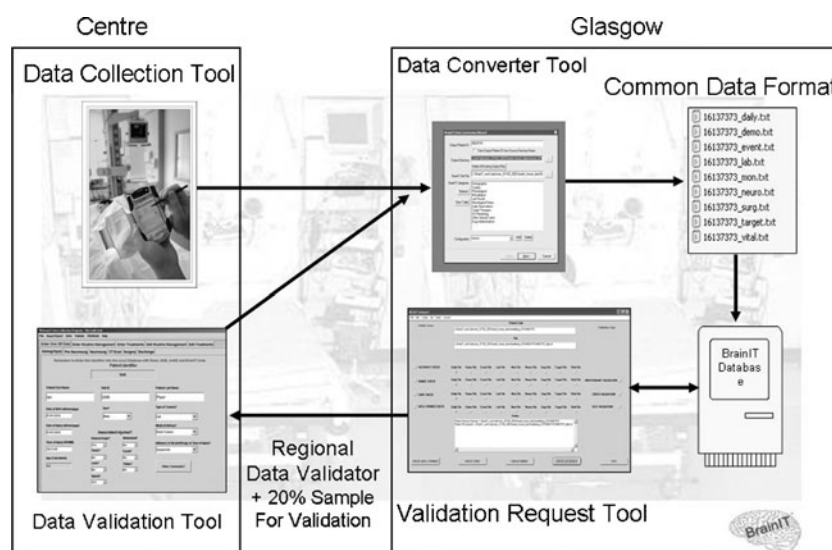
also provides data entry in six European languages. An anonymisation routine removed patient identification elements from the collected data and labelled the patient data file with a unique BrainIT study code generated from the BrainIT website. The hand-held PDA data collection tool would not allow exporting of data from the device until a valid eight-digit BrainIT project code was downloaded from the BrainIT website. Once entered, the export routine stripped out any patient identifiers (name, dob, centre name) and all patient data for that patient was only linked to the anonymous eight-digit BrainIT project code in the exported data file. 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 converted data from centre specific format into a standardised 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 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 (e.g. ICP, SaO<sub>2</sub>) were selected and validation staff asked to manually enter the hourly recorded values from the nurse's chart (or local gold standard data source) for the first and last 24-h 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.



**Fig. 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 converter converts data into the series of common data format files which are put 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

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## Assessing feasibility

To assess feasibility, we sought answers to specific questions including:

1. What data cleaning was necessary prior to analysis?
2. What proportion of missing data was found in each data category?
3. How accurate is the data that was collected?
4. What are the known limitations of the existing IT methods for collection of the data?

## Results

### Data description

Over a 2-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 h of monitoring data which fell outside our inclusion criteria leaving 199 patients in the feasibility study dataset. Twenty centres contributed data to this dataset. The average number of patients contributed per centre was ten (median five) with a centre maximum of 45 patients and a centre minimum recruitment of one. Seventy-five percent of centres contributed four or more patients to the 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 in such series. Using the TCDB classification on worst CT, 100 patients were coded with diffuse injury and 60 with mass lesions. Using the 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 (PNSH) 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 unpredictable times. These data types included “ICU monitoring” categories describing, for example, the location and type of medical monitoring device placed (e.g. right frontal ICP bolt), neurological status (ICU Glasgow Coma Scale (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 the 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

**Table 1** Demographic and clinical features of feasibility study data set ( $n=199$ )

Sex			Traumatic Coma Database (TCDB) (worst)	
Sex	Male	162	Diffuse1	9
	Female	37	Diffuse2	51
Age			Diffuse3	34
	Mean	36.1	Diffuse4	12
	Range	4–83	Mass	60
	<14-years old	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

category, there was on the 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. Figure 2 is a histogram plot showing the quantity and spread of time-series data for the main monitored channels: ICP, BP, CPP, CVP, SaO<sub>2</sub>, Core Temperature, ETCO<sub>2</sub> and PtiO<sub>2</sub>. The number of data points sampled per channel ranges from 89,524 for PtiO<sub>2</sub> to 1.98 million samples for BPm (BPm=1,979,284, ICPm=1,748,423, CPP=1,719,166, CVPm=541,524, SaO<sub>2</sub>=1,656,614, Tc=1,372,641, ETCO<sub>2</sub>=502,524, PtiO<sub>2</sub>=89,524).

