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Ratio Ictal SPECT Co-registered with MRI visualizes a greater extent of the ictal onset zone in focal refractory epilepsy

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Abstract
Background: *Until recently, the main non-invasive technique to evaluate the ictal onset zone has been Subtraction ictal SPECT coregistered with MRI (SISCOM). While SISCOM provides useful information about the ictal onset zone, the case we report herein suggests the possibility that multiple regions are involved in a more complex network[7], whose identification can improve the patient's prospects for resective epilepsy surgery.*
Case: *The 23 year old right handed female case under discussion illustrates how Ratio Ictal SPECT coregistered with MRI (RISCOM) findings better guided the invasive evaluation with a more precise targeting of the subdural grids. Here, the concordance between the noninvasive technique (RISCOM) and the invasive evaluation (chronic electrocorticography) allowed a better determination of the seizure onset zone for resective epilepsy surgery. In turn, the resected tissue included a more extended area (orbitofrontal), which was not seen by SISCOM. Importantly, the case also allows for a better understanding of the relationship between the epileptogenic lesion and the ictal onset zone, and their role in the postsurgical outcome. The patient achieved seizure freedom (Engel 1A).*
Conclusion: *A more accurate determination of the ictal onset zone by this novel noninvasive technique not only greatly impact in the postsurgical outcome of patients with focal refractory epilepsy. It may also indicate that the ictal onset zone can be the expression of interlobar connections that does not necessarily include the epileptogenic lesion of patients with malformations of cortical development.*
Key Words: *SISCOM, RISCOM, Chronic electrocorticography.*

Introduction

Epilepsy surgery is a multidisciplinary specialty directed to the identification and localization the epileptic focus[2], mapping its spatial relationships with functional cortical area(s), and ultimately resecting the epileptic focus to achieve seizure freedom[2 3 6]. The main goal of any resective epileptic surgery is to reduce the number of seizure, preserving the functionality and improving the quality of life[1]. Selection criteria for resective epilepsy surgery are pharmacoresistence and absence of potential damage to eloquent cortex from the surgery preserving ability of the remaining brain to carry on normal functions[1]. While targeted resection often cures epilepsies with resectable foci (lesional or nonlesional focal epilepsies)[1 4], the rate of seizure freedom after temporal resective epilepsy surgery is 70-80%[6] and mostly depends on the ability to completely resect the epileptogenic zone[6]. It is believed that the early postoperative failures are due to the inability to localize and/or resect the entire epileptic focus, whereas late recurrences are likely due to development/maturation of a new and active epileptic focus (de novo epileptogenesis)[2]. We use different techniques such as magnetic resonance imaging (MRI), video-electroencephalography (EEG), subdural grids, depth electrodes, magnetoencephalography (MEG), Single Photon Emission Computed Tomography (SPECT), positron emission tomography (PET) and neurocognitive testing in order to localize the potential epileptogenic zone[1 2 8 9]. In order to get a more precise definition (determination) of the epileptogenic zone that is hypothetically defined area the resection of which leads to seizure freedom[5 6]. It should be inferred after presurgical evaluation defining other areas (the epileptogenic lesion, the ictal onset, symptomatogenic, irritative, and epileptogenic zones) and finding explanations for the discrepancies, if any, between these areas. In some cases, however, there is not a clear concordance among these areas and invasive monitoring complemented by functional imaging modalities is necessary to localize the epileptogenic zone.[11]

Single photon emission computed tomography (SPECT):

Ictal onset zone is the area from which seizures originate on ictal EEG. Electrocorticography (ECoG) is considered the gold standard investigatory mean to know about the ictal zone but the issue is that ECoG is an invasive procedure and needs a previous planning in order to put the electrodes over the area closest to the ictal onset zone, which can only be found by other investigatory methods[5 6]. Seizure activity causes blood flow changes in the brain. These changes are predominant in the ictal onset zone and are detected by single photon emission computed tomography (SPECT)[5]. SPECT is used to localize the ictal onset zone in the presurgical evaluation of patients with refractory focal-onset epilepsy. 99mTc-HMPAO is injected at the time of seizure. Both high resolution (3-4 mm voxel) inSpira (Neurologica Corp, Danver, MA) scanner that is 72-detector focused collimator ring scanner system and conventional 2-headed detector SPECT scanner i.e Seimens (Hoffman Estates, IL) with 7-10 mm voxel resolution are used to get the SPECTS.

