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Multimodal MRI Evaluation in Intractable Epilepsy with Pathologically Confirmed Mesial Temporal Sclerosis

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1. Introduction

Medial temporal lobe epilepsy (MTLE) is a common syndrome. Many of the cases of medial temporal lobe epilepsy often remain resistant to drug therapy. Surgical resection of the affected temporal lobe is often final option to control/reduce the seizure frequency. Mesial temporal sclerosis which can be unilateral or bilateral is the most common cause of medial temporal lobe epilepsy. Accurate preoperative lateralization of the mesial temporal lobe sclerosis is essential, because the surgical strategy and outcome is distinctive in this group of patients. Currently many non-invasive methods like MRI, EEG and neuropsychological assessment are used to achieve this goal.

Number of studies have shown role of various MRI techniques in lateralizing the seizure focus in cases of mesial temporal sclerosis (1-8). Newer quantitative MRI along with qualitative MR techniques has improved the overall sensitivity of MRI for the detection of MTS (9-12). We planned to examine the relative sensitivity of specific MRI sequences in patients with pathologically confirmed MTS.

2. Materials and methods

We reviewed results of MRI scans of 44 patients who were subjected to anterior temporal lobectomy and had pathological confirmation of MTS. The definition of intractable epilepsy is taken when patient is having at least two episodes of seizures per month even after being on at least two antiepileptic drugs for at least two years. We compared each combination of test results to resected tissue pathology to determine the association with MTS. Patients were excluded if imaging revealed other pathologies such as tumors or vascular lesions. Epileptogenic temporal lobe was identified by detailed physiological studies (EEG, VEEG) and neuropsychological studies in all patients.

MRI studies- MRI studies were performed using a standard protocol in a Siemens Magnetom Vision 1.5 T magnet in all patients.

Following images were obtained in the temporal lobe protocol- T1(TR-650 ms;TE-14 ms; slice thickness-3 mm), PD-T2(TR-2300ms;TE-17 & 102 ms; slice thickness-3mm) and FLAIR(TR-9000 ms;TE-105 ms;TI-1800ms;slice thickness-3 mm) images in a plane parallel

and perpendicular to the long axis of hippocampus (fig 1) and 3D volume acquisition of the entire brain using T1 W MPRAGE sequence(TR-9.7 ms;TE-4 ms; flip angle- 12;FOV-250;slice thickness-1 mm).
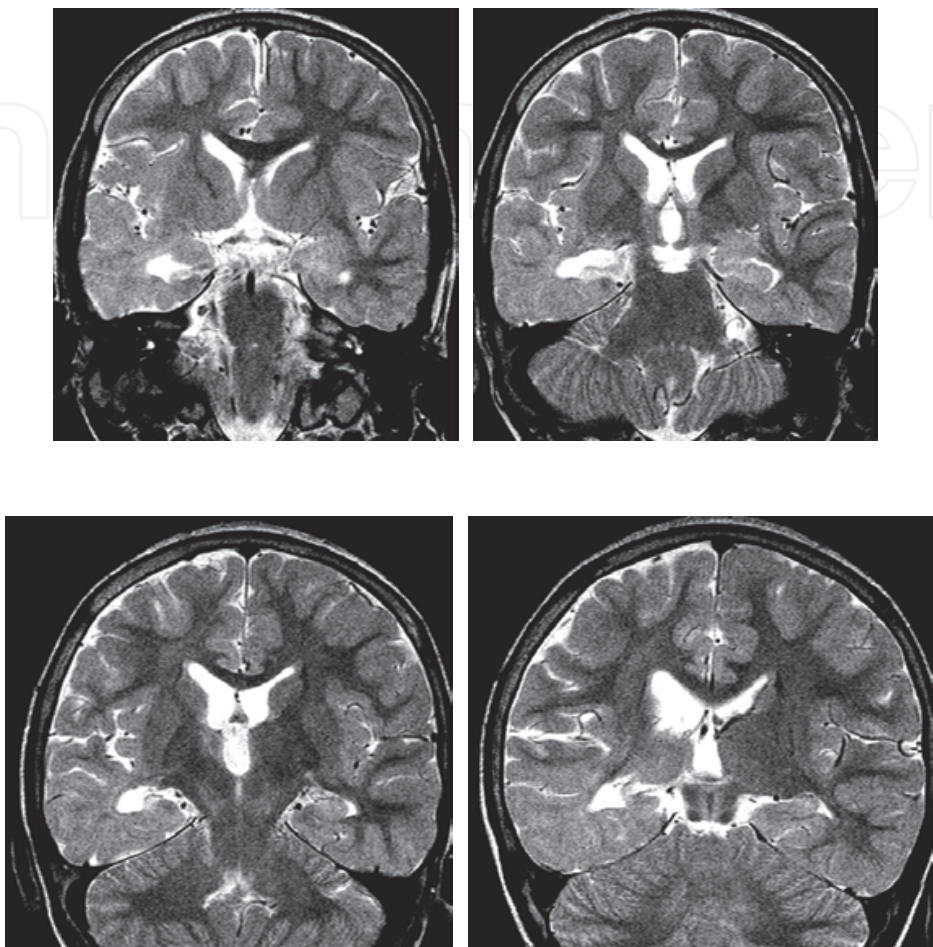