### Data cleaning

On the 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 needed 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

**Table 2** Summary of data collected

Data type	Number of fields	Average number of rows per patient
Demographic (e.g. PNSH/NSH)	109	1
ICU monitoring (e.g. types of device/location)	12	15.0
Neurological status (e.g. GCS/pupils)	10	42.3
Other clinical events (e.g. blood samples, suction...)	20	230.9
Surgery	11	1.4
Target therapies	59	69.6
Daily observations (e.g. daily summaries of management)	11	8.4
Total	232	–

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 3 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: (1) One third of the fields with significant amounts of missing data were one-off laboratory data values (eg: glucose, Haematocrit, PaCO<sub>2</sub>) which should have been obtained from admission notes from either the PNSH or the NSH. (2) 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

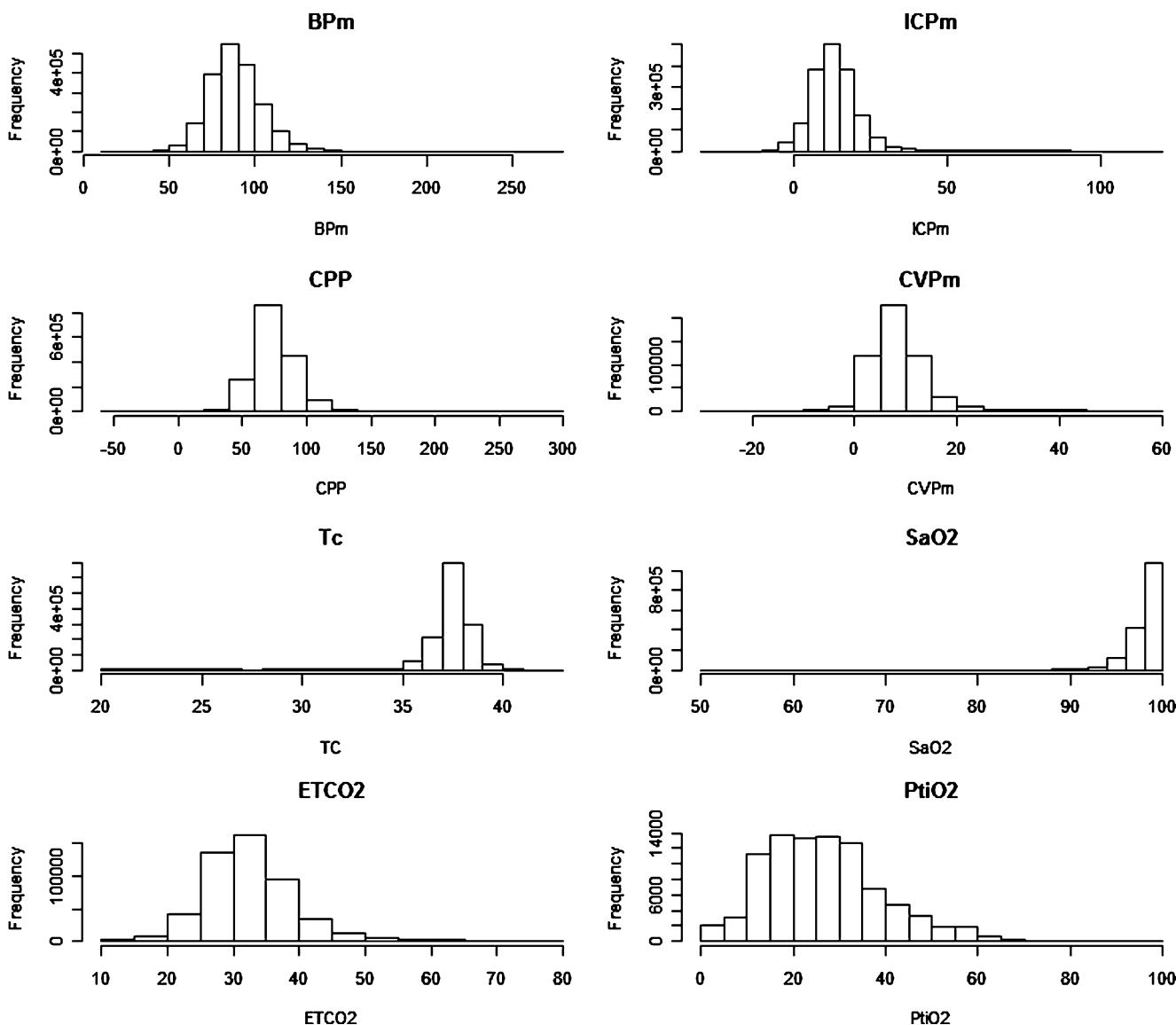
whether or not specific pathologies were seen on CT such as SAH, pneumocephalopathy, hydrocephalus, etc. (3) Fifteen percent of the missing data fields were explanatory variables associated with the 6-month Glasgow Outcome Scale data. These included fields such as “who was the main respondent” to the 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 unpredictable 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 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

