Electrical impedance tomography with cortical or scalp electrodes during global cerebral ischaemia in the anaesthetised rat

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Abstract. The performance of a prototype impedance imaging (Electrical Impedance Tomography, EIT) system using cortical or scalp electrodes has been assessed in a model of global cerebral ischaemia in the anaesthetised rat. In preliminary calibration experiments using a circular array of electrodes around a tank of saline, the centre of a polythene rod could be localised with a mean error of 4% of the tank diameter, and two such rods could be discriminated when separated by 22% of the tank diameter. Cerebral ischaemia was produced by diathermy of the vertebral arteries and reversible occlusion of the common carotid arteries for 15 min. A bimodal impedance increase of about 50 - 200% was recorded with a ring of cortical electrodes in the fronto-occipital plane. With a similarly orientated ring of scalp electrodes, a unimodal impedance increase of about 10% was observed. In both cases, impedance reversed after cerebral reperfusion. Similar but irreversible changes were observed *post mortem*. As the reconstruction algorithm assumes constant initial resistivity, this suggests that modifications to allow for initial conditions would be needed for more accurate imaging with scalp electrodes.

1. Introduction

Electrical Impedance Tomography (EIT, also termed Applied Potential Tomography, APT) is a recently developed imaging technique which enables images of the impedance distribution within a subject to be obtained from measurement with a ring of external electrodes. One potentially fruitful application of this technique lies in imaging the impedance increases of tens of per cent which occur in the brain in conditions such as cerebral ischaemia, epilepsy or spreading depression (Van Harreveld and Schadé 1962, Holder 1992a, b). The common feature of these conditions is that neurones outrun their energy supplies and as a result ions and water move from the extracellular to the intracellular compartment. With measurement at frequencies below about 100 kHz, most current travels in the extracellular space, so this causes an impedance increase (Van Harreveld 1972).

For clinical use it would be most desirable to image such changes with scalp electrodes. In a previous study (Holder 1992a), it was shown that reproducible impedance increases could be measured with scalp electrodes during cerebral ischaemia, which were still observed when changes in local scalp impedance or temperature were excluded. They were, as expected, attenuated in comparison to impedance changes measured with cortical electrodes.

There is currently considerable interest in the technical development of EIT (Webster 1990) but, to the author's knowledge, only one system, 'The Sheffield EIT system', has been constructed and is available for clinical use. Being a prototype, it has various limitations.

Images can only be obtained with respect to a specified reference image; the reconstruction algorithm assumes that the electrodes are equally spaced in a circle, and that the initial resistivity of the subject is uniform. The reconstruction algorithm is relatively crude, and uses a single iteration. Its advantages are that a complete data set sufficient to produce an image can be collected in 79 ms, and image reconstruction takes about 5 s. Unlike more sophisticated algorithms, the method is relatively insensitive to deviations in electrode spacing. The device is physically small – about the size of a video recorder, attached to a microcomputer – and operates at 51 kHz with an applied current of 5 mA. It is therefore non-invasive and would be suitable for continuous imaging at the bedside (Barber and Seagar 1987, Brown and Seagar 1987).

Preliminary images of ECG gated changes in the adult head measured with the Sheffield EIT system (McArdle *et al* 1989), and of intraventricular haemorrhage in the neonate with a different imaging system (Murphy *et al* 1987) have been published. They were obtained with scalp electrodes; examples of images are shown, but their correspondence to intracranial impedance was not investigated. There do not appear to be any other studies of impedance imaging of the head in human or animal subjects.

This study was therefore undertaken to assess the performance of the Sheffield EIT system by comparing images obtained with scalp electrodes during cerebral ischaemia with the actual impedance changes in the brain measured with cortical electrodes. This was performed in a model of cerebral ischaemia in the anaesthetised rat, previously investigated with single channel impedance measurements (Holder 1992a). In addition, the performance of the system in imaging other known impedance changes in physical phantoms, or in the rat *post mortem*, was assessed. The purpose of the study was to use this data to investigate whether the Sheffield EIT system appears suitable for imaging cerebral ischaemia in human subjects and, if not, to suggest appropriate technical modifications.