Fig. 1. T2 W images perpendicular to long axis of hippocampus showing Right mesial temporal sclerosis

Demographic variable	Measure

No of patients
    Male
    Female
	44
	30
	14

Mean age of the patients	28 yrs(11- 45 yrs)
Mean age of seizure onset	12 yrs(3 mth-32 yrs)
Mean duration of seizure	17 yrs(3-37 yrs)
Lt temporal resection	22
Rt temporal resection	22

Table 1. Demography of patient population-

Quantitative analysis: This included T2 relaxometry and volumetry.

T2 relaxometry was calculated in a multiple coronal slices from dual echo sequences obtained at TEs of 17 and 102 ms with a slice thickness of 3 mm. Hippocampal T2 relaxometry maps were generated manually from the measured image intensities in the hippocampal structures. T2 values were obtained from a predetermined region of interests. Measurements were taken from each ROI inside the hippocampus excluding the temporal horn CSF (fig 2).
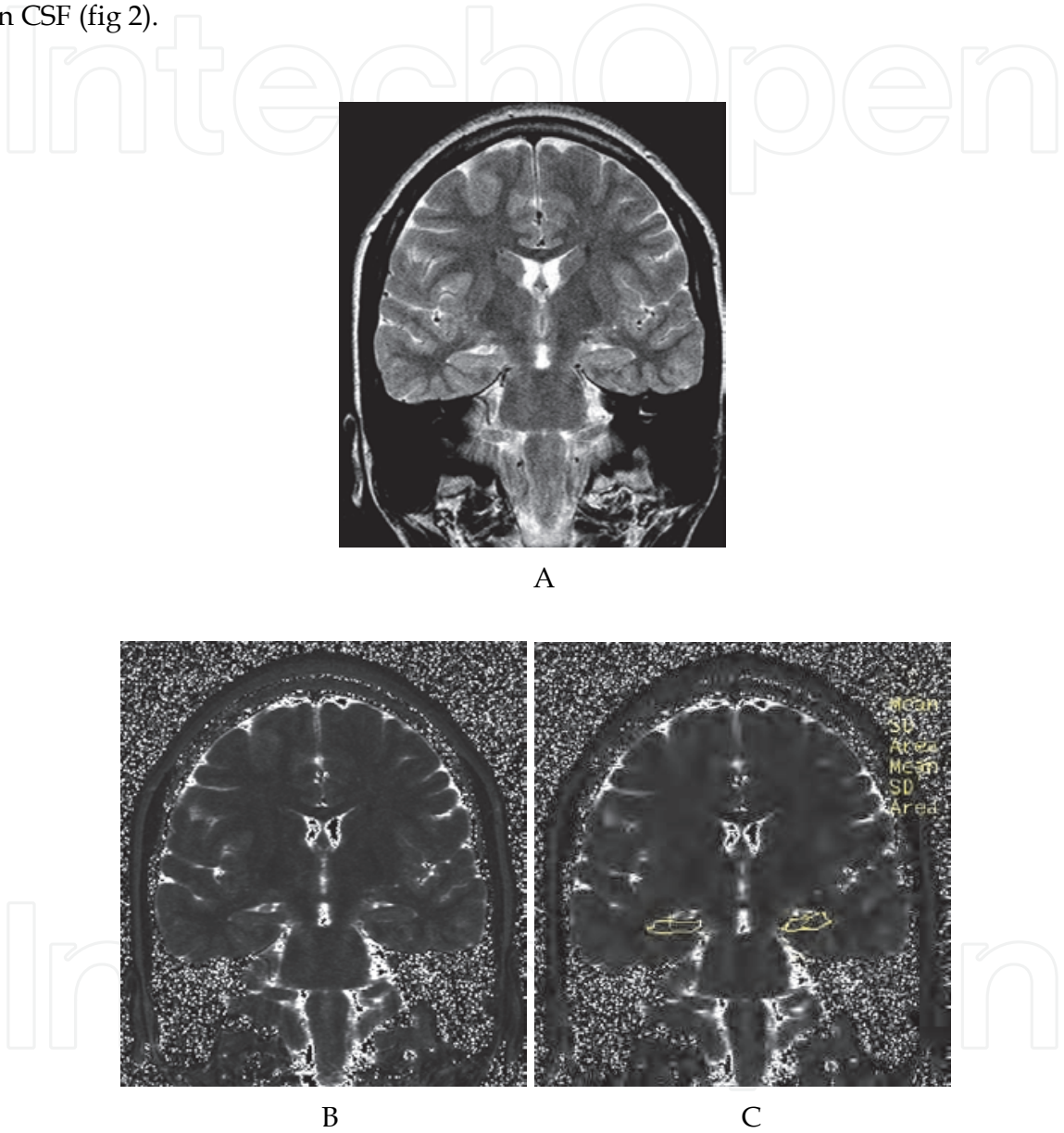

