ELECTRICAL IMPEDANCE TOMOGRAPHY (EIT) FOR BRAIN FUNCTIONAL IMAGING

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ABSTRACT: *Imaging of brain function -- to monitor either haemodynamic responses occurring over seconds or neuronal activity taking place at sub-second time-scale -- is a major application in medical tomography. In this paper, after an introduction of electrical impedance tomography (EIT), a review of the existing brain functional imaging techniques has been presented. Based upon their comparison viz-a-viz the properties of temporal & spatial resolutions, depth sensitivity and portability, it has been argued that EIT has emerged as a strong candidate technique for the application of low-cost and portable imaging of brain function.*

Key Words: Tomography, Medical Imaging, Radiology, EIT, Brain function

1. INTRODUCTION TO TOMOGRAPHY AND ELECTRICAL IMPEDANCE TOMOGRAPHY (EIT)

The word *tomography* has been described by Oxford English Dictionary as "a method of Radiography displaying details in a selected plane within the body". Tomography is generally defined as the process of plane-wise imaging the internal properties of a subject using various types of probing signal. A complete tomography system consists of the processes of energizing from a source, measurement, data acquisition and data inversion (image reconstruction).

Tomography techniques are non-intrusive, and ideally, non-invasive as well. One categorisation of tomographic systems is from the point of view of the principles on which they are based, namely transmission, emission and diffraction/scattering tomography. Then there are different types of tomography based on the choice of the probing signal (modality) e.g. electrical, magnetic, electromagnetic, acoustic, infrared or optical.

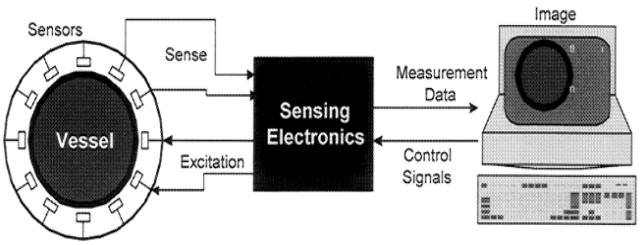

Figure 1. An electrical tomography system [1]

In Electrical Tomography (figure 1), the excitation is in the form of either current being injected into the subject or voltage being presented across the subject. There are single- as well as multi-frequency [2] electrical tomography systems. The frequency of the applied signal can be in the range starting from a few tens of Hz up to a few MHz. Electrical tomography having probing signal frequency in GHz range is considered separately as microwave tomography. Electrical tomography provides, from the measured signals, sensitivity to a bulk electrical property like conductivity or permittivity of the matter of the subject, thus giving rise to the names electrical impedance tomography (EIT) [3] or electrical resistance tomography (ERT). If the applied probing signal is a magnetic field, then this is magnetic induction tomography (MIT). The bimodal technique of magnetic resonance EIT (MREIT) is a combination of magnetic resonance imaging (MRI) and EIT.

In voltage-source EIT systems, measurements are made of the current passing through the boundary electrodes, while in current-source EIT systems, the boundary voltages are measured between electrodes. The voltage-source design is simpler. On the other hand, the current-source design has the advantage of reduced sensitivity to electrode placement, higher accuracy in conductivity images and better suppression of high frequency noise [4].

Within current-source EIT systems, there are further variations of current strategy: Applied potential tomography (APT) systems use a single current source for serial injections; Adaptive current tomography (ACT) systems use multiple current sources for multiple simultaneous current injections, which is an obvious complication in hardware. The main issue in multiple simultaneous injections is to achieve the necessary accuracy in both the amplitude and phase of all the current signals so that the sum of all the currents, i.e. the common mode current, is equal to zero [4]. This is not easy to achieve.

Unless separate injection and measurement electrodes are provided, ACT instruments perform bipolar or 2-terminal measurements, i.e. the same pair of electrodes are involved in both injection and measurement; this brings in the effect of electrode contact resistance [5]. On the other hand in APT systems, the pair of electrodes being used for measurement is other than the ones being used for injection; this is called tetrapolar or 4-terminal measurement [6].