2. Methods

2.1. Animal preparation

The method of producing cerebral ischaemia has been described elsewhere (Holder 1992a). In brief, rats were anaesthetised with inspired halothane, paralysed with pancuronium bromide, and artificially ventilated. The vertebral arteries were occluded by diathermy, and then the common carotid arteries were occluded reversibly for 15 min. More than one hour elapsed between successive episodes of ischaemia. Cortical or scalp temperature was measured using a thermocouple placed over the right parietal region. During cerebral ischaemia *in vivo*, cortical or scalp temperature was maintained as close as possible to the resting level by raising or lowering a table lamp placed over the rat's head.

In some animals, EIT images were collected from the time of death for a period of 30 min. (The observed impedance changes were only due to post-mortem processes; no other manipulation was performed). Below, these records are termed 'post-mortem'; 'during cerebral ischaemia' refers to measurements made during cerebral ischaemia *in vivo*.

2.2. EIT image collection

EIT images were obtained using an approximately elliptical array of sixteen electrodes placed either on the cortex or in the scalp. All electrodes were made of silver; exposed surfaces were chlorided. The cortical electrode array consisted of blocks of silver set at regular intervals into a ring of dental acrylic about 4 mm wide. The silver blocks were connected to a flexible lead with a driven screen 12 cm in length by a solder join which was sealed

into the acrylic. The acrylic ring was made to correspond to the contours of the rat brain in the plane from the frontal to occipital lobes. Its internal dimensions were 21 mm in the sagittal and 13 mm in the coronal directions (termed Y and X axes respectively below). Each electrode surface was an area 3 mm high and 1 mm wide on the inside of the array. The array was applied to the brain through an approximately elliptical craniotomy made by drilling with a dental burr 1 mm in diameter. It was about 5 mm wide and stretched from the frontal lobes, about 18 mm anterior to the bregma, caudally to the occiput immediately above the foramen magnum. The dura immediately over the venous sinuses was left intact. Any exposed cortex was covered with PVC clingfilm.

Scalp electrodes were made of Ag wire, 0.5 mm in diameter. One end was soldered to a 12 cm length of multistranded copper wire, 1 mm outer diameter. The solder join was insulated with silicone rubber glue, and 4 mm of wire was left exposed. Flexible unscreened leads were used in order to minimise traction on the scalp. The electrodes were inserted at regular intervals in the fronto-occipital plane in a direction radial to the vertex. The dimensions of the approximate ellipse formed by the mid-points of the wires was about 25 and 18 mm in the sagittal and coronal directions respectively. A layer of PVC clingfilm was placed over the leads and scalp and this was secured with a tubular elastic net (Netelast, size 'B', Roussel medical).

The leads attached to the electrodes were connected to the front panel of the EIT device by screened leads which were 4 mm in outer diameter and 30 cm long. Common mode feedback was applied through a chlorided silver electrode placed in the animal's tail.

One EIT image was recorded each minute, and consisted of 200 complete data sets averaged to reduce noise. The reference phase of the phase sensitive detector in the EIT system was set at the value which gave the least variability in the EIT image when saline in tanks containing the cortical or scalp array (see below) was varied from 0.118 - 0.354% g l^{-1} of NaCl. The Sheffield EIT system is based on a four electrode method for measuring impedance, and so measures the in-phase component of the complex impedance. Below, the term 'impedance' refers to this resistive component of the complex impedance.

2.3. Experimental arrangements for calibration

The different arrangements were:

(1) *Large cylindrical tank.* Sixteen brass bolts were placed halfway up and equally spaced around a plastic cylinder, 15.3 cm in diameter and 24 cm high. They were 3 mm in diameter and projected 15 mm into the tank.

(2) *Cortical array tank.* The cortical electrode array was set in a roughly cylindrical tank, constructed so that its internal cross-section was the same as the inner dimensions of the electrode array. The walls were constructed of a rolled up flexible acrylic sheet, which was bonded to the electrode array, and a Perspex base with silicone rubber glue. The electrode array was placed halfway up the tank, which was 5 cm high.

(3) *Scalp array tank.* The sixteen scalp electrodes were inserted at equal intervals through holes in an acrylic plate so as to form an ellipse 21 × 16 mm along its axes. A rolled flexible acrylic sheet was glued with silicone rubber glue to the upper surface of the acrylic plate so as to form an ellipsoidal tank. This was filled with saline to a height of 3.5 cm.

