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Intracranial Electrical Impedance Tomography: A Method of Continuous Monitoring in an Animal Model of Head Trauma

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Abstract

Background—Electrical impedance tomography (EIT) is a method that can render continuous graphical cross-sectional images of the brain's electrical properties. Because these properties can be altered by variations in water content, shifts in Na⁺ concentration, bleeding, and mass deformation, EIT has promise as a sensitive instrument for head injury monitoring to improve early recognition of deterioration, and to observe the benefits of therapeutic intervention. This study presents a swine model of head injury used to determine the detection capabilities of an inexpensive bed side EIT monitoring system with a novel intracranial pressure (ICP)/EIT electrode combination sensor on induced intraparenchymal mass effect, intraparenchymal hemorrhage, and cessation of brain blood flow. Conductivity difference images are shown in conjunction with ICP data, confirming the effects.

Methods—Eight domestic piglets (3–4 weeks old, mean 10kg), under general anesthesia, were subjected to four injuries: induced intraparenchymal mass effect using an inflated, and later,

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Attestation: Preston Manwaring approves this manuscript and attests to the originality of the work and integrity of the data collection and analysis. This author is also the archival author.

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deflated 0.15mL Fogarty catheter; hemorrhage by intraparenchymal injection of 1mL arterial blood; and ischemia/infarction by euthanasia. EIT and ICP data were recorded 10 minutes prior to inducing the injury until 10 minutes post-injury. Continuous EIT and ICP monitoring were facilitated by a ring of circumferentially disposed cranial Ag/AgCl electrodes and one intraparenchymal ICP/EIT sensor-electrode combination. Data were recorded at 100 Hz. Two-dimensional tomographic conductivity difference () images, rendered using data before and after an injury, were displayed in real-time on an axial circular mesh. Regions of interest (ROI) within the images were automatically selected as the upper or lower 5% of conductivity data depending upon the nature of the injury. Mean within the ROIs and background were statistically analyzed. ROI was compared to the background after an injury event using an unpaired, unequal variance t-test. Conductivity change within an ROI post- injury was likewise compared to the same ROI prior to the injury utilizing unpaired t-tests with unequal variance.

Results—Eight animal subjects were studied, each undergoing four injury events including euthanasia. Changes in conductivity due to injury showed expected pathophysiologic effects in an ROI identified within the middle of the left hemisphere; this localization is reasonable given the actual site of injury (left hemisphere) and spatial warping associated with estimating a 3D conductivity distribution in two dimensional space. Results are shown as mean $\pm$ 1 SD. When averaged across all eight animals, balloon inflation caused the mean within the ROI to shift by -11.4 ± 10.9 mS/m; balloon deflation by $+9.4 \pm 8.8$ mS/m; blood injection by $+19.5 \pm 11.5$ mS/m; death by -12.6 ± 13.2 mS/m. All induced injuries were detectable to statistical significance ($p < 0.0001$).

Conclusion—This study confirms that the bed-side EIT system with ICP/EIT combination sensor can detect induced trauma. Such a technique may hold promise for further research in the monitoring and management of traumatically brain-injured individuals.

Introduction

Electrical impedance tomography (EIT) is an imaging method that can create a cross-sectional image of a region of the body utilizing an array of electrodes typically placed on the skin or surface of an organ being imaged.^{1,2} EIT has been actively investigated since the 1980s in modeling transthoracic and cranial disease processes.³ Because electrical impedance is highly sensitive to water content, it has also been applied to various tissues such as the human breast for cancer screening and to possibly distinguish early neoplastic transformation from benign cystic processes.^{4,5} While such sensitivity to water content could be anticipated to benefit interrogation of various brain pathologies, the cranium has been an impediment to deeper or more central imaging due to its electrically insulating properties limiting high frequency current penetration.⁶ Numerous studies exploring cerebral impedance imaging methods for brain injury detection discuss this shortcoming.^{7,8,9,10,11,12} However, the unique benefits of EIT, which include continuous imaging without risk of ionizing radiation, warrant further refinement of the method.

EIT uses small magnitude currents and voltages, which are driven and sensed, respectively, between different groups of electrodes. A computational algorithm is implemented to transform these electrical measurements into cross-sectional images of electrical conductivity.¹³ Equipment required to make such measurements can be relatively inexpensive.

A promising adaptation of previously employed circumferential electrode arrays has been recently described by our group to circumvent the impediment to cranial current penetration.¹⁴ It is based upon extending an external array to include an implanted centrally located EIT electrode. Holder, *et al.*¹⁵ showed that a multitude of implanted electrodes significantly increases sensitivity within the cranium. Such techniques generally remain

impractical outside of an exploratory acute animal model and are typically dismissed by clinicians due to increased risk for infection. However, certain presently employed standard of care monitoring techniques in injured patients include the use of invasive devices and thus lend themselves well to doubling as an internally located electrode. The addition of even one such electrode forces current through the less conductive cranium, and deeper into the central brain, improving resolution and sensitivity in that region.

