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Measuring the local electrical conductivity of human brain tissue

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The electrical conductivities of freshly excised brain tissues from 24 patients were measured. The diffusion-MRI of the hydrogen nuclei of water molecules from regions that were subsequently excised was also measured. Analysis of these measurements indicates that differences between samples' conductivities are primarily due to differences of their densities of solvated sodium cations. Concomitantly, the sample-to-sample variations of their diffusion constants are relatively small. This finding suggests that non-invasive *in-vivo* measurements of brain tissues' local sodium-cation density can be utilized to estimate its local electrical conductivity. © 2016 AIP Publishing LLC.

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I. INTRODUCTION

Tomographic analyses of electroencephalographs (EEGs) and magnetoencephalographs (MEGs) could be improved by non-invasively establishing the local electrical conductivities of a patient's brain and cranium. Presuming that electrical currents in the brain are primarily carried by sodium cations, we explore whether MRI measurements of local sodium concentrations can generate reasonable estimates of their electrical conductivities.

To address this question, we measured (1) the electrical conductivities of samples of brain tissue that were excised from pediatric epilepsy surgery patients and (2) the *in-vivo* diffusion-MRI of water molecules' hydrogen atoms at the locations from which brain tissues were subsequently excised. These measurements were performed with the same apparatuses that were described in prior publications.^{1,2} However, the measurement described here utilizes a new and significantly enlarged cohort of patients. Only findings that remain significant with this expanded study are discussed. More importantly, we analyze our results in a novel manner which suggests how non-invasive MRI measurements can be used to estimate the local electrical conductivity. The present work complements a recent study that focuses on how the temporal decay of a dc conductivity measurement provides a measure of the characteristic distance charge carriers move before encountering a blockage.³

II. CONDUCTIVITY AND MRI MEASUREMENTS

The room-temperature low-frequency ($<10^3$ Hz) electrical conductivities of twenty-four bulk (1 cm^3) samples of freshly excised brain tissue from pediatric epilepsy surgery patients were measured both perpendicular and parallel to their brains' pia. The results presented in the second and fourth columns of Table I show conductivities ranging from

0.05 S/m to 0.24 S/m with an average value of ~ 0.12 S/m. The very high correlation between measurements made parallel and perpendicular to the pia (R-value/p-value: $+0.79 / <0.0001$) indicates that the electrical conductivity of these bulk samples is essentially isotropic.

Diffusion-MRI (i.e., spin-echo nuclear magnetic resonance, NMR) measurements of the hydrogen nuclei of water molecules in brain tissue were acquired on 30 mm^3 voxels and averaged over 1 cc volumes at the locations from which samples were subsequently excised (determined at surgery using intraoperative neuro-navigation). These *in-vivo* measurements yield diffusion constants for water molecules' hydrogen nuclei perpendicular and parallel to their brains' pia averaged over each voxel. As presented in the seventh and ninth columns of Table I, these diffusion constants ranged between $D_{MRI} = 0.7 \times 10^9\text{ m}^2/\text{s}$ and $D_{MRI} = 1.5 \times 10^9\text{ m}^2/\text{s}$. The high correlation of the diffusion constants in these two directions (R-value/p-value: $+0.88 / <0.0001$) indicates that the diffusion constant is nearly isotropic. Its value is $D_{MRI} \sim 10^9\text{ m}^2/\text{s}$.

III. ANALYSIS

The general expression for an isotropic dc conductivity, $\sigma = (q^2/kT)nD$, can be utilized to estimate the charge carriers' room-temperature diffusion constant D .³ Presuming the charge carriers to be monovalent, sodium cations ($q = e$) with the concentration typical of brain tissue, $\sim 2.4 \times 10^{25}\text{ m}^{-3}$, yield the room-temperature diffusion constant $D \sim 10^9\text{ m}^2/\text{s}$.

The average charge-carrier diffusion constant deduced from our measurements of the conductivity D is seen to be comparable to the average diffusion constant characterizing the motion of water molecules' hydrogen nuclei. This relationship can be understood as resulting from sodium cations being solvated. In particular, in the absence of charge carriers, water molecules' dipole moments foster their short-range parallel alignment.^{4,5} By contrast, the presence of a sodium cation fosters surrounding water molecules being directed toward the

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TABLE I. The room-temperature electrical conductivities of freshly excised samples from the brains of 24 epilepsy patients measured perpendicular and parallel to each brain's pia are listed in the second and fourth columns. The systematic error estimated for each measurement is given following its value, in columns three and five. The directionally averaged electrical conductivity (AEC) is listed in column six. The room-temperature diffusion constants of water molecule's hydrogen atoms perpendicular and parallel to the brain's pia measured with diffusion-MRI (spin echo NMR) are listed in columns seven and nine. These measurements were made at the locations from which bulk samples ($\sim 1 \text{ cm}^3$) were subsequently excised. The standard deviation (SD) of each measurement's listing is presented in columns eight and ten. The directionally averaged diffusion constant (ADC) of these measurements is listed in column eleven.