(4) *Post-mortem calibration.* One experiment was performed *post mortem* in an animal in which scalp electrodes had been placed. It was placed in a supine posture on an acrylic mould which preserved the cervical lordosis and the position of the scalp electrodes. The mandible and palate were removed, and the ventral surface of the brain was exposed by removing the roof of the nasopharynx with bone clippers. The brain was evacuated and replaced with saline solution or air.

An Ag/AgCl common mode feedback electrode was placed at the top or bottom of the tank in (1 - 3) and in the tail in (4). The tanks were filled with saline, which consisted of 0.118 g l^{-1} (20 mmol l^{-1}) NaCl, unless otherwise stated; this had a resistivity similar to that of brain. Measurements were made at room temperature. (Temperature of saline in the tanks was not specifically controlled, but room temperature altered by less than one degree during the 30 min or less required to make any one series of measurements. This temperature difference would not have contributed significantly to baseline variability, as the impedance of saline varies by approximately -1.3% per °C (see Holder 1992a).

2.4. Data analysis

The EIT images have been displayed as three-dimensional surfaces. The X and Y axes correspond to the axes in the plane of the electrodes; the Z axis represents the change in impedance with respect to a specified reference frame. The orientation of the display is identified by a diagram of a corresponding slice through the rat's head. Only the central 812 pixels out of a 32×32 pixel matrix represent the image; surrounding pixels were set to zero.

A program was written (in Microsoft Quickbasic, version 4.5) which enabled manipulation and analysis of these images on an IBM compatible AT 286 microcomputer. Each pixel in *in vivo* images was corrected separately for baseline shift. The baseline was taken to be the extrapolation of the linear regression of the period of 10 min prior to carotid artery occlusion. Images from different ischaemic episodes were combined by taking the average for each pixel. Estimates of the blurring of objects imaged by EIT have been made by approximating Gaussian curves to impedance profiles in one or two dimensions. The standard deviation in the XY plane was calculated on this basis. A peak in the image was defined as a point where up to three pixels of equal value were greater than all of the pixels in a surrounding grid of 5×5 pixels, and where this was separated from any peak with a greater magnitude by a trough whose value fell to $1/e$ times the average of the two peaks. Statistics regarding such a peak were calculated with respect to the area around the peak where the pixels had a value greater than the (peak value)/e. An estimate of the standard deviation for individual peaks was taken to be the radius of a circular area approximating to this area. The average pixel value was calculated as the mean pixel value over this area, and the volume under a peak was calculated as the sum of all the values of the pixels in it. The full width at half maximum (FWHM) was calculated as 1.665 times the standard deviation in the XY plane. Results are presented as mean $\pm$SE.

3. Results

3.1. Calibration studies

Baseline drift was assessed by comparing the mean and standard deviation of the pixels in an image measured under resting conditions 10 min after a reference image (table 1). The standard deviations of the impedance changes in different pixels were about ten times greater for measurements *in vivo* than for those made in tanks. The correlation coefficients for the mean impedance change against time, sampled at intervals of 1 min over typical resting periods of 10 min, were 0.76 ± 0.19 ($n = 5$ in 2 rats, $P < 0.05$ in 4 out of 5 records) and 0.83 ± 0.06 ($n = 9$ in 4 rats, $P < 0.05$ in all records), for cortical and scalp records respectively, for both linear and logarithmic regression. It was therefore considered justifiable to correct for linear baseline shift in subsequent *in vivo* measurements (see section 2.4).

Table 1. Changes in impedance under resting conditions in different experimental situations. The average and population standard deviation refer to the mean impedance change of images collected 10 min after a reference image.

Experimental arrangement	Electrode arrangement	Difference in δZ measured at 0 and 10 min (%) over whole image		n
		Mean	SD	
Large cylindrical tank + saline	Brass bolts	-0.12 ± 0.10	0.35 ± 0.03	3
Tank + saline	Rat cortical array (Ag/AgCl)	0.03 ± 0.02	0.29 ± 0.07	3
Tank + saline	Rat scalp model (Ag/AgCl)	0.30 ± 0.24	0.22 ± 0.06	3
In vivo	Rat cortical array (Ag/AgCl)	-0.41 ± 0.24	2.78 ± 0.39	5 (2 rats)
In vivo	Scalp electrodes (Ag/AgCl)	-0.42 ± 0.45	2.17 ± 0.43	9 (4 rats)

EIT images were acquired as the cortical or scalp array tanks were filled with saline solutions of varying concentrations (conductivities varied over the ranges of 50 - 300% or 50 - 200% compared to 0.118 g l⁻¹ NaCl for cortical or scalp array tanks respectively). These ranges were approximately equivalent to the impedance variations encountered experimentally. The resistivities of the salines were measured with a single channel impedance measuring device operating at 50 kHz (Holder 1992a) using four chlorided silver wire electrodes. The mean image impedance change varied linearly with respect to saline resistivity (r = 0.98, 0.98 ($P < 0.05$), slope = 0.94, 0.98, n = 11, 9, for the cortical and scalp arrays respectively. The standard error of impedance changes within any one image was less than 0.3%.