A routine assessment tool for the clinical management of head trauma in the comatose patient with a Glasgow Coma Score of 8 or less is the insertion of an external ventricular drain for measurement of intracranial pressure (ICP) and drainage of cerebrospinal fluid (CSF) as needed to improve management of rising ICP with brain edema.¹⁶ The external ventricular drain is available in various designs. A typical unit consists of a 3 mm outer diameter silicone catheter connected to an external saline column strain gauge or a fixating cranial bolt tapped into the cranium with insertable tubing and ICP sensor.^a Some implanted ICP and external ventricular drain systems have recently incorporated additional sensing transducers for tissue oxygen tension^{b, c} A simple (TcO₂), pH, temperature, and thermal diffusion as a measure of blood flow. adaptation of any of these designs with an insulated conductive sleeve or wire extending to the tip could provide a central EIT electrode at the deep parenchymal level just superior to a lateral ventricle.

In an effort to demonstrate the detection capability and potential practical application of EIT in human patients suffering severe head trauma, a swine model is described, which incorporates a circumferential scalp electrode array and a cranial bolt for positioning both a combined ICP sensor and intracranial electrode.

Various commonly employed manipulations were adapted to simulate aspects of human head trauma and to assess the potential strengths of continuous axial imaging of impedance change. These included induction of mass effect by inflation and deflation of an implanted intraparenchymal balloon, injection of intraparenchymal blood, and cessation of cerebral blood flow by heart stoppage. This manuscript further describes the approach used for continuous EIT, an analysis of the multi-animal trial, and results and discussion of the applicability and potential of EIT to monitor TBI in a patient.

Methods

Animal Protocol

Eight^d domestic piglets (age range 3–4 weeks, weight average 10 kg) were sedated with midazolam followed by induction and maintenance of anesthesia with endotracheal isoflurane 1–2.5%. This regimen was selected to minimize impact on cerebral blood flow. The acute study protocol with animal termination at conclusion was approved by the Institutional Animal Care and Use Committee (IACUC) of Dartmouth-Hitchcock Medical

^aCSF External Drainage Devices. [cited 2012 Feb 11]; Available at: <http://emedicine.medscape.com/article/1982472-overview#aw2aab6b2>

^bLICOX INFO [cited 2009 Oct 19]; Available at: <http://www.integra-ls.com/home/search.aspx?qry=licox>

^cIntraoperative Cerebral Blood Flow Measurement: Quantitative CBF Monitoring techniques. [cited 2012 Feb 12]; Available at: http://www.medscape.com/viewarticle/405659_3

^dConductivity change due to blood injection represents the limiting manipulation; inflation of an insulative balloon has an almost infinite conductivity contrast compared to brain. Nominal conductivity of brain and blood are 127 mS/m and 680 mS/m, respectively. The conductivity estimation algorithms employed in EIT typically do not recover the full contrast actually present; to account for this, the mean expected contrast between pre- and post-injury was conservatively assumed to be 1:3 with standard deviations of 50% (e.g. blood injection would be detected as three times the background conductivity irrespective of the actual value). The standard deviation represents an estimate of variation between animals for one particular injury (e.g. hematoma creation by blood injection). Five samples are necessary to achieve a power of 0.80 with a 95% confidence interval for a 2-tailed student t-test. Eight samples provide added assurance.

Center. After instrumenting the animal for arterial blood pressure, oxygen saturation, and end-tidal CO₂, each animal was positioned prone. A midline incision along the sagittal suture allowed exposure of the paramedian cranium. A paramedian burr-hole was placed 1 cm lateral to the sagittal suture and 1 cm anterior to the coronal suture. A modified hydraulically-sealed cranial tapping bolt was inserted into this hole to the level of the dura. A Teflon insulated stainless steel EIT electrode tube incorporating an ICP sensor (Codman Microsensor, Raynham, MA) was inserted through the bolt to the level of deep white matter just above the right lateral ventricle (Figure 1). A contralateral paramedian burr-hole was created followed by placement of a 3-french cannulated 0.15mL Fogarty catheter (Edwards Lifesciences Corp., Irvine, CA) to the deep parenchyma at the level of the lateral ventricle (Figure 2). An array of 8 EIT scalp electrodes 1 × 1.5 cm constructed from modified Ag/AgCl ECG pads (Kendal CA-310, Covidien, Mansfield, MA) was placed upon the scalp in a coplanar orientation surrounding the lateral ventricles centrally, and extending from the frontonasal region to occiput and overlying temporalis and occipitalis musculature.