**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
SaO <sub>2</sub> (arterial oxygen saturation: %; pulse oximetry)	164
Tc (core temperature: °C)	149
CVP (central venous pressure: mmHg; mean)	105
ETCO <sub>2</sub> (end tidal CO <sub>2</sub> : mmHg)	79
NIBP (blood pressure: mmHg; systolic, diastolic, mean)	50
Tp (peripheral temperature: °C)	17
PtiO <sub>2</sub> (brain tissue oxygen partial pressure: mmHg)	11
SjO <sub>2</sub> (jugular venous oxygen saturation: %)	10
CO (cardiac output: ml/hour)	7
brTemp (brain temperature: °C)	3
PrX (bp-icp reactivity: dimensionless)	1



**Fig. 2** Figure 2 is a histogram plot showing the quantity and spread of time-series data for the main monitored channels: ICP, BP, CPP, CVP, SaO2, Core Temperature, ETCO2 and PtiO2. The number of data points sampled per channel ranges from 89,524 for PtiO2 to 1.98

million samples for BPm (BPm=1,979,284, ICPm=1,748,423, CPP=1,719,166, CVPm=541,524, SaO2=1,656,614, Tc=1,372,641, ETCO2=502,524, PtiO2=89,524)

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 shortcomings in the acquired episodic data have implications for the design of future data collection/validation tools as well as project training procedures.

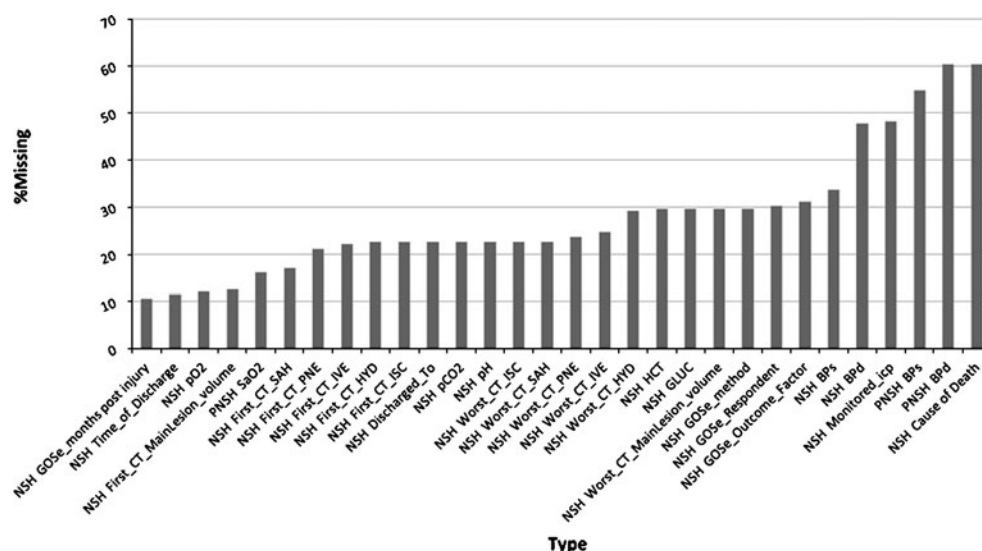
**Data accuracy**

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) (Fig. 4). 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: (1) ICP placement, (2) evacuation of mass lesion, (3) elevation of depressed skull fracture, (4) removal of foreign body, (5) anterior fossa repair for CSF leak, (6) placement of extra