The correspondence of the peak impedance change and physical position of a polythene rod suspended vertically in either the large cylindrical or cortical array tanks is shown in figure 1. The difference (expressed in per cent of the axis dimensions of the tank) between the position of the peak impedance change in the image and the centre of the rod was $3.9 \pm 0.17\%$ (n = 9, as the rod was moved in increments of 10% from X, Y coordinates of 50%, 10% to 50%, 50% to 10%, 50%) in the large cylindrical tank, and $7.4 \pm 0.35\%$ (n = 9, increments of 20% from 50%, 90% to 50%, 10%, and 90%, 50% to 10%, 50%) in the cortical array tank. The ratio of the FWHM along the Y compared to the X axis was 0.99 ± 0.03 and 1.3 ± 0.03 for the large cylindrical and cortical array tanks respectively. Under the same conditions, extrapolation from a series of images suggested that a rod placed centrally could be discriminated from a second rod when their centres were 32% or 26% apart for the large and cortical array tanks respectively. The respective gaps between the rods at these points would be 22% and 18% respectively.

Post mortem, a change in the contents of the cranial cavity from saline to air produced an approximately gaussian central increase in impedance measured with scalp electrodes (figure 2). The FWHM of the increase was 27.5% of the image diameter. In reality, the cranial cavity occupied about 80% of the length of the scalp electrode array along both the X and Y axes.

3.2. EIT images collected during cerebral ischaemia in vivo, *and* post mortem *(figures 3 and 4)*

In images made during cerebral ischaemia with the cortical electrode array, two major areas of impedance increase were observed, which reversed on reperfusion. Both were bilateral

but their peaks were slightly to the right of the midline. There was a broad fronto-parietal increase of about 70% and a sharper posterior increase of over 200%, present to a greater or lesser extent in all four of the individual images collected in two rats. In images collected *post mortem*, impedance increased in a similar distribution to records *in vivo*, but the increase in the first 15 min was greater than *in vivo* by about 25%, and continued for the duration of the period of recording.