After a 10 minute settling period, each animal underwent the following sequentially induced injury events (Figure 3a):

- stabilization period without any induced injury
- inflation of the parenchymal balloon (Fogarty catheter) with 0.15 mL CT contrast dye for 10 min, followed by deflation
- instillation of 1 ml of arterial drawn, unclotted blood into the white matter
- termination with heart stoppage by IV Euthasol (Virbac, Ft. Worth, TX) injection

No manipulations were made during the stabilization period. Recording during this period provided a reference with which to examine signal variance.

EIT

Real-time EIT was recorded at 100 frames-per-second using custom time-division multiplexing-hardware based upon a National Instruments (Austin, TX) data acquisition platform. The excitation frequency was 50kHz with 5mA peak of applied current. Each electrode was driven in round-robin fashion such that at any time two electrodes provided the current excitation and all other electrodes recorded the resulting electrical potential. All electrode combinations are used and cycled through 100 times per second. Electrode 1 is the central electrode and 2–9 are the scalp surface electrodes. This represents a 4-electrode or tetra-polar measurement scheme.

Intracranial pressure, pCO₂, and invasive ABP were recorded in synchrony with EIT acquisition using a CardioCap/5 (GE Healthcare, Pollards Wood, UK) or a MP150 (Biopac, Goleta, CA) system. Real-time 2D tomographic reconstructions were computed with the pig snout oriented to the right (3 o'clock position) with no attempt to warp a circular axial finite-element mesh (the image reconstruction domain) to the ovoid shape of the intracranial space. The data were post-processed in MATLAB (Mathworks, Natick, MA) for statistical analysis using an average of 100 EIT frames about the time the event occurred. EIT images were scaled in color with red representing the most conductive and blue the least conductive regions. Thus, an insulator such as a silicone balloon, imaged at the frequency employed in this study (50kHz), would appear blue; saline, CSF, and blood would appear red.

The same method of single-step differential computational analysis and image rendering for real-time vascular changes used by Halter, *et al.* was employed.^{13,14,17} This approach produces an image of the change in conductivity between two time points (e.g. pre- and post-balloon inflation). Similar to difference imaging in computed tomography, EIT baseline

data are collected before an event, and subsequently subtracted from post-event data. A conductivity difference () image is computed based on this subtraction (e.g. post-injury – baseline; Figure 3b). Specifically, a circular finite element grid consisting of 1345 nodes is used to define the imaging domain; the computation produces a at each of the grid nodes or intersections, the magnitude of which is represented by a colored pixel in the reconstruction image. Regions of interest can be analyzed from each of these images by extracting the nodes and associated values from within the specified ROI.

The benefits of difference imaging are that electrode positions do not need to be exact, systematic signal errors specific to the instrumentation are reduced, and computations are faster. Every injury image was created in this fashion. The nodal conductivity differences are reported in terms of mS/m (mS = milli-Siemens, $S = 1/\text{ohm}$). Image accuracy in EIT is dependent upon a number of factors including the assumed geometry of the reconstruction domain. As discussed previously, the reconstruction domain is not warped to match the shape of the head because imaging methods, such as CT, were not available at the time of data acquisition. The nodal values are therefore not expected to accurately reflect the actual change in absolute conductivity (because of a mismatch in the reconstruction geometry and actual cranial geometry); however, because the same geometry was used for computing all images, the relationships between the for the different manipulations and events are expected to be valid representations of relative conductivity changes.

Specific time points associated with the different induced injury events were logged within the data acquisition software and were synchronized with the physiological and EIT data. Each time point was selected for analysis of synchronized ICP, ECG, and ABP data (Figure 3).

One region of interest (ROI) was selected from each image based upon the observed change. The ROI was chosen as the 5% of nodes (68 of 1345 nodes) corresponding to the most or least conductivity change depending on if the manipulation resulted in an increase or decrease in conductivity, respectively. In the example of Figure 3, the blue region would be identified by selecting the lower 5% of all nodes (decrease in conductivity associated with the inflating balloon), while in Figures 4 and 5 the upper 5% of all nodes would be selected (increase in conductivity associated with balloon deflation and blood injection). Figure 4 has the automatically selected ROI nodes for that particular experiment superimposed over the reconstructed image. In one of the 24 cases (8 animals $\times$ 3 induced injury events), a few of the initially identified nodes within the lower 5% (during balloon inflation) were found outside the primary population (i.e. at the boundary of the image); these nodes were removed from the analysis so that the ROI consisted of a single contiguous population of nodes. No generally accepted method for selecting ROIs in EIT exists at present; this approach of selecting 5% of the nodes enables consistent inter-examiner results.