A

B   C

Fig. 2. *A*- T2 W image perpendicular to the long axis of hippocampus. *B*- T2 relaxometry map of the same image. *C*- Outline of hippocampus in cross   section on a T2 relaxometry map.

For volumetric analysis images were transferred to Siemens Magnetom vision workstation. Volumetric measurements were performed by outlining the region of interest (ROIs) manually on a magnified image (fig 3). Anatomical guidelines for outlining the hippocampal formation followed previous protocols (9, 13).

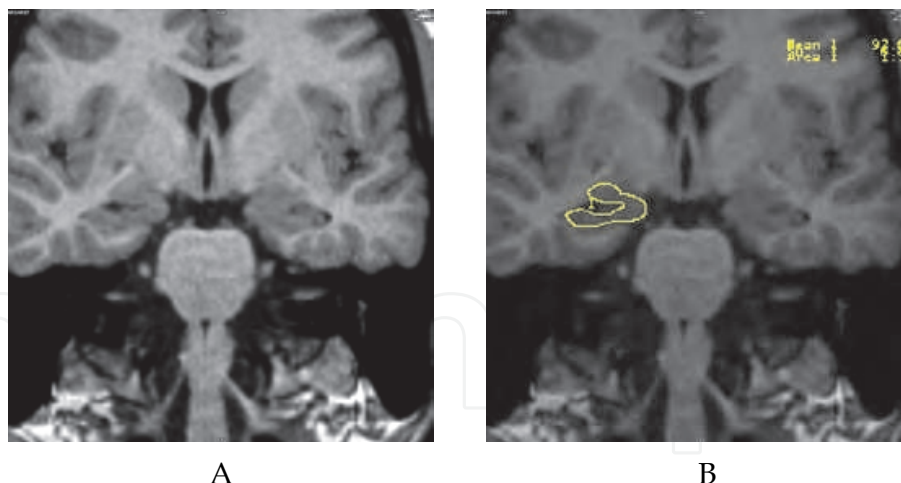A   B

Fig. 3. A-T1W MPRAGE 1mm thick image perpendicular to the long axis of hippocampus.
B- Outline of hippocampus in cross section.