In images made during cerebral ischaemia with scalp electrodes, a predominantly central impedance increase occurred, which reached a maximum of about 10% of the increase when measured with cortical electrodes. The impedance returned to the baseline on reperfusion, but with greater variability than the cortical records. The change consisted of a single
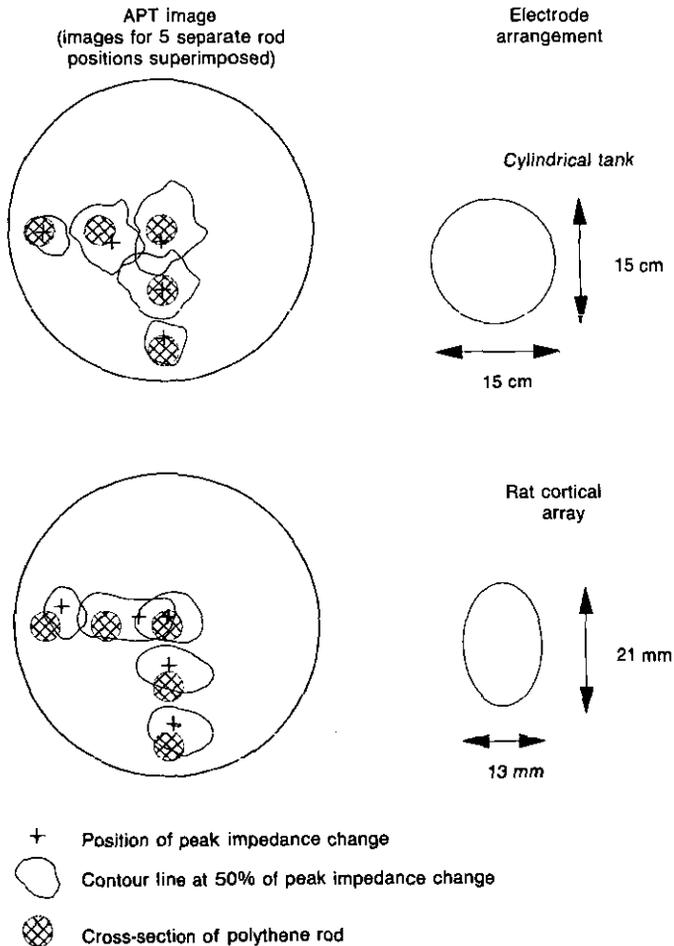
Figure 1. Localisation of a polythene rod in the large cylindrical or cortical array tanks. A polythene rod was suspended vertically in various positions in saline in either tank. The diameters of the polythene rods were 15 mm and 1.5 mm for the large cylindrical and cortical array tanks respectively. Each rod extended vertically more than twice the tank diameter in both directions. The peaks and boundaries of the FWHM of the image impedance change and the positions of the rods have been superimposed for several rod positions. The positions of the rod relative to the elliptical cortical electrode array are represented as a proportion of axis lengths so as to be comparable in the circular EIT image.
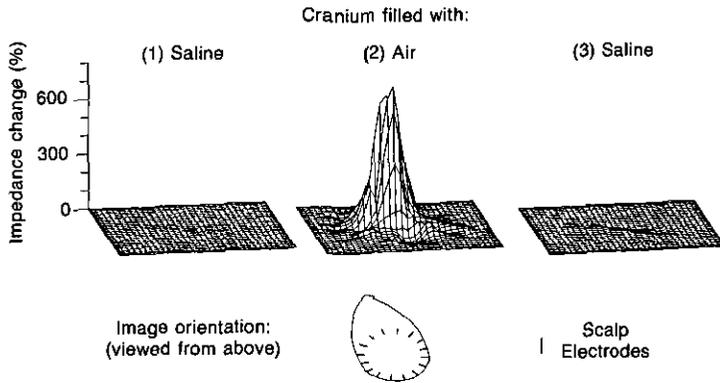
Figure 2. *Sensitivity of* EIT *measured with scalp electrodes to replacement of cranial contents by air. Measurements were made with scalp electrodes about one hour* post mortem. *The brain was evacuated but the meninges were left intact. A reference image was made with the cranial cavity filled with saline. The images shown were made 3, 12 and 13 min later, when the cranial cavity was filled successively with saline, air and saline.*

central major peak. *Post mortem*, the impedance increase was more widespread and irregular, and continued to increase until the end of the period of measurement. In images collected with scalp electrodes *post mortem*, the impedance increased uniformly throughout the period of measurement.

In both sets of cortical records, total image impedance, and that of the two major peaks, increased rapidly for the first 5 min or so, and was then followed by a more gradual increase. A similar biphasic initial time course may be seen in the impedance changes of the whole image and single major peak in the scalp records obtained during cerebral ischaemia (figure 4).

4. Discussion

4.1. Implications of calibration results for interpretation of images made during cerebral ischaemia

An ideal imaging system would accurately measure a specified variable in a slice of defined thickness. With the prototype EIT system used, sensitivity varied over the image, and the 'slice' was biconvex in an ill-defined way. The calibration studies were intended to define the limitations of the device; some would be present even if the device could be used under ideal conditions, others derive from the need for a practical experimental protocol for use on the head of rat.

4.1.1. Spatial resolution. This has been investigated by Eyuboglu *et al* (1989), using a suspended ball in a tank containing saline and the same EIT system as used in this study. The spatial resolution was worse centrally in the tank, and improved in an asymmetric fashion nearer the edge. This may be mainly attributed to current spread from the electrodes, which is in all directions. The current density is therefore less in the centre of the image than at the edges. No other calibration studies have been published. The calibration results from the present study show, as expected, that single objects can be well localised when placed in a medium of initially constant resistivity. Two objects could be distinguished towards the centre of the image when separated by about 20% of the electrode array diameter.