Analysis

ROI nodes based on the post-injury images (ROIa; post-injury – baseline) were identified for each animal and injury as described above. This same set of nodes was also used to define an ROI within the pre-injury images (ROIp; pre-injury – baseline). Nodal values were extracted from each ROIa and ROIp and bootstrapped (random re-sampling with replacement) 5000 times. The mean of the bootstrapped values within individual ROI and backgrounds were found to be normally distributed (based on Q-Q plots and Lilliefors tests). While this step may have been unnecessary, because the results (means and standard deviations) from the bootstrapped data were the same as for the raw data, these inputs guarantee the requirements of normality for the statistical tests are met. EIT reconstructions often lack normality because of inherent spatial structure in 2D EIT images and electrode artifacts often observed on the boundary.

Two statistical tests were performed to assess how significant changes in conductivity were. First, a ROIa-to-background unequal variance unpaired t-test was run on each injury event imaged to assess whether the medians of the ROI and background conductivity groups are statistically different from each other. There are 1277 background nodes and 68 ROI nodes due to the 5% selection scheme described above. Second, the post-injury 68 ROI nodes (ROIa) were compared to that of the pre-injury image nodes (ROIp) using the same unpaired t-test with unequal variance. The unpaired t-test was used because it is impossible to randomize the order of before and after injury measurements, as one would desire for a paired t-test analysis. In this scenario, the degrees of freedom do not need to be adjusted, even when there is a positive correlation between the before/after cases.^{18,19} This second test yields information about how statistically significant the observed change in conductivity between pre- and post-injury is. The ICP sensor data are also reported for reference. All values reported are based on 1 standard deviation. All results are calculated based upon 95% confidence intervals. Results are shown as mean $\pm$ 1 SD.

Results

Control

Control measurements were made for all 8 pigs during the stabilization period. The 8 pigs had a mean conductivity difference of 0.12 ± 0.18 mS/m across the entire imaging domain. As a control, the conductivity difference over the 10 minute period should be near zero. ICP remained within a range of 4–10 mmHg. Mean baseline ICP values were pig dependent (5.87 ± 3.48 mmHg). pCO₂ was maintained between 36–42 mmHg during this and all other manipulations.

Balloon Inflation

Following the injection of 0.15 ml contrast dye into the balloon over a 6–10 second period (Figure 6), ICP increased from an average pre-inflation baseline of 7.9 ± 3.8 mmHg to an average immediately post-inflation value of 8.8 ± 3.8 mmHg. This pressure increase is not statistically or clinically significant, though it is detectable within individual experiments. The balloon emerged graphically in the EIT tomogram in the blue scale (decreasing conductivity) in the correct anatomic location given a 2-D representation²⁰ (i.e. the ROIs appear in the central left hemisphere region of the reconstruction, where the injuries occurred). ICP stabilized within minutes post-event and then began to increase gradually. Mean σ decreased to -11.4 ± 10.9 mS/m and was detected by automatic ROI selection in every case (Figure 3, Table 1). This effect was significant to a $p < 0.0001$ level for all experiments (Table 1). The standard deviation of the means from all experiments is high, but the standard deviation within a single experiment is low as expected.

Balloon Deflation

The radiopaque dye was extracted over a ~30 second period. ICP generally decreased to pre-balloon inflation levels; from 9.56 ± 3.56 mmHg to 8.1 ± 3.47 mmHg. Because of the small size of the balloon, this pressure change is not statistically significant but is detectable. Pre-deflation pressure is higher than immediately post balloon inflation. Automatic ROI selection was possible in all cases except experiment 8. Experiment 8 suffered from CSF leaking onto the electrodes that changed the imaging domain, causing erroneous data to be collected during deflation and was omitted from the mean calculation. This, however, did not affect the other manipulations performed on experiment 8. Mean ROI σ increased to $+9.4 \pm 8.8$ mS/m with experiment 8 omitted (Figure 4, Table 2). Again, the standard deviation of the means from the group of all experiments is high, but the standard deviation within a single experiment is quite low. All 7 remaining animal experiments showed this

manipulation to be statistically significant at a $p < 0.0001$ level. The ROI locations appear similarly located in the central left hemisphere of the reconstruction.

Intraventricular Injection of Blood

Following the injection of 1 ml of unclotted arterial blood into the white matter above the left lateral ventricle, ICP increased from an average baseline of 9.1 ± 3.1 mmHg to a peak of 24.4 ± 7.17 mmHg. It stabilized initially then began to climb after a few minutes. A marked increase in conductivity is seen as a red circular region in the EIT tomogram (Figure 5). The mean conductivity difference increase for the pigs was $+19.5 \pm 11.5$ mS/m (Table 3). The standard deviation of the means from the group of all experiments seen in the table is high, but low within single experiments as is expected. A decrease in conductivity is seen in the cortical margins on the same side. Six animal experiments showed this manipulation to be statistically significant ($p < 0.0001$), with two experiment outliers being omitted. While significant in the ROI test, the conductivity change of experiments 1 and 5 were opposite in magnitude to the other experiments and not physiologically realistic. These two results were therefore omitted from the mean. The ROIs in this manipulation appear more central to the reconstruction than in the mass effect injuries due to migration and distribution of the blood into the subdural space.