Here is how a typical EIT measurement takes place in a single current-source system. Current is repeatedly injected serially at different electrodes, thus forming various current injection patterns, and both active and reactive components of the resulting boundary voltages are measured at all the other electrodes placed around the subject. If only the active (real) components of the boundary voltages are measured, then this is ERT (electrical resistance tomography). There are many possible types of current drives for single current source (figure 2), namely cross, polar, pseudopolar and adjacent. Polar drive current patterns (figure 2 (c)) are generally considered to produce high EIT sensitivity to impedance changes deep inside the subject [8], though [7] have differed. Using the measured active (and reactive) components and the image reconstruction software, images of the conductivity (and permittivity) distribution within the subject are formed.

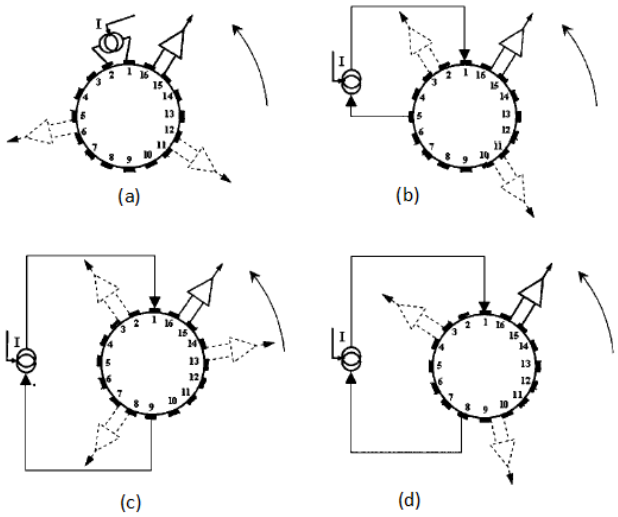

Figure 2. Current drives for single current source EIT systems (a) adjacent (b) cross (c) polar (d) pseudo-polar [7]

Thus overall, the choices are made between the different approaches mentioned above to design an optimal EIT system for a given application. From the application point of view, tomography can be categorized into two main types, namely i) Industrial process tomography and ii) Medical tomography. The field of industrial process tomography is the application of tomography to engineering processes, e.g. imaging of oil and gas in pipelines. More details of this field are available in [9, 10]. Medical tomography is discussed next.

2. MEDICAL TOMOGRAPHY

The use of tomography for medical imaging has traditionally been called Radiology. The medical imaging techniques currently in use in hospitals are based on the following major methods, namely i) X-ray transmission ii) Radio-nuclide emission iii) Nuclear magnetic resonance and iv) Ultrasound [11, 12].

X-ray imaging has been used since the early 1900s, after Rontgen discovered X-rays in 1895. It uses attenuation of the transmitted X-ray beam to image the density of the subject medium. In the 1960s, the combination of X-ray attenuation and computer-based processing gave birth to the technique of computerised tomography (CT). For the development of CT, the Nobel Prize for medicine was awarded in 1979 jointly to Godfrey Hounsfield (of EMI Central Research Laboratories, Hayes UK) and Allan McLeod Cormack (of Tufts University, Massachusetts USA).

The radio-nuclide emission imaging method detects emissions from radio-active isotopes injected into the subject. It is used in the techniques of gamma camera imaging, positron emission tomography (PET) and single-photon emission computed tomography (SPECT) [13]. The first successful PET scanner was developed in the mid-70s, by the team headed by Michael Ter Pogossion [12]. The techniques of PET and CT carry a health hazard due to the subject being exposed to ionising and other potentially harmful radiation.