Qualitative MR analysis: included three parameters signal changes, loss of internal architecture and volume loss.

Visual analysis was performed on T1, T2 and FLAIR images to assess following

Surgical technique and histological tissue analysis- All surgical procedure was performed by neurosurgeon. The resection included a standard neocorticotomy of anterior temporal lobe, sparing the superior temporal gyrus. Amygdala and anterior half to two-third of hippocampus were resected and sent for pathological analysis.

The diagnosis of mesial temporal sclerosis was based on the presence of hippocampal neuronal loss and gliosis.

Statistical analysis-Sensitivity of each tests were calculated individually and in multiple combinations. The results of each technique are then compared with the outcome results of the surgery.

3. Results

Visual analysis

Atrophy: Unilateral hippocampal atrophy was detected in 36 of 44 patients (81%). Bilateral atrophy was noted in 2 patients and 6 were normal.

Signal changes: 39 of 44 patients (88.6%) had signal changes which correspond to the site of surgery. 2 patients had bilateral signal changes and lateralization was not possible by signal changes.

Quantitative analysis

Of the 44 patients only 20 patients could be analysed by the quantitative MR analysis because of the non-availability of the raw data.

T2 relaxometry: Higher abnormal T2 values were noted in 16 of 20 patients (85 %) on the side of surgery performed. Normal mean value was taken as 100.2 ± 4.18 msec (right-100.5 msec; left-98.9 msec). The cutoff was set 2 SD above the average and was 109 msec (14). Of these 16 patients 13 had unilateral abnormality and 3 had bilateral abnormality. In patients with bilateral abnormality T2 values were higher on the affected side than the contralateral side.

Volumetric analysis: 18 of 20 patients (90%) showed decreased volume corresponding to the resected side(normal mean value taken as 3571 ± 311 cmm for left and 3696 ± 310 cmm for right)(7). Of these 15 were unilateral and correctly lateralized. The remaining 3 had significant bilateral atrophy with the smaller size corresponding to the affected side in all the patients. Using the right/left volumetric ratio of hippocampal formation, 19 of 20 patients (95%) showed marked differences, with the ratio correctly lateralizing the affected side. The volumetric analysis was normal in one patient.

MRI sequences	Sensitivity
Qualitative	80 %
T2 relaxometry	85 %
Volumetry	90 %

Modality correlation

Visual analysis which took into account both the FLAIR signal changes and visual qualitative atrophy led to correct lateralization in 39 of 44 patients(88.6%). Remaining 5 patients did not have either volume loss or signal changes.

Of the 20 patients in which we had quantitative data only 16 (80%) could be correctly lateralized by the visual qualitative analysis. Of the remaining four patients 2 patients had higher T2 relaxation values with correct lateralization and 3 had smaller volume lateralizing to the affected side. With combined visual analysis and T2 relaxometry analysis 18 patients (90%) were lateralized correctly. When we combined the results of visual analysis and volumetric analysis 19 patients (95 %) were lateralized correctly. On combining all the three modalities all the 20 patients (100%) patients were lateralized correctly; one patient who had normal volume bilaterally was showing high T2 values on the surgery side.

MRI sequences	Sensitivity
Qualitative	80 %
Qualitative + T2	90 %
Qualitative + volumetry	95 %
Qualitative+ T2 + volumetry	100%

4. Discussion

We compared the sensitivity and relative utility of different MR sequences in patients with MTS. This study was specifically designed to assess the sensitivity of the MRI sequences in population of highly selected patients with histologically confirmed MTS. Similar to

previous studies we found that qualitative and quantitative analysis are both highly reliable in experienced hands with individual sensitivity ranging from 85-95%.

This study shows that the use of multiple MR techniques in the investigation of patients with intractable mesial temporal lobe sclerosis offers advantages over individual modalities. The combined sensitivity of all the MR techniques together was 100% for correct lateralization of the epileptogenic temporal lobe.