Cerebral Blood Flow Arrest by Heart Stoppage

Euthanasia by intravenous injection of Euthasol demonstrated an almost immediate, marked and symmetric decrease in cerebral conductivity over the entire image for each animal (Figure 7); ROI's analysis was not used because the effect is global. The decrease in conductivity continued for up to 10 minutes post-mortem until data recording was ended. ICP after a minimum of 5 minutes post-mortem was 6.38 ± 3.01 mmHg. Mean between the period just prior to euthanasia and at a minimum of 5 minutes post mortem throughout the region sensed was -12.6 ± 13.2 mS/m.

Discussion

This study investigated pathophysiologic effects common to severe human head injury to determine sensitivity to detection by enhanced EIT utilizing a central electrode which doubled as an ICP sensor. The manipulations included mass effect by intraparenchymal balloon inflation, injection of freshly drawn, nonclotted arterial blood into the parenchyma to simulate delayed intracerebral hemorrhage, and cessation of cerebral blood flow by heart stoppage during euthanasia. Each of these effects showed a statistically significant change in electrical conductivity and rendered anatomically correct regions of change in the axial tomogram. It is interesting to note that the balloon mass effect and localization was statistically detectable with volume injections of only 0.15 ml contrast dye, but the rise in ICP was both statistically and clinically insignificant (7.9 to 8.8 mmHg). While one could expect a much larger ICP rise if a 1 ml volume of dye were injected (this remains to be established in subsequent studies), this sensitivity points to the potential usefulness of the difference imaging approach for early detection of worrisome change. It was expected, and we believe, that the rapid inflation of the balloon was injurious to the tissue promoting cerebral edema, which is evidenced by gradual increases in ICP until the time of balloon deflation.

Despite the statistically significant changes observed, there is relatively large variability in conductivity difference for the group of experiments (i.e. the means between animals undergoing the same injury do not tightly cluster). This is simply due to the fact that no two experimental setups are alike. However, variability within a single experiment is potentially

attributable to several factors such as drift, which may be inherent to the EIT instrumentation, electrode drift due to gel ionic transport, cable movement.

EIT system drift is not a likely source based on our previous laboratory investigations of saline tank phantoms and resistor phantoms that showed good repeatability in measurements over many hours, an essential requirement for difference imaging. Electrode drift due to gel ionic transport across the skin or oxidation could have influenced stability if data sets were far removed temporally from the event of interest. Such drift usually occurs over extended periods of time. Each experimental manipulation was 10 minutes and not far removed from the baseline measurements. Cable movement is also not a significant contributor because each cable is actively shielded and carefully fixed in place during the experiments.

The most dominant cause of variability in conductivity measurements within the 10 windows is likely attributable to respiratory effects. Depending upon ventilator settings, 100 EIT signal averages may cover a fraction of or more than one breathing cycle. A bias in the averaged data will occur when less than a whole breathing cycle is employed for analysis or the effects are otherwise mitigated (e.g. temporarily halting ventilation). Inspiration impedes blood outflow through the jugulars, thereby momentarily causing blood-logging or engorgement of the brain and holding ICP at higher values.

This source of variability was explored in one experiment by creating a new set of measurements using ABP data to determine diastolic and systolic phases of the heart. By averaging EIT frames acquired during the two phases over several seconds of data, a difference image could be created between the diastole and systole data sets. The breathing signal was removed by rejecting data points with ICP excursions clearly caused by ventilation. The method appeared to refine the blood perfusion pattern in the anterior and middle cerebral arterial regions (Figure 8).

The method is sensitive to physiological changes, but the variability presents a challenge for specificity. Ways of decreasing variability in mean by normalizing parameters to individual cases, instead of looking at the data as a whole, as done here, may be advantageous and should be explored. Another option, once sufficient data are collected, will be to look at data trends and establish statistical thresholds that suggest significance in image conductivity. Another option, suggested by Gómez-Laberge *et. al.*, may be to utilize a pixel grouping algorithm in conjunction with threshold values, as demonstrated in a series of ventilated pigs.²¹

Mean resting ABP was observed to vary from animal to animal. Several animals appear to be hypotensive. Low blood pressure may affect the change in conductivity beat-to-beat as blood flow is limited, but this was not explored. Mass effect by balloon inflation, intracerebral hematoma, and blood flow cessation are large effects unlikely to be affected by low ABP.