Nuclear magnetic resonance (NMR) measurement forms the basis of magnetic resonance imaging (MRI). In MRI, the distribution of protons (hydrogen nuclei) in water molecules is determined, and ultimately imaged. This is done by placing the subject in a strong static magnetic field and detecting the variation of RF signals due to magnetic alignment of the protons when RF electromagnetic field coils are turned on and off. For their discoveries concerning MRI, the Nobel Prize for medicine was awarded in 2003 jointly to Peter Mansfield and Paul Lauterbur.

Ultrasound-based medical imaging (also called ultrasonography) [14] uses acoustic waves of frequency around 1-6 and 7-18 MHz for, respectively, deeper and superficial structures of the human body. It detects attenuation due to the acoustic impedance of the subject being imaged.

Besides these long-established medical imaging techniques, there are several other relatively new imaging techniques. These include optical molecular imaging, optical coherence tomography, diffuse optical tomography (DOT) [15], event related optical signal (EROS) [16] and EIT. These techniques either are under extensive research or have been taken up by clinicians, for medical applications.

The medical imaging techniques can be further classified into one of two types in terms of their objective: anatomical (or structural) and functional. The former type is used to image the structure or anatomy of some part of the subject (e.g. imaging of bone or tissue) whereas the latter type performs imaging of some function taking place within the subject (e.g. imaging of cardiac function).

An imaging technique can be suitable for anatomical imaging, but not for functional imaging, e.g. CT. Yet another imaging technique can be suitable for both anatomical and functional imaging. For example, MRI, originally developed as an anatomical imaging technique for soft tissues, has a functional version called fMRI i.e. functional MRI [17]. fMRI is sensitive to either the blood volume (using the injected magnetic resonance contrast agents) or the blood oxygen level, the latter technique being called BOLD (blood oxygenation level detection) fMRI. Similarly, the ultrasound technique can perform anatomical imaging (e.g. of a tissue, based on its varying acoustic impedance) as well as functional imaging (e.g. of blood flow, by detecting the Doppler shifts in the received ultrasound waves).

The Radio-nuclide emission imaging techniques (PET and SPECT) are more functional in nature and these image/measure the absolute physiological and biochemical activity taking place inside the body, though PET is also indirectly used for anatomical imaging. The diffuse optical tomography technique of near-infrared spectroscopy (NIRS) is under research for both anatomical and functional applications [15]. In NIRS, light of a specific wavelength is passed through the subject's body and collected by the light detector. The analysis of the absorption and scattering spectra of the received light gives information about either the tissue structure, for anatomical purposes or the changes in the deoxygenated and oxygenated haemoglobins, reflecting the haemodynamic activity.

For some practical applications, a combination of different imaging techniques is used, which is referred to as multi-modal imaging, e.g. combination of PET with MRI [18].

EIT is under research for both anatomical and functional imaging applications, and is discussed next.

Table 1. Comparison of characteristics of functional imagingtechniques * For a comparison, spatial resolution of anatomical imaging techniques of CT and MRI is less than 1 mm.

[a][43]; [b][16]; [c][17]; [d][40]; [e][45]; [f][13]; [g][14]; [h][15]; [i][41]; [j][42]; [k][47]; [l][48]; [m][46]; [n][20]

Functional Imaging Technique	Characteristics			
	Temporal resolution	**Spatial Resolution***	**Depth-Sensitivity**	**Portability**
fMRI	100 msec at best[a,b] ; typically a few seconds[c]	From a few mm down to 0.1 mm[c,d]	Up to 2-3 cms[e]	No
PET	Over seconds[a]	From a few mm down to 1 mm[f]	--	No
Ultra-sound	Over seconds	Down to 2 cm[g]	Up to 16 cm[g]	Yes
DOT / fNIRS	A few tens of msec[h]	1-2 cm[b,h]	Up to 1-2 cm[a,b]	Yes
EROS	From a few to 100 msec[b]	A few mm[b]	Up to 3-5 cm[b]	Yes
EEG	From sub-msec to 100 msec[c,i,j]	From several cm down to 1-2 cm[c,j]	Up to 4-5 cm[k]	Yes
MEG	From 4 msec to 100 msec[c,j]	From several cm down to 3 mm[c,j]	Up to 1-2 cm[k]	No
EIT	Down to 2 ms[l]	Down to 7-8 mm, for 546 independent measurements[m] (as in fEITER)	At least 5-6 cms[n]	Yes