Visual analysis of FLAIR sequences and T1 W sequences for atrophy demonstrated abnormalities in 88.6%. Other published studies show similar results (11). Jack et al reported identification of atrophy by visual analysis in 83 % and by signal changes on T2 W images in 79% of patients of MTS (15). A more recent study using FLAIR found abnormalities in 97% of the patients with MTS (16). This suggests that with current MRI techniques the sensitivity of visual identification across different centers is relatively reliable.

However the identification of bilateral hippocampal atrophy by visual analysis may be difficult. Only 2 of the 4 patients with bilateral hippocampal atrophy by absolute hippocampal volumes demonstrated visually detected bilateral atrophy. The FLAIR sequence detected bilateral signal changes in only 2 of these patients. Therefore visual analysis is accurate in detecting unilateral MTS but may not be adequate to identify bilateral hippocampal atrophy in some patients.

However visual analysis correctly lateralized the most abnormal hippocampus in most of those with volumetric based bilateral hippocampal atrophy. In 3 of the 4 patients with bilateral hippocampal atrophy, the more affected side was localized by visual analysis. Though our results were influenced by the selection of the patients (only operated patients) previous study by Jack et al demonstrated that even in those patients with bilateral symmetric hippocampal changes, lateralization and successful surgery is possible (17).

Some studies have reported that T2 relaxometry is a reliable method to detect MTS. Jackson et al originally reported that T2 relaxometry maps were abnormal in all patients with MTS (18). However other groups have reported relatively lesser sensitivity (19), in our study the sensitivity of T2 relaxometry to identify the affected side is only 85 % similar to other study.

Majority of the patients who had loss of volume also had longer T2 relaxation. This result indicates a strong relationship between the volumetry and T2 relaxometry. However literature shows discrepancy between the two techniques (7).

The different results of T2 relaxometry across studies may be considered to be due to different technical reasons. Previously published studies had used multi-echo sequences using 8-16 different TEs (7, 18) whereas we have used only dual echo sequences. Other point of difference is that earlier studies have used shorter TR (1500 ms) while we have used TR of 2300 ms (11).

Convergence of all MRI findings in MTS increases the likelihood of a correct diagnosis. Correct lateralization was possible in majority of the patients by qualitative visual analysis; quantitative techniques may provide useful information in the rest. Volumetric measurements using differential right –left volumes provided localization in 90 % of patients, compared to T2 relaxometry which was abnormal in only 85%. Visual analysis failed to recognize the signal changes in only one patient who had abnormal T2 relaxation.

The results of this study suggest that visual qualitative analysis is sensitive in the detection of MTS in most patients. Although quantitative techniques increase the sensitivity of lateralization these are technically demanding and time consuming with the exception of T2
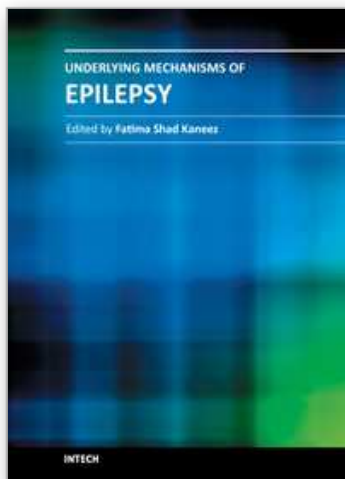
relaxometry. So for routine clinical purpose simple strategy will be to use visual analysis and T2 relaxometry to lateralize the MTLE first. If this is not successful then volumetry can be used as an additional technique.

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Underlying Mechanisms of Epilepsy

Edited by Prof. Fatima Shad Kaneez

This book is a very provocative and interesting addition to the literature on Epilepsy. It offers a lot of appealing and stimulating work to offer food of thought to the readers from different disciplines. Around 5% of the total world population have seizures but only 0.9% is diagnosed with epilepsy, so it is very important to understand the differences between seizures and epilepsy, and also to identify the factors responsible for its etiology so as to have more effective therapeutic regime. In this book we have twenty chapters ranging from causes and underlying mechanisms to the treatment and side effects of epilepsy. This book contains a variety of chapters which will stimulate the readers to think about the complex interplay of epigenetics and epilepsy.

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