A limitation of the computational method employed here is that a 2D circular rendering was used to represent a more complex 3D geometry, in which not all electrodes were co-planar and the imaging domain is not circular. Forcing these data acquired from the 3D environment to fit a 2D solution will cause some distortion in the tomogram and localization of the ROIs. Simulation and laboratory experiments have demonstrated that objects tend to move more centrally in such circumstances.²⁰ 3D models for EIT are becoming more common in the research setting as computational power has improved. However, these implementations are typically performed post-acquisition and not in real-time using expensive high-end computational hardware and sophisticated computationally intensive algorithms. Our approach represents a technology capable of performing EIT in real-time using a mid-range portable computer. While this approach has been demonstrated to provide

information regarding pathological changes in the cranium, localization is not perfect. As higher speed, lower cost computation platforms become available, it would be worth incorporating more anatomically correct 3D renderings into this technology to enhance precision of localization.

Another limitation of the method is that difference imaging requires a baseline. It is difficult to generate images of injury if a pre-injury baseline is unavailable. Therefore, the method of difference imaging must be seen as a trend monitor to observe deterioration and the effects of intervention. To be optimally useful in a clinical environment, we anticipate that the baseline data and image obtained following instrumentation with the ICP and EIT central catheter should be closely correlated to timing and perhaps overlaid as an anatomic graphic to the baseline CT scan of the head. Such graphical overlays highlighting areas of functional change are familiar to intensivists, neurologists, and neurosurgeons and include examples of functional MRI and EEG maps.

Absolute imaging in EIT is an option when a baseline or standard reference values of impedance are not available. That method, however, is more sensitive to noise, model inaccuracies, and electrode position and condition (e.g. contact impedance). It is also a much more computationally intensive problem making rapid tomographic rendering a challenge. In the environment of craniocerebral trauma, where scalp and cranium are injured with evolving patterns of edema and hematoma, such absolute imaging may be of less value than trend detection within the cranium.

This animal study was designed to explore the potential benefits and feasibility of a continuous axial image rendering of the human brain. The manipulated variables of mass effect by balloon inflation, intracranial hemorrhage, and cerebral blood flow cessation represent challenging issues of urgent recognition in the intensive care environment in patients who have suffered severe head injuries. At present, such patients undergo intermittent CT imaging with repeat imaging based on the clinical course and protocols for discernment of otherwise unrecognized changes by clinical examination or routinely measured parameters, e.g. ICP and TcO₂. As these patients are often deeply sedated or induced into pharmacologic coma and muscular relaxation to optimize control of ICP, a means of monitoring is desirable that can more effectively signal dangerous changes. Furthermore no transducers presently provide a cross-sectional map of the brain. Local sensing such as TcO₂ and thermal or laser CBF flow monitoring cannot be confidently generalized to the brain. CT and MRI imaging normally require transportation to a radiology center with the attendant risks of detachment from monitoring and the stress of movement.

The electrical path of the very low level, high frequency current used in EIT is not straight between two electrodes but rather it constitutes a diffuse field following the path of least electrical impedance. This nature of EIT makes high-resolution images (such as in x-ray tomography) difficult. No practical algorithm to fully address this physical limitation is presently anticipated. However, its resolution can be improved by increasing the number of electrodes used, keeping in mind however, that an excessive number may become encumbering to care. The simplicity of 8 circumferential contacts by corkscrew, staple, or adhesive electrodes in the clinical context of typical scalp swelling, lacerations, postoperative scars, skull fracture, or even decompressive craniectomy becomes a limiting necessity. A further practicality is that our present 8x1 array can render 100 image updates per second with the computational power of a portable bedside computer. Bedside manipulations such as transient venous occlusion increase in positive end expiratory pressure (PEEP), and injection into an external ventricular drain of saline for clearance or compliance testing should become readily apparent in the continuously rendered tomogram.

From an electrical safety standpoint, the described levels of current used in this study are non-injurious and are within accepted safety guidelines for externally applied currents²² though long term effects of an active internal electrode on brain tissue should be established in further studies. By way of comparison, EIT currents may be smaller in magnitude and lower in duty-cycle than typical deep-brain stimulators.

While several other EIT research groups have explored the effects of intraperitoneal and intracranial hemorrhage,^{22,23,24} to the best of our knowledge, the novel EIT implementation described in this manuscript is at present the only study to show *in-vivo*, real-time, tomographic reconstructions of mass-effect, hemorrhage, and cessation of blood flow. Wang *et. al.*²⁵ show in-vivo hematoma creation and detection with 16 external electrodes. Interestingly, their results show a decrease in conductivity with injection of 5mL of blood. In contrast, this study shows an increase, which corresponds well with literature indicating that blood is more conductive than brain.