3. MEDICAL EIT

Key reviews of medical EIT are given in [19, 20]. The seeds of the EIT technique were sown by the use of resistivity measurements for geophysical applications in the 1920s. Since then, ERT has been routinely used in geological [21] and archaeological [22] fields, though with dc excitation only. The use of EIT/ERT for medical applications goes back to the work on thoracic impedance measurements and impedance pneumography during the 1950s and 1960s [23]. This work did not include imaging. The first few electrical resistance / impedance measurement systems capable of imaging were presented by [24, 25] and [26] – the last one being for geophysical application. The first tomographic in-vivo resistance image to be published was by [27], showing the image of a human forearm.

Since the development of these electrical resistance/impedance imaging systems in the late 70s and early 80s, research in the field of medical EIT has grown steadily, for both anatomical and functional imaging applications [19]. The anatomical EIT is generally concerned with imaging the conductivity and permittivity of tissues, in order to differentiate between malignant and benign tissues for diagnostic purposes. Thus, routine application of anatomical EIT by clinicians is in prospect for breast cancer detection [28]. Similarly, the functional version of EIT is also under extensive research or use by clinicians for monitoring / imaging of lung, brain, cardiac and gastrointestinal functions as well as of blood perfusion [29, 30, 31].

4. FUNCTIONAL ACTIVITY IN THE BRAIN

two different time-scales. The more familiar one takes place over a few seconds, i.e. at supra-second time-scale. This functional activity is generally of a physiological nature, e.g. variations in blood flow / volume, cell swelling or metabolic activity, and is called the haemodynamic response [29]. This activity occurs typically 5 sec after a neural stimulus is applied and it causes relatively large changes in the brain impedance, i.e. from a few per cent to many tens of percent [32, 33].

The less familiar timescale, in terms of imaging, is the electrical activity happening over a few tens of msec, i.e. at sub-second level. This activity is due to the neuronal signalling and associated synaptic – both electrical and chemical -- transmissions. The fastest chemical synaptic transmission takes place over 1-5 msec, and is still slower than the electrical synaptic transmission, which is over a fraction of a msec, at the level of a single synapse [34]. The overall neuronal signalling in response to a given stimulus is the transmissions across the billions of synaptic clefts present in brain and an evoked response is their accumulated effect, which is developed over a few tens of msec. For example, in monkeys and cats, neural processing after the application of a stimulus takes place over a period of 20 to 500 msec [35]. Similarly, in humans, it takes 50 msec to transmit information from the retina to the brain's visual cortex, whereas the awareness of the stimulus is developed 500 msec after the stimulus starts in the cortex [36]. On the other hand, a single pulse delivered to the skin can evoke a potential impulse in the cortex in 20 msec [36]. For research on consciousness, a minimum time-duration of 250 msec has been suggested as meaningful [37]. The evoked response causes relatively small changes in the brain impedance.

Brain functional imaging applications that require the sub-second level of temporal resolution as well as depth sensitivity include research in neural and cognitive sciences, e.g. studying consciousness [37] and the effects of anaesthetics [38]. The hippocampus, thalamus and amygdala, which control cognitive functions like consciousness & memory and the integration of brain-processes, are deep-lying sub-cortical areas [34, 39] and their electrical activity can only be imaged by a system having both sub-second temporal resolution and depth sensitivity.

