

## Noninvasive Evaluation of Electrical Conductivity of the Normal Brain and Brain Tumors

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**Target Audience:** Clinicians, scientists and technologists engaged in brain tumor imaging

**Background and Purpose:** The knowledge of electrical tissue properties is expected to be beneficial for clinical diagnosis and therapy monitoring. Electric Properties Tomography (EPT) is a recently developed technique which measures the tissues' electrical conductivity noninvasively through post-processing the radiofrequency (RF) transmit field map of a standard MRI scan<sup>1</sup>. In attempt to explore the clinical applicability of noninvasive conductivity measurements, this study evaluated the repeatability of conductivity measurements by EPT and the conductivity values of the normal intracranial compartments, normal-appearing brain parenchyma and intra-axial brain tumors.

**Methods:** This study included 1 normal subject and 25 patients with intra-axial brain tumors (4, 5, 4, and 12 patients with WHO grade I, II, III, and IV tumors, respectively). EPT was performed, using a 3-dimensional steady state free precession sequence (3D-SSFP) (3.0T scanner, FOV = 220 × 220 × 170 mm<sup>3</sup>, resolution = 1.3 × 1.1 mm<sup>2</sup> in plane, 1 mm slice thickness, sagittal slices, non-selective RF pulses,  $\alpha = 25^\circ$ , TR/TE = 3.5/ 1.7 ms, 2 averages, total scan time = 3:40 min). The axial fast spin echo T2WI was also performed in all participants. The axial fast FLAIR imaging and the axial pre- and post-contrast-enhanced T1WI were also performed in the patients. To evaluate repeatability of the conductivity measurements, a total of seven acquisitions were done in the normal subject. The conductivity maps were calculated from the phase images of the 3D-SSFP sequence, using the formula  $\sigma(\mathbf{r}) = (2 \mu_0 \omega)^{-1} \Delta \phi(\mathbf{r})$ , where  $\sigma(\mathbf{r})$  = conductivity,  $\mu$  = magnetic permeability of the body,  $\omega$  = Larmour frequency,  $\Delta$  = Laplacian operator, and  $\phi(\mathbf{r})$  = transceive phase. The gray matter, white matter and the cerebrospinal fluid (CSF) of the normal subject were segmented, using the T2weighted images. The normal-appearing brain parenchyma and the non-enhanced and enhanced tumor components of the patients were also segmented, using the T2-weighted, FLAIR, and pre- and post-contrast-enhanced T1-weighted images. These segmented components were then superimposed onto the corresponding conductivity maps which were co-registered with the aforementioned anatomical images. The histograms were extracted for each component, and the histogram metrics (the normalized peak height, peak position, maximum, and histogram width) were compared among the normal and normal-appearing intracranial compartments, between the tumors and the adjacent normal-appearing brain parenchyma, and among the tumors with varying grades. The influence of gender and age on the regional conductivity values was also evaluated.

**Results:** Very good agreement was achieved among the seven measurements made in the normal subject (intra-class correlation coefficient  $\geq 0.90$ ), suggestive of high repeatability of the noninvasive conductivity measurements by EPT. There was significant gender difference in the regional conductivity values — women having higher normalized peak height of the normal and normal-appearing white matter histograms (two sample t-test,  $P = 0.035$ ). No significant correlation was observed between the histogram metrics and age (Pearson's product-moment correlation analysis,  $P > 0.05$ ). The normal and normal-appearing gray matter, white matter and CSF had significantly different width, maximum, and normalized peak height and peak position of the histograms (One way ANOVA and post-hoc Bonferroni tests,  $P < 0.017$ ) (Fig 1). The representative conductivity maps of the low and high-grade tumors are shown in Fig 2. For both low and high-grade tumors, the histogram metrics of the enhanced and non-enhanced components of the tumors differed significantly from the adjacent normal-appearing brain parenchyma (the width, maximum and peak position for high grade tumors, and the width and maximum for low-grade tumors) (paired t-tests,  $P < 0.05$ ). The peak histogram position of the non-enhanced hyperintense component of the tumors showed moderate positive correlation with the tumor grade (Spearman's rank-correlation analysis,  $\rho = 0.48$ ,  $P = 0.018$ ), and its value of 850 mS m<sup>-1</sup> distinguished the grade IV tumors from the other tumors with the sensitivity of 83.3% and the specificity of 75.0% (Fig 3).

**Discussion:** Gender difference in the histogram metrics may suggest a variation in the number and size of the axons and myelin — which form insulation against the electrical flow, between the two gender groups<sup>2</sup>. Variation in the histogram metrics among the normal and normal-appearing intracranial compartments is considered to reflect their varied tissue compositions; for instance, the white matter which is composed mainly of insulating axons and myelin has a lower peak histogram position. The altered conductivity metrics of the tumors are thought to be due to changes in water and tissue composition and breakdown of the insulating cell membranes and myelin<sup>3</sup>. Higher conductivity values with higher tumor grades may imply that these tumors have a larger degree of tissue alterations and breakdown.

**Conclusion:** EPT provides information about the tissues' electrical conductivity noninvasively and in vivo. Its high repeatability, the observation of significantly different conductivity histogram metrics between the tumors and adjacent normal-appearing brain parenchyma, and possible differentiation of the grade IV tumors from the others may suggest that EPT can become a tool for the diagnosis and monitoring of brain tumors.

**References:** (1) Katscher U, et al. Recent progress and future challenges in MR electric properties tomography. *Comput Math Methods Med.* 2013; 2013: 546562. (2) Polak K, et al. Sex difference in Onuf's nucleus homologue in the Asian musk shrew. *Brain research* 2010; 1346: 62-68. (3) Bullard DE, et al. Measurement of tissue impedance in conjunction with computed tomography-guided stereotaxic biopsies. *J Neurol Neurosurg Psychiatry* 1987; 50: 43-51.

**Figure legends:** Fig 1 (below, left). The average histograms of the normal and normal-appearing gray matter (red), white matter (blue), and CSF (green). The histogram metrics differed significantly among these compartments (one way ANOVA and post-hoc Bonferroni tests,  $P < 0.017$ ). Fig 2 (below, middle). The conductivity maps showing (a) a diffuse astrocytoma (WHO Grade II) and (b) a glioblastoma (WHO Grade IV). The tumors are indicated by arrows. The look-up table shows the conductivity values in mS m<sup>-1</sup>. Fig 3 (below, right). The box plots showing range and the median values of the peak histogram positions for the non-enhanced hyperintense components of the grade IV and other tumors. The dotted line represents the peak histogram position of 850 mS m<sup>-1</sup> at which the grade IV tumors are distinguished from the other tumors with the sensitivity of 83.3% and the specificity of 75.0%.