(a) Cerebral ischaemia

Time: 10 min   25 min   50 min

Carotid artery occlusion

Temperature change: +0.4±0.1°C   +1.0±0.4°C

Cortex — Impedance change (%)

Temperature change: −0.1±0.1°C   +0.1±0.2°C

Scalp

(b) Post mortem

Time: 1 min   15 min   30 min

Temperature change: −1.3°C   −2.2°C

Cortex — Impedance change (%)

Temperature change: −2.9±1.2°C   −3.8±0.8°C

Scalp

Image orientation:
(viewed from above)   Electrode
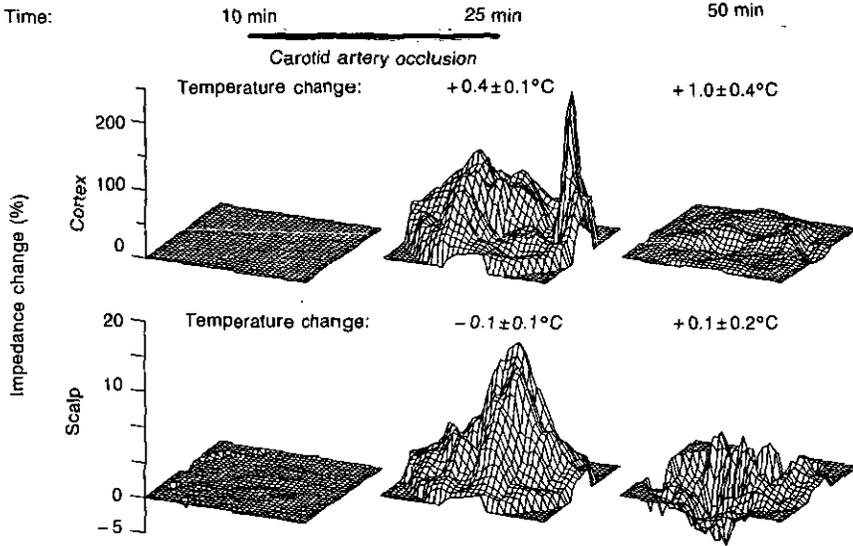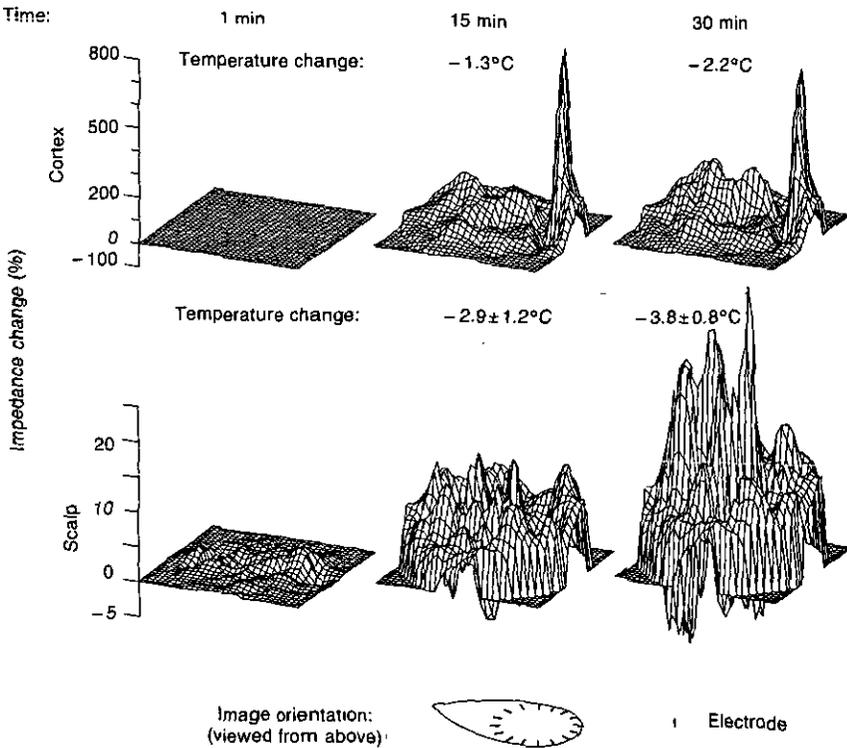
Figure 3. Averaged EIT images collected with either cortical or scalp electrodes during cerebral ischaemia (a) $n = 4$ in 2 rats in each case, or *post mortem*, (b) $n = 1$ and 2 respectively. Carotid artery occlusion was performed from 10 to 25 min after a reference frame taken at 0 min. In post-mortem records, the images are referenced to an image taken just before the time of death. Temperature changes are with respect to the onset of cerebral ischaemia or the temperature 1 min after the reference image in the post-mortem records.