**Fig. 3** Graph showing one-off demographic and clinical data fields with greater than 15% of missing data



ventricular drain, (7) active external decompression (with bone removal and duroplastia), (8) other. This classification system was used in an attempt to simplify and reduce 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.

The detection rate of acute events was also examined (e.g. 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

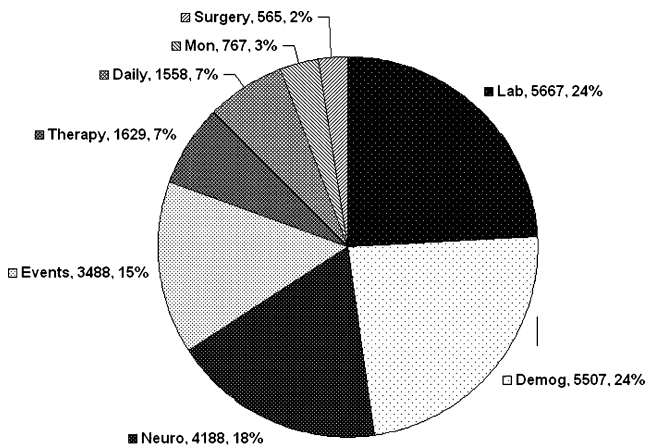
theatre were more likely to be not recorded. Through discussions with local nursing and data validation staff, it is believed that the intense nursing activity just prior to and following a transfer is more likely to lead to omissions in recording these events on research systems.

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 six data types with the most recorded nursing chart values. Data is expressed in terms of bias (+/-95% CL) between the nurse's 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, Fig. 5 shows a scatter plot of computer-monitored minute by minute ICP data averaged over 60 min (ICPavg) plotted against nurse's chart end-hour

**Table 4** Therapy type vs missing end-times

Therapy	Start entries	End entries	Missing end entries
Sedation	1,108	499	55%
Analgesia	1,032	574	44%
Paralysis	741	460	38%
Volume expansion	1,674	1,308	12%
Inotropes	614	199	68%
Anti-hypertensives	63	22	65%
Anti-pyretics	788	505	36%
Hypothermia	22	10	55%
Steroids	51	6	88%
Cerebral vasoconstriction	0	0	0
Osmotics (mannitol)	807	538	33%
Barbiturates	90	45	50%
Other	2,576	2,026	21%
Total	9,566	6,192	35%



**Fig. 4** 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)

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 6 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 nurse's 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 was designed to allow 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 one third of the therapies annotated to have missing end-times.

#### Discussion

Good laboratory practice dictates that as part of clinical trial design, acquired data must be checked for accuracy against the primary data sources using research nurse staff. 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.

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 investigator led environment [3].

#### 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 nurse's 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 [2, 4, 16]. Our results here confirm those of other investigations [13] 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.

**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	pCO <sub>2</sub> , FiO <sub>2</sub> 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 ( $\pm 95\%$  CL) between nurse's chart recorded values vs computer collected end-hour averages

Value	Data type				
	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
<i>n</i>	749	558	457	499	223

However, the key question remains unanswered as to whether missed adverse events using higher-resolution sampling significantly influences clinical outcome [14].