5. IMAGING OF BRAIN FUNCTION

There is a long list of techniques which are currently either being used in clinics or under research for monitoring and imaging brain function at the supra-second timescale, i.e. haemodynamic responses. These include fMRI [17, 40], PET / SPECT [13], ultrasound [14], electroencephalography (EEG) [41], magneto-encephalography (MEG) [42], DOT technique of functional NIRS (fNIRS) [15], EROS [16] and EIT. Table 1 presents a comparison of the characteristics of temporal

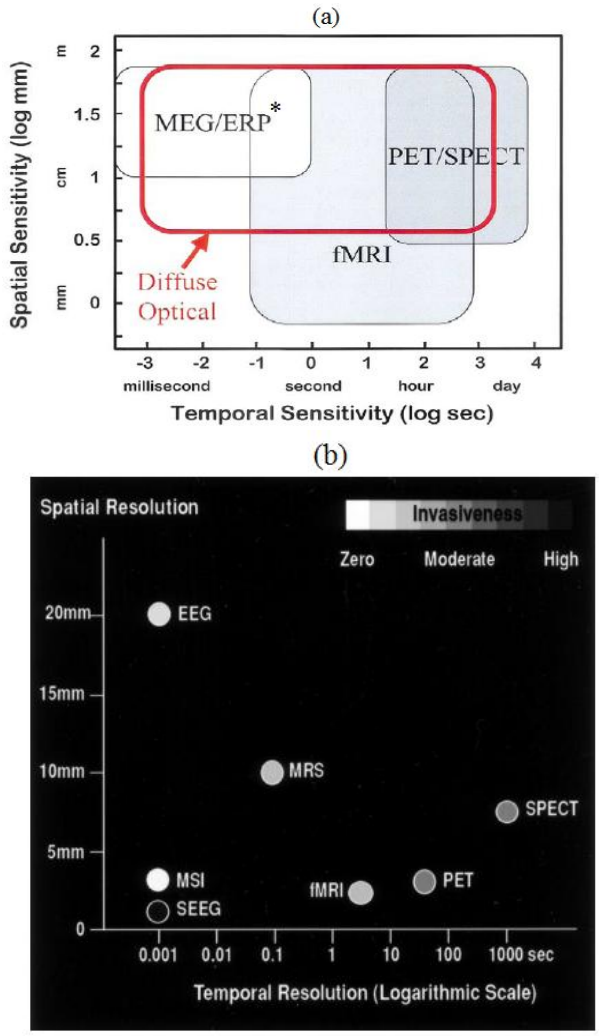

Figure 3. Comparisons of spatial and temporal resolutions of different neuroimaging techniques (a) [43] (b) [42]

resolution, spatial resolution and depth sensitivity for these Out of these techniques, fMRI, PET/SPECT and functional imaging techniques. Non-invasive EEG is portable, but it is not directly sensitive to the deep structures within the brain [34]. MEG is not portable as it requires a large shielded room due to the weak signals involved.

ERP (event related potential) is event-triggered EEG

ultrasound have the limitation of not having sub-second temporal resolution (figure 3). Thus if required to monitor brain function at sub-second timescale, then these techniques perform this task indirectly, through monitoring the haemodynamic response and assuming a direct link of cause-effect between neural activity and haemodynamic response. However, it has been reported that this assumption of a direct link may not always be correct [44]. [40] mentions the experimental findings when haemodynamic responses were present and visible in BOLD fMRI signal, but the neuronal spiking was entirely absent. These observations are important in neuroscience research, as they cast doubt on the concept of indirect monitoring of neural activity through haemodynamic response. This also raises the requirement of an imaging modality having sub-second temporal resolution and direct sensitivity to the brain's electrical activity.