(*a*) Cortical electrodes

Cerebral ischaemia   Post-mortem

(*b*) Scalp electrodes

Total image   Peak 1   Peak 2   Peak 3
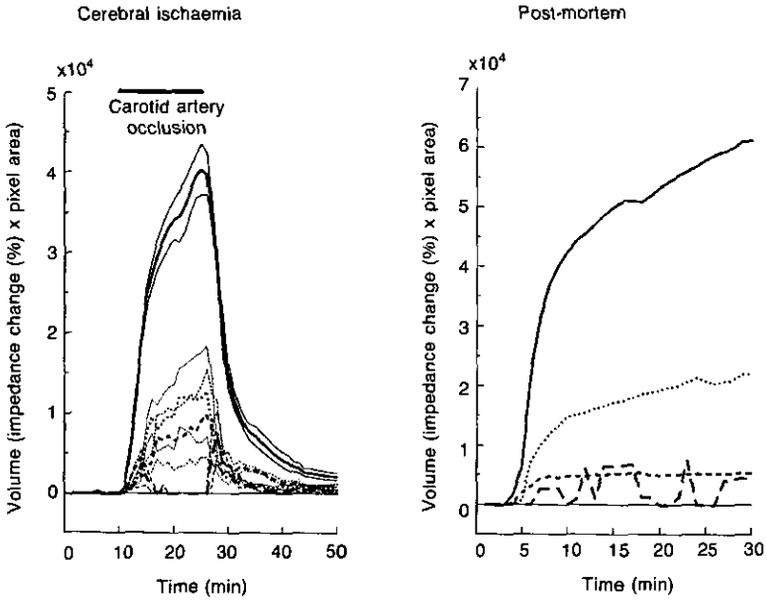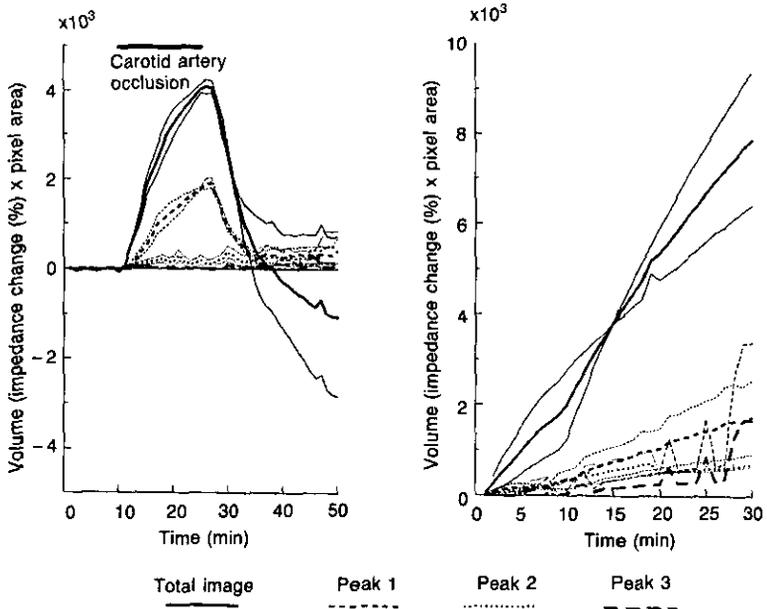
Figure 4. The volumes of the whole image and largest three peaks with respect to time of the images in figure 3. Heavy and light lines represent the mean and limits of ± 1 se respectively.

4.1.2. Elliptical electrode arrays. These led to distortion of test objects, but in a predictable way.

4.1.3. Assumption of reconstruction algorithm that the initial resistivity of the object is uniform. This is reasonably true for measurement with cortical electrodes. It is clearly not the case when scalp electrodes are used, as the resistivity of the skull is approximately thirty times greater than that of the brain or scalp (see Holder 1992a). In calibration experiments *post mortem*, this had two effects: (i) The thickness of the skull was greatly over-represented. (ii) Any intracranial impedance changes were blurred into a small central area of the image.

4.1.4. Off-plane impedance changes. Eyuboglu *et al* (1989) observed that the sensitivity to off-plane impedance changes was greater towards the centre of the image. They could therefore lead to errors in interpretation of an image because an impedance change which extended over the entire area of an image, but some distance off-plane, could appear as a centralised impedance disturbance.