Our adaptation of the external ventricular drain or ICP monitor into a central electrode may be promising to extend the depth of resolution and sensitivity into the central brain region. This technology may improve monitoring and guidance for therapeutic intervention in other pathologic conditions beyond head injury where edema, Na⁺ shifts, and mass effect participate. These include stroke, hydrocephalus, and postoperative changes.

Conclusions

We have described a novel and practical combination of a simple circumferential and intracranial electrode EIT system with a standard of care pressure transducer that for the first time, has been used to monitor intracranial injuries *in-vivo*, in real-time, with statistically significant detectability.

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Figure 1.

A modified cranial bolt for simultaneous deep parenchymal ICP monitoring and EIT sensing. The PTFE insulated tube (except at the tip) forms a central electrode for impedance measurement at a depth of 3 cm. The conductor emerging at the upper right is an electrical contact point for interfacing with the EIT hardware.

Figure 2.

The instrumented cranium of the piglet with an array of 8 circumferential electrodes and one central electrode with integrated ICP sensor. The contralateral left cranial catheter for intraventricular blood instillation is also seen. For clarity, all EIT reconstructions and radiographs reported here share this same caudal-rostral orientation. The same orientation is employed for difference imaging tomograms.

Figure 3.

Timeline of experiment progression (a) and an example data stream recorded intraoperatively along with a reconstructed image (b). The green and red vertical lines in the ICP plot represent the time at which the baseline and post-injury data are taken, respectively, for the post-injury image reconstruction. Each of these data vectors is computed by averaging 100 consecutive EIT frame acquisitions to improve signal to noise ratio. In this example, the green and red lines straddle an increase in ICP caused by the inflation of the Fogarty balloon catheter. The large amplitude oscillations in the ICP waveforms are caused by positive-pressure ventilation. The smaller perturbations are ICP variations due to blood pumping. The figure in the right column shows the EIT reconstruction. The slightly off-centered large insulative (blue) region in the image represents the effect of the balloon inflation. The snout is oriented toward the 3 o'clock position. A pre-injury difference image would similarly be created by utilizing an average of data at that location (i.e. from time = ~1290 s to ~1300 s) minus the baseline.

Figure 4.

Axial electrical impedance tomogram after balloon deflation. The baseline image was taken just prior to deflation. Once the insulative inclusion is removed, the resulting void fills with the more conductive parenchyma or fluid such as CSF thereby presenting a more conductive (red) region in the reconstructed image. The X's represent electrode locations within the mesh. The snout direction is at the 3 o'clock position as in figure A.

Figure 5.

The reconstruction of the injection of 1 ml of blood (arrow) into the left hemisphere of the brain. Also shown is the simultaneously recorded increase in ICP and ROI vs. time. Similar graphs are readily created for all manipulations, confirming that the effects are genuine. While physically co-located with the Fogarty inflations, blood injections do not always appear co-located in the reconstructions. This is probably due to blood dissecting out of the region into which the catheter has been placed.

Figure 6.

A lateral cross table radiograph of the instrumented cranium. The left arrow points to the inflated Fogarty catheter with 0.15mL contrast dye. The right arrow points to the position of the central electrode. The tip of the electrode is lower than the balloon. The dark objects above are the cranial bolts.

Figure 7.

Simultaneous ICP, ECG, and ABP synchronous to EIT during euthanasia. Note that as the pentobarbital sodium cocktail takes effect (arrow), ECG stops and ICP and ABP immediately begin to drop. The small excursions seen after drop in ICP are due to positive pressure ventilation, which ceases at time 8835s. During this time there is a near symmetric loss of perfusion (seen as a decrease in conductivity in both hemispheres) as the brain becomes more ischemic post heart stoppage.

Figure 8. Difference conductivity image with the baseline and later frame data created by averaging EIT acquisitions from diastolic and systolic phases of the heart cycle while excluding ventilator induced breathing artifact. The arrows point to effects caused by the presumed and “unmasked” anterior (2) and middle cerebral (1) artery blood distributions. The scale has been adjusted to enhance the conductive regions.