6. EIT FOR BRAIN FUNCTIONAL IMAGING

[32, 33] provide good reviews of EIT for brain functional imaging. Compared with the other functional imaging techniques mentioned earlier, EIT has the advantages of portability and overall low-cost (including operating costs). On the other hand, the main disadvantage of EIT is its relatively poor spatial resolution. One important reason for systems like X-ray tomography to have good spatial resolution is that the applied X-ray beam travels in a straight line. Equation 1 shows the relationship for the intensity-ratio of the X-ray beam passing through the subject [11].

$$\ln\left(\frac{I_0}{I(x,z)}\right) = \int \mu(x,y,z)dy \qquad (1)$$

where:

y = Direction of travel of X-ray beam

I = Transmitted intensity of X-ray beam

I_0 = Exit intensity of X-ray beam from the source

μ = Attenuation coefficient of the subject matter; a function of position

Due to the effect of absorption of low-energy photons (called beam hardening), an object of uniform μ incorrectly appears as non-uniform. When equation 1 is modified for its correction, the result is that the right-hand side factor of $\int \mu(x,y,z)dy$ becomes $\int d(x,y,z)dy$, where d is the density of the material. Thus it can be seen that only the material that is on the geometrical path of the beam contributes to the line integral of whether attenuation coefficient or density, as shown above. This is why X-ray tomography is called a "hard-field" tomography system.

On the other hand, EIT is a "soft-field" tomography technique as the applied current spreads in the whole subject and an object of high conductivity contrast anywhere in the subject contributes to all boundary voltage measurements V_m, for all current patterns. This effect is shown in equation 2 [11].

$$V_m = \int\int\int \sigma(x,y,z)\nabla\phi\nabla\psi dxdydz \qquad (2)$$

where:

V_m is the boundary voltage measured at mth electrode-pair

σ is conductivity of the subject at the point x,y,z

$\nabla\phi$ is potential gradient at the point x,y,z due to unit injected current

$\nabla\psi$ is the field which would be produced at the point x,y,z if unit current is passed through the measurement electrode-pair

As σ is to be calculated (the inverse problem) from the measured boundary voltages V_m in equation 2, the volume integral in these calculations makes the inverse problem less well-defined and hence the detection of small perturbations in brain conductivity is very difficult [10]. This is why doing 3D, instead of 2D, tomography measurements improves the spatial resolution in EIT images. The 3D tomography requires a multi-plane, instead of single-plane, electrode configuration, with both intra- and inter-plane current drives. The types of imaging used to date have been 2D, 3D interpolated from 2D and true 3D [49].

It is worth noting here that the spatial resolution depends on the sensitivity maps that result from the various current injection patterns, the number of independent voltage measurements that can be achieved, and the signal-to-noise ratio (SNR) of those measurements [50]. Indeed, in the "soft-field" technique of EIT, the issue of improving spatial resolution in images is an important question for ongoing research [51]. One possibility for use of EIT images may be by co-registering these with another high spatial resolution modality like MRI, as is done for EEG / MEG [52].

EIT has a potential danger too, in the form of injected current; however as long as the current amplitude is within the limits defined by IEC60601_1 safety standard, EIT can be considered safe [53].

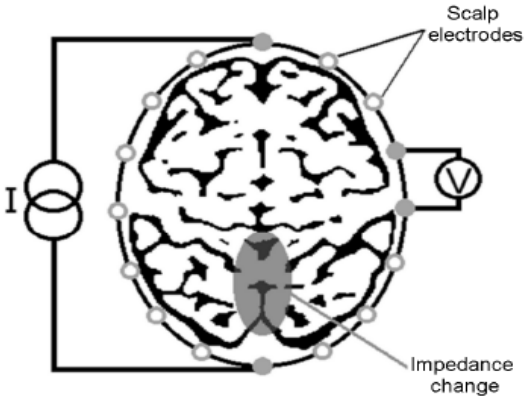

Figure 4. Brain EIT [54]

The use of EIT for imaging of brain function at supra-second timescale, i.e. for haemodynamic responses, has been demonstrated by [29, 54] (figure 4). Extensive research is going on to develop EIT-based brain functional imaging systems for various clinical applications, such as intensive & neo-natal care and brain monitoring during anaesthesia and neurological disorders like Alzheimer's, stroke, epilepsy, edema etc. [30, 32, 33, 55, 56]. The critical aim of stroke monitoring is to ultimately differentiate between ischemic and haemorrhagic stroke in order to decide about using thrombolytic drugs [56].