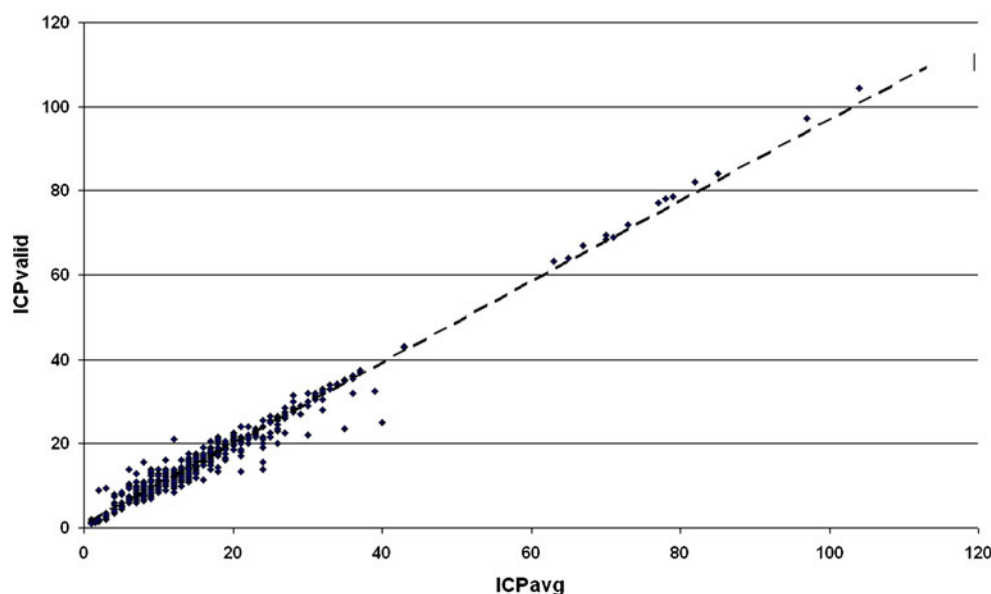
### Validation costs

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. Such large overhead for an academic network is prohibitively expensive and not sustainable and a more cost-effective solution for data validation must be found. One promising approach now being assessed by the BrainIT group is developing collaborative research with experts in Grid-based middleware technology. Grid technology comes in a variety of forms and 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 open-source 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]. It was a considerable challenge to overcome

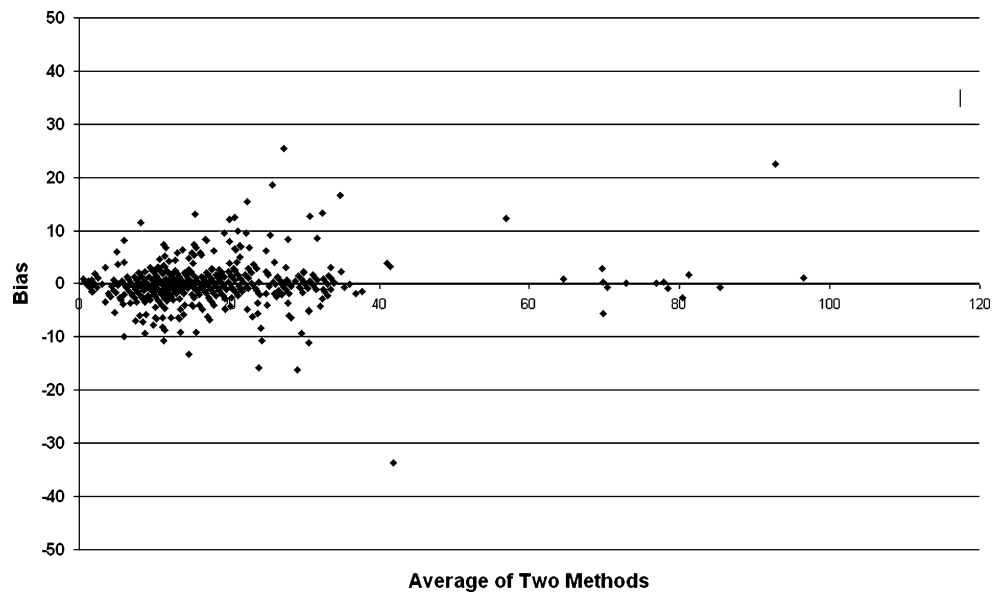
legitimate concerns by IT and data protection staff that research systems could access local data sources behind hospital firewalls. To overcome such concerns, it is critically important to collaborate with a Grid group that have considerable experience and a track record in working within the hospital and medical domain. Richard Sinnott's group have such a track record as demonstrated by being given honorary NHS staff appointments. Security is paramount and industry standard techniques including symmetric key encryption/authentication, use of advanced firewall and port monitoring together with using a high-end MS Essential Security platform. Also, all Grid services work entirely on a “push” model which means local software systems working behind hospital firewalls only push anonymised data out of the hospital environment, ensuring there is no direct access to data sources from outside the hospital firewall.