Table 1

Balloon Inflation Injury			
Experiment	Mean of ROIp	Mean of ROIa	Mean of Background
1	-0.2 ± 0.1	-6.0 ± 1.0	0.2 ± 1.2
2	0.2 ± 0.2	-3.8 ± 0.3	-0.6 ± 1.2
3	0.1 ± 0.1	-27.3 ± 5.3	1.7 ± 5.0
4	-0.1 ± 0.3	-5.1 ± 0.7	-0.6 ± 1.4
4	-0.7 ± 0.4	-7.2 ± 1.5	0.4 ± 1.7
6	0.0 ± 0.1	-3.4 ± 0.7	0.4 ± 0.8
7	-6.3 ± 0.6	-30.2 ± 2.5	-6.1 ± 9.5
8	0.0 ± 0.3	-8.1 ± 0.5	-1.9 ± 2.3
Mean	-0.9 ± 0.3	-11.4 ± 1.6	-0.8 ± 2.9
SD	2.2	0.2	1.7
			2.4
			3.0

Mean and standard deviations of (change in conductivity in mS/m) values before and after the balloon inflation injury. Conductivity change values within the region of interest prior to injury (ROIp; prior to injury data – baseline) are the difference in conductivity between the baseline and three breaths prior to balloon inflation. These values should be close to zero because no injury has occurred. After the injury occurs, we see an expected decrease in conductivity in the automatically selected ROIa (region of interest after injury; post injury data – baseline). The t-tests described in the text are used to identify statistically significant differences between ROIa and ROIp and between ROIa and the post-injury background nodes. Background nodes are all nodes that are not part of the image ROI. All t-tests show statistically significant differences ($p < 0.0001$) between the ROI data before and after an injury within the single experiments (i.e. experiment 1 ROIp to ROIa, and ROIa to background). The wide variation between the results of individual experiments and the mean of all experiments suggests differences within setups, but does not indicate a lack of overall significance.

Table 2

Experiment	Balloon Deflation Injury			
	Mean of ROIp	Mean of ROIa	Mean of Background	
1	0.0 ± 0.1	4.4 ± 0.4	0.3 ± 1.0	
2	0.0 ± 0.2	6.0 ± 0.4	1.4 ± 1.4	
3	0.1 ± 0.2	10.8 ± 0.7	3.1 ± 2.8	
4	0.2 ± 0.4	7.0 ± 0.7	1.4 ± 1.8	
4	0.2 ± 0.7	4.6 ± 0.4	0.8 ± 1.4	
6	-0.2 ± 0.1	4.0 ± 1.4	-1.8 ± 1.4	
7	0.5 ± 0.3	28.6 ± 2.1	7.6 ± 8.8	
8	1.3 ± 0.4	*	-1.4 ± 3.3	
Mean	0.3 ± 0.3	9.4 ± 0.9	1.4 ± 2.7	
SD	0.5	0.2	8.8	3.0
				2.6

Mean and standard deviations of values (in mS/m) before and after balloon deflation. ROIp (prior to injury data – baseline) values are the change in conductivity between the baseline and three breaths prior to balloon deflation. These values should be close to zero because no injury has occurred. After the injury occurs, we see an expected increase in conductivity in the automatically selected ROIa (post injury data –baseline). The * indicates a deviation from the expected change in conductivity. This outlier was omitted from the statistical analysis because an electrode contact had changed due to fluid found leaking onto it. All t-tests show statistically significant differences ($p < 0.0001$) between the ROI data before and after an injury within the individual experiments (excluding omitted experiment 8). As mentioned previously, variation between the results of individual experiments and the mean of all experiments suggests differences within setups, but does not indicate a lack of overall significance.

Table 3

Hematoma Formation Injury				
Experiment	Mean of ROIp	Mean of ROIa	Mean of Background	
1	0.0 ± 0.1 *	-	-0.7 ± 6.9	
2	-0.2 ± 0.3	17.5 ± 3.7	-1.4 ± 3.3	
3	-0.4 ± 0.6	30.8 ± 6.8	-3.7 ± 6.8	
4	0.4 ± 0.3	14.0 ± 2.7	-1.0 ± 3.2	
4	-0.5 ± 0.7 *	-	0.4 ± 1.4	
6	0.1 ± 0.3	4.0 ± 1.4	-1.8 ± 1.4	
7	-1.7 ± 4.1	15.3 ± 2.2	1.1 ± 3.8	
8	0.2 ± 1.0	35.1 ± 6.2	-4.2 ± 11.0	
Mean	-0.3 ± 0.9	19.5 ± 3.7	-1.4 ± 4.7	
SD	0.7	11.5	2.2	3.3

Mean and standard deviations of values (in mS/m) before and after hematoma creation. ROIp (prior to injury data – baseline) values are the change in conductivity between the baseline and three breaths prior to the intraparenchymal blood injection. These values should be close to zero because no injury has occurred. After the injury occurs, we see an expected increase in conductivity in the automatically selected ROIa (post injury data – baseline). The * indicates a deviation from the expected change in conductivity. These outliers were omitted from the statistical analysis. All t-tests show statistically significant differences ($p < 0.0001$) between ROIp and ROIa within the single experiments (excluding omitted experiments 1 and 4). The variation between the results of individual experiments and the mean of all experiments does not indicate a lack of overall significance, but rather a difference in experimental setup.