At the sub-second time-scale, the concept of measuring changes in brain impedance/resistance evoked by applied stimuli may be traced back to the simultaneous measurements of cortical resistivity and evoked electrical activity, reported during the 1950s and 1960s. There are different values for these changes reported in literature, i.e. from a few percent down to mostly a few hundredths -- even thousandths -- of a percent. [57] reported an about 3 % decrease in resistivity of cat brain during direct cortical stimulation. Klivington, Galambos and Velluti, in their pioneering work (e.g. [58, 59], reported a new phenomenon then, of evoked resistance shift (ERS) in conjunction with recordings of evoked potentials (EP), in the audio and visual cortex of anaesthetised and unanaesthetised cats. The reported measured values of ERS due to audio/visual stimuli were 0.0025 % [58] and 0.1 % [59] in the audio and visual cortex, and 0.002-0.005 % in the subcortical nuclei, of anaesthetised and unanaesthetised cats. Their series of papers extended to a determination of the source(s) of these ERS responses, which was firmly attributed to changes in synaptic electrical properties [59]. They also reported variations in the ERS characteristics over different brain regions.

Since the late 1980s, the University College London (UCL) research group has been doing extensive research on the application of functional EIT of evoked responses. [60] reported the human brain conductivity changes of 0.002 % and 0.02 % during sensory and visual evoked responses. Later, a prototype system was presented [61] having a 5 Hz square-wave excitation, for monitoring the sub-second neuronal depolarization. For human brain, [8, 54] reported slow changes (over tens of seconds) of up to 1 % due to visual and 0.3 % due to somatosensory stimulus in human brain. Their recent research on rat brain is presented in [51] and [62], the latter being in collaboration with KH Univ. (Korea) group.

At the University of Manchester, [63, 64] presented pilot study results of sub-second functional brain imaging using an adapted industrial EIT system. Encouraged by these results, a full 32-electrode system, namely fEITER (functional Electrical Impedance Tomography of Evoked Responses), was developed [65]. Its results of the hospital tests on humans have been reported in [65, 66, 67, 68].

Other research groups who are conducting extensive research in both supra- and sub-second brain functional imaging using EIT are FMM Univ. China [7, 30, 55] and more recently, University of Bologna Italy [69].

Thus, research is on to establish EIT as the technique of choice where low-cost & portable brain functional imaging, whether for supra- or sub-second time-scale, is required.

7. CONCLUSIONS

There are different medical tomography techniques available for brain functional imaging applications. However, their temporal & spatial resolutions, as well as the characteristics of depth sensitivity, portability and overall cost are the major factors which dictate their suitability of use for specific applications.

For example, brain functional imaging having both sub-second temporal resolution and depth sensitivity is required in many neuroscience research applications like studying consciousness and the effects of anaesthetics. For such applications, the medical imaging techniques not having sub-second temporal resolution perform this task indirectly, i.e. by assuming a direct link of cause-effect between neural activity & haemodynamic response and monitoring the latter. However, this assumption may not always be correct, casting doubt on the concept of indirect monitoring of neural activity through haemodynamic response. This emphasizes the requirement of an imaging modality having sub-second temporal resolution and *direct* sensitivity to the brain's electrical activity. This is where EIT is a strong candidate technique.

EIT has, in addition, got the characteristics of portability and overall low cost. However, its major drawback is the poor spatial resolution in images. Many research groups are at present conducting extensive research in the use of EIT for both supra- and sub-second brain functional imaging. It can be expected that, in near future, EIT will emerge as the technique of choice where low-cost & portable brain functional imaging is required, such as in operating room, intensive care unit (ICU) and emergency diagnostic services.

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