Lateralization of Temporal Lobe Epilepsy using a Combinational Model of Electroencephalographic and Imaging

Fariborz Mahmoudi[1,2], Mohammad-Reza Nazem-Zadeh[1], Jason M. Schwalb[3], Ellen L. Air[3], Hassan Bagher-Ebadian[1], Manpreet Kaur[3], Rushna Ali[3], Saeed Shokri[1], Kost V. Elisevich[4], and Hamid Soltanian-Zadeh[1,5]

[1]Departments of Radiology, Research Administration, Henry Ford Health System, Detroit, Michigan, United States, [2]Computer and It Engineering Faculty, Islamic Azad University, Qazvin Branch, Qazvin, Qazvin, Iran, [3]Departments of Neurosurgery, Henry Ford Health System, Detroit, Michigan, United States, [4]Department of Clinical Neurosciences, Spectrum Health System, Grand Rapids, Michigan, United States, [5]CIPCE, School of Electrical and Computer Engineering, University of Tehran, Tehran, Iran

Purpose: Mesial temporal lobe epilepsy (mTLE) is the most common type of refractory focal epilepsy. Concordant electroencephalographic, neuropsychological and Magnetic Resonance Imaging (MRI) findings often lateralize the epileptogenic side permitting surgical resection of the mesial temporal structures, without further investigation. MRI findings include atrophy of temporal lobe structures on T1-weighted and hyper-intensity in FLAIR (fluid-attenuated inversion recovery) images ipsilateral to the side of seizure onset. However, for cases with insufficient structural asymmetry or discordance between imaging, electroencephalographic and neuropsychological findings, information from additional studies, such as Wada (intracarotid sodium amobarbital procedure) and Single photon emission computed tomography (SPECT) are used in the decision making process. However, recruiting additional diagnostic procedures can increase the chance of discordance. In cases of unclear lateralization, implantation of intracranial electrodes for long term monitoring (Phase II) is needed to localize the epileptogenic zone. Unfortunately, Phase II monitoring may lead to infection, intracranial hemorrhage, and elevated intracranial pressure. In this study, we have developed, a combinational model based on imaging and other diagnostic procedures to try to reduce the need for Phase II monitoring. We estimated the weights of individual diagnostic procedures and imaging models in final decision making. Based on most important ones, we designed a fusion function for mTLE lateralization with better accuracy as a final combinational model. Briefly the purpose of this study is, developing a model that would not only enhance patient safety, but also would reduce economic burden.

Methods: The model was developed from a data set of 91 unilateral mTLE patients who underwent resection of the mesial temporal structures and achieved postoperative Engel class IA outcomes, 52 females aged 40.8±11.4 years and 39 males aged 38.9±12.5 years. Forty-two of these patients had undergone implantation of intracranial electrodes to localize the seizure onset zone (left vs. right and/or temporal vs. extra-temporal). The patients underwent a 3.0T MRIs (Signa, GE, Milwaukee, USA) to acquire coronal T1-weighted (using inversion recovery spoiled gradient echo, IRSPGR protocol, TR/TI/TE = 10.4/4.5/300 ms, flip angle = 15◦, voxel size = 0.39×0.39×2.00 mm^3) and coronal T2-weighted (using fluid attenuated inversion recovery, FLAIR protocol, TR/TI/TE = 9002/2250/124 ms, flip angle = 90◦, voxel size = 0.39×0.39×3.00 mm^3) images. Forty-five of patients underwent preoperative SPECT imaging with a triple-head gamma camera imaging system with high-resolution fan-beam collimators (Picker International, Inc., Cleveland Heights, OH) within 2-3 hours after the injection of 99mT ethylcysteinate diethylester at a dose of 550 MBq.

Results of three diagnosis procedures EEG_1, Wada, neuropsychological tests and five different imaging characteristics for mTLE lateralization were used to develop the model. These five characteristics are: M_1: hippocampal volumes [1], M_2: means of FLAIR intensity in left and right hippocampi [1], M_3: standard deviations of FLAIR intensity in left and right hippocampi [1], M_4: means of normalized "ictal ‐ interictal" SPECT intensity in left and right hippocampi [1], M_5: a multi-structural volumetric model which works based on features extracted from hippocampus, amygdala and thalamus from T1-weighted MRI [2]. In order to select most important decision functions from these eight functions, wrapper algorithm are was applied. Then, logistic regression with a ridge estimator was applied on the selected functions. This regression resulted in a combinational linear model that performs the role of a fusion function for mTLE lateralization.

Results: After applying the wrapper algorithm on the above eight functions, three functions, EEG_1, M_2 and M_5, were found to be the most promising functions for mTLE lateralization. Then, by applying regressing logistic function on these selected functions, a combinational linear model is obtained as equation (1).

$$M_6 = 10.6 + 47.2*EEG_1 + 12.6*M_2 + 57.6*M_5 \quad (1)$$

Table 1 Data and Models Specifications

	Diagnosis Procedures			Imaging Models					Combinational Model
	EEG1	Wada	Neuropsychology	M_1	M_2	M_3	M_4	M_5	M_6
Missing Cases	1	5	12	0	0	0	46	23	0
Undecided Cases	4	18	30	2	3	6	7	0	0
Decided Cases	86	68	49	89	88	85	38	68	91
Accuracy	96.5%	94.1%	85.7%	82.0%	83.0%	85.9%	97.4%	98.5%	100.00%

Based on the coefficients of equation (1), M_5 (volumetric multi-structural model) and EEG_1 have more weight for lateralization decision making than M2. Table 1 presents the classification results for the proposed model (M_6) using leave-one-out cross-validation evaluation. The proposed model had an mTLE lateralization accuracy of 100% without any undecided cases or false alarms. In this model, the range of the posterior probability for correct lateralization for the left side is 0.99±0.06. This probability for the right side is 1.00±0.00. These values demonstrate complete reliability on classification by the logistic function.

Conclusion: This study introduces a combinational model using three non-invasive functions based on electroencephalographic phase I, intensity features of hippocampus from FLAIR images, and multi-structural volumetric features extracted of hippocampus, amygdala, and thalamus from T1-weighted MRI, to determine the epileptogenic side in mesial temporal lobe epilepsy patients. Using the proposed model, we succeeded in establishing laterality in all cases, including those that had required Phase II monitoring to define the epileptogenic site. The proposed model holds promise as a way to obviate the need for Phase II monitoring and its associated risks and costs. The results of this pilot study imply that the neuropsychological and Wada tests despite being considered as the standard care for TLE patients prior to resection, show less promising role on localizing the epileptogenic zone compared to the other diagnostic tests such as imaging and EEG. However, considering the fact that each diagnostic test might have different information content that might differently affect on the final decision making, ranking the performances of these tests demands further study.

Acknowledgement: The authors acknowledge the National Institutes of Health for the financial support of this study (NIH grant R01EB013227).

References:

[1] Nazem-Zadeh, M.-R., et al., "Lateralization of temporal lobe epilepsy by multimodal multinomial hippocampal ..." Journal of the neurological sciences (2014);
[2] Mahmoudi F., et al., "Roles of Various Brain Structures on Non-Invasive Lateralization of Temporal Lobe Epilepsy", ISVC'14, 2014;
[3] Kohavi R., John GH., "Wrappers for feature subset selection", Artificial intelligence, 1997; 97(1):273-324;
[4] Le Cessie S., Van Houwelingen J., "Ridge estimators in logistic regression", Applied statistics, 1992:191-201;