Patient	$\sigma_{\perp}$ (mS/m)	% $\delta\sigma_{\text{sys}}$	$\sigma_{\parallel}$ (mS/m)	% $\delta\sigma_{\text{sys}}$	AEC (mS/m)	$D_{\perp}$ ($10^{-9} \text{ m}^2/\text{s}$)	SD	$D_{\parallel}$ ($10^{-9} \text{ m}^2/\text{s}$)	SD	ADC ($10^{-9} \text{ m}^2/\text{s}$)
1	62.6	9.6	66.9	9.0	65.5	1.08	0.46	1.18	0.46	1.06
2	137.5	4.7	119.0	5.3	125.2	1.03	0.36	1.16	0.31	1.05
3	97.6	6.3	99.8	6.2	99.1	1.22	0.26	1.38	0.25	1.22
4	80.5	7.6	96.2	6.4	91.0	1.17	0.44	1.29	0.46	1.19
5	109.2	5.7	90.8	6.8	96.9	1.28	0.34	1.12	0.33	1.13
6	116.8	5.4	110.2	5.6	112.4	1.04	0.24	1.24	0.20	1.10
7	243.2	3.2	185.3	3.6	204.6	1.24	0.38	1.33	0.39	1.23
8	104.7	6.0	107.9	5.7	106.9	1.21	0.57	1.25	0.42	1.14
9	96.0	6.4	103.2	5.9	100.8	0.95	0.35	1.15	0.42	1.00
10	97.8	6.4	103.1	6.1	101.4	1.14	0.24	1.37	0.26	1.21
11	86.0	7.1	100.1	6.2	95.4	1.06	0.24	1.12	0.27	1.04
12	138.8	4.6	111.0	5.7	120.3	0.97	0.29	1.11	0.28	1.00
13	124.1	5.2	132.0	4.8	129.4	0.79	0.30	0.86	0.32	1.06
14	163.4	4.2	118.9	5.3	133.7	1.23	0.53	1.25	0.51	1.19
15	191.9	3.6	137.6	4.6	155.7	0.72	0.22	0.83	0.37	0.97
16	69.6	8.6	76.3	7.9	74.0	1.10	0.26	1.15	0.26	1.08
17	116.5	5.4	120.8	5.3	119.4	1.12	0.30	1.17	0.29	1.09
18	100.1	6.1	119.6	5.3	113.1	1.11	0.30	1.13	0.29	1.08
19	181.3	3.8	164.6	4.1	170.2	1.00	0.14	1.19	0.15	1.06
20	97.8	6.3	129.2	5.0	118.7	1.12	0.57	1.29	0.53	1.18
21	103.9	6.0	98.7	6.2	100.4	1.15	0.39	1.30	0.35	1.18
22	128.1	5.0	112.2	5.6	117.5	1.00	0.59	1.14	0.70	1.02
23	101.1	6.2	152.4	4.4	135.3	1.41	0.71	1.46	0.67	1.05
24	85.3	7.2	54.3	11.0	64.6	0.71	0.31	0.85	0.28	0.99

FIG. 1. The directionally averaged electrical conductivity (AEC) of excised samples of human brain in units of S/m is plotted against the directionally averaged diffusion constant of hydrogen nuclei of brain's water molecules (ADC) in units of $10^{-9} \text{ m}^2/\text{s}$ from a voxel within the region from which the corresponding brain sample was subsequently excised. Significantly, the fractional variation of the AEC ($\sim 50\%$) is much larger than that of the ADC ($\sim 10\%$) with there being no significant correlation between these two quantities. That is, variations of the electrical conductivity are not primarily associated with variations of the average diffusion constant.

solvated cation.^{6,7} In other words, the presence of a sodium ion alters the orientations of surrounding water molecules. Then, the rate with which water molecules surrounding a solvated sodium cation reorient is comparable to that with which a cation moves. Thus, the diffusion constants measured by D-MRI are indicative of carriers' diffusion constants: $D_{\text{MRI}} \sim D$.

The electrical conductivity $\sigma = (e^2/kT)nD$ is linearly dependent on two variables, n and D . Fractional changes of the conductivity are therefore the sum of that of the solvated-sodium-cation density and that of the diffusion constant: $\Delta\sigma/\sigma = \Delta n/n + \Delta D/D$. To assess the relative importance of these two contributions, consider the relationship between the directionally averaged MRI-diffusion constant (ADC) and the directionally averaged electrical conductivity (AEC) listed in Table I. Figure 1 shows a plot of the AEC against the ADC. The relative variation of the ADC is only $\sim 10\%$. By contrast, the relative variation of the AEC is much larger, $\sim 50\%$. As a result, there is no significant correlation (R -value/ p -value: $= 0.13/0.54$) between the ADC and the AEC. That is, different samples exhibit relatively small variance between their diffusion constants. In other words, the electrical conductivities of our bulk samples of freshly excised brain tissue depend primarily on the densities of their diffusing ions.

IV. CONCLUSION

All told, this study suggests that measurements of the local density of sodium cations in human brain tissue

can provide a reasonable estimate of the local electrical conductivity. We will now pursue this approach further by using sodium MRI to provide a direct non-invasive *in-vivo* means of assessing the local density of sodium cations.

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