Such an approach, provided local IT policy staff is satisfied with the system security, will enable remote data validation systems to directly query hospital-based primary data sources for the purpose of checking the quality of previously uploaded data. Towards this end, the BrainIT group as part of an EC-funded Framework 7 project are now assessing such an approach in a group of neuro-intensive care centres equipped with the latest Grid technology. This

**Fig. 5** Scatter plot of computer-monitored minute by minute ICP data from an example patient showing the data averaged over 60 min (ICPavg) plotted against nurse's chart end-hour values (ICPvalid). Linear regression best fit  $R^2$  value=0.9773



**Fig. 6** 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 nurse's chart end hourly recorded values collected by the validation nurses



project—the AVERT-IT project [18] has installed 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 20 min, data is stripped of patient identifiers, encrypted and “pushed” out of local hospital networks to an external secure server cluster hosted at the University of Glasgow National eScience Centre [<http://www.nesc.ac.uk>]. Local databases will be maintained which link local patient identifiers with an anonymous patient identifier. Systems running at the BrainIT coordinating centre in Glasgow allow remote monitoring of the data acquired from all six participating BrainIT centres. Such a remote monitoring service in quasi real-time (updates every 20 min) will allow more efficient collection and validation of hospital-based data collected for research purposes while the patient (and their notes) are still within the ITU environment. This infrastructure will also support monitoring of patient management for adverse events (such as treatments given for arterial hypotension) and will enable testing and tracking adherence to study protocols.

### Lessons learned

A number of lessons have been learned during this feasibility study. First, 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, then it is possible that the local research nurse who originally entered the data and the research nurse who has been tasked to validate the surgery type may have interpreted the primary reason for surgery to be different. To overcome this ambiguity, we must provide a scheme for ensuring a consistent classification response. To accomplish this, 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.

Second, 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 PDAs. Increasingly, nursing and medical staff have good IT and data-entry skills and as a result we have developed new PC-based data collection tools. Also, our data tools (although state of the art at that time), did not provide sufficient local validation features such as preventing export and upload of empty data fields. Most IT technology nowadays can be configured to explicitly specify required fields and prevent upload of missing or incorrect 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 bedside nurse. The web-client software now includes data-validation routines which will prevent upload of missing data in any required fields. Patients cannot be fully discharged from the system until all required data is entered. Patients with missing data can be partially discharged from the system (when they are discharged from the ITU) but they remain in a visible list “patients with missing data”. A single web page displays all missing fields in red and must be completed before the patient can be fully discharged.

### Current status and future direction

The aim of the BrainIT group and their implementation is a staged process. We have successfully defined a core dataset standard, developed some 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 have been made to address those issues prior to starting future studies. Inevitably, with each new project, problems will arise and solutions will be found in 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 [<http://www.brainit.org/bit2web/faces/Papers.jsp>]. We are currently using the second database release with a third release planned, and what is encouraging is that the existence of the database resource was directly responsible for generating and testing the hypothesis about application of Bayesian neural network methods for prediction of arterial hypotension adverse events which lead to a project now funded under the seventh EC information and communications technology framework [<http://www.avert-it.org>]. 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 international management guidelines are for the most part adhered with [5]. However, there is a risk with surveys that there may be differences in results between what users believe to be the management 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 [11]. 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 a patient's 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 have been started at the recent BrainIT group meeting (Vilnius, September 2009) and the current 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 about the weaknesses with our data collection methods have been met with advances in client/server tools providing improved validation support. We anticipate that the second generation of BrainIT data collection tools (now 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 to do so will require more direct electronic access to hospital-based clinical data sources for both data validation purposes and for reducing the research nurse time needed for double data entry of data currently not accessible from hospital-based systems.

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