4.1.5. Baseline shift. Impedance recordings in biological tissue tend to have a drift (see Holder 1992b), which is likely to vary with each combination of the 16 electrodes used in this study. This was worse in *in vivo* recordings. This problem was addressed by empirically correcting each pixel separately in EIT images for baseline drift over a defined period prior to recording. This could be justified because preliminary measurements showed that such drift was linear. In practice, this gave reasonably level baseline images (e.g. figures 2 and 3).

4.2. Interpretation of EIT images made during cerebral ischaemia or post mortem

During cerebral ischaemia measured with cortical electrodes, impedance increased in the frontoparietal and occipital areas, but most markedly in the latter. In studies in the same four vessel model of cerebral ischaemia in the rat as that used in this work, blood flow measured by dye perfusion (Pulsinelli and Brierley 1979), or ^{14}C-iodoantipyrine autoradiography (Furlow 1982, Jorgensen and Diemer 1982) decreased markedly in frontoparietal areas, but was generally preserved in the cerebellum and brainstem. These experiments were all performed in rats which were allowed to recover after vertebral artery occlusion, unlike this study, in which all procedures were performed at one operation. The preservation of posterior territory blood flow may have been related to this. Regional cerebral blood flow has also been measured by hydrogen clearance using platinum electrodes in rats in which vertebral and carotid artery occlusion were performed at the same operation (Todd *et al* 1986). The blood flow after 15 min of cerebral ischaemia decreased to 5 - 8% of the resting value in frontal, parietal and occipital areas. The large occipital impedance increase observed in this study is therefore unexpected. Further studies would be needed to establish whether it represented a true cerebral impedance disturbance, or was in some way artefactual, perhaps due to movement of the electrode-tissue interface as a result of the cerebral ischaemia. (During these experiments no separation of the brain from the electrode array was visible by eye.) This could be investigated by using spring-mounted electrodes to maintain electrode pressure at a constant level.

During cerebral ischaemia measured with scalp electrodes, impedance increased reversibly over one central area. The position of the peak was near the midline, between the peaks recorded with cortical electrodes. This suggested that the two peaks seen in the cortical images were blurred together. The impedance increases during cerebral ischaemia measured with cortical or scalp electrodes had similar biphasic time courses, which supports

the contention that the observed scalp impedance changes reflected cortical impedance. However, a small peripheral impedance increase was present at the periphery of images made with scalp electrodes during cerebral ischaemia. This was not present in calibration images made *post mortem*, when the cranial contents were altered (figure 2). This suggests that small local increases in scalp impedance occurred as a result of carotid artery occlusion.

The EIT images collected *post mortem* were similar to those seen during ischaemia, except that the changes did not reverse and were larger. Post-mortem impedance changes have been investigated with applied current at 1 kHz in rabbit cerebral cortex (Van Harreveld and Ochs 1956). A resistance increase of 155% was observed 25 min *post mortem*. The impedance changes were attributed to anoxic depolarisation, cooling, draining of fluids such as the cerebrospinal fluid, and emptying of blood vessels. These processes presumably caused the larger impedance increases observed in this study. The post-mortem images collected with scalp electrodes also showed impedance increases around the periphery which were presumably due to drainage of blood from the scalp and cooling of the head.

The blurred shapes of the impedance increases are probably partly due to the poor spatial resolution. In scalp images, no ring of minimal impedance change is seen, which might have been expected to represent the skull. This is presumably because the large central change is blurred and extends peripherally into the region in which the skull would have been represented. It is also surprising that the impedance increases are largest centrally; cortical impedance increases are large and might have been expected to produce a cylindrical appearance to the images. This is presumably due to off-plane impedance increases, both because the head is spherical, and because off-plane sensitivity is greatest centrally (see above).

4.3. Implications for use of EIT in imaging brain functional changes

These results indicate that, at present, this EIT system would have the greatest application in localising single, rapid impedance changes in a homogeneous medium. These conditions would best be met if EIT were used with intracranial electrodes − for instance, to localise an epileptic focus in patients being assessed for curative surgery. The images collected with scalp electrodes appear to blur the intracranial contents together and so do not seem to give much more information than that obtained with single channel impedance measurement. Before proceeding to clinical studies with scalp electrodes, it would be essential to improve the reconstruction algorithm so that imaging could be performed through the extracerebral layers.

Acknowledgements

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