Ictal SPECT and baseline SPECT are processed and then co-registered on MRI to get the SISCOM (Subtraction ictal SPECT co-registered to MRI) and RISCOM (Ratio ictal SPECT co-registered to MRI). SISCOM is broadly based on the difference (subtraction) between regional blood flow or perfusión during seizure activity and the baseline blood flow. We developed a new technique for detecting brain perfusion changes related to ictal activity i.e RISCOM. RISCOM technique is based on the determination of the relative changes of the blood flow during seizure compared to baseline blood flow taking the ratio of ictal and baseline regional brain perfusion in subjective terms.

History and Examination

The patient is a 23 year old right handed female with past medical history of right hemisphere closed-lip schizencephaly with dysgenesis of the corpus callosum, left hemiatrophy, hemiparesis, hypothyroidism, premature ovarian failure, right eye blindness, mild mental retardation, and intractable seizures epilepsy since age 4. Her family described that seizure begin with head turning to the right and rub her hands together with altered mental status lasting 60-90 seconds with occasional secondary generalization. She was taking phenytoin and levetiracetam, but was still having seizures 1 to 2 times a week. Patient states she does normally have an aura consisting of headache prior to her seizures and that this can occur up to 5 minutes preceding the seizures. Her physical examination showed normal speech and orientation, with mild (4/5) left hemiparesis including the face, slightly wide-based gait and left foot drop. Visual field fixation was preserved in left eye and could only detect light in right eye.

Non Invasive EEG Monitoring

The patient was evaluated with Video Electroencephalography (vEEG) recording, during which typical complex partial seizures (CPS) were captured. Electrographic findings suggested the ictal onset zone over the right temporal lobe with irritative cortex extending to the bifrontal region, peri-sylvian and intra-sylvian cortex.

Presurgical MRI

Closed clip schizencephaly in the right temporal region with dysgenesis of the corpus callosum, absence of the septum pellucidum and hypoplasia of the optic chiasm was visible in MRI (Fig.3). There was apparent increased relative cerebral volume/permeability within the right frontotemporal region.

Invasive EEG Monitorning

Patient underwent a right temporal craniotomy with placement of subdural electrodes. Frequent epileptiform discharges were seen over the right orbito-frontal region, the right anterior subtemporal region, and the anterior temporal pad. There were also frequent runs of electrographic seizures localized to the anterior subtemporal strips and anterior temporal region on the temporal pad. These findings were consistent with a partial seizure disorder of the right that is likely localized to the anterior temporal region as well as the orbitofrontal region. Fig. 7 shows the placement of electrodes intra-operatively and Fig. 6 is CT/MRI showing the position of electrodes post-operatively.

Preoperative SPECT Imaging

The patient was injected with 99mTc-HMPAO at 11th sec after the clinical onset (unspecific aura) of seizure (Fig.2). SISCOM post processed images (Fig.4) showed activation (hyperperfusion) of the right temporal region (Fig.1a), RISCOM images confirmed this finding but also showed activation of the ipsilateral orbitofrontal cortex (Fig.1b & Fig.5). These results were taken in account to plan the placement of the intracranial subdural electrodes.

Preoperative Functional mapping

Electrical stimulation of the subdural electrodes suggested that electrodes FP4-FP5 and TP7-TP8 produce a clear reproducible bilateral eye movement to the left. This most likely represented premotor motor cortex such as frontal eye fields. Neighboring rows of electrodes TP19-TP24 and TP27-TP32 produced relatively low voltage after discharges and long electrographic runs that propagated along the temporal pad. No behavior changes were seen during this activity. No spontaneous or stimulated seizures occurred. However, stimulation of RST1-RST2 induced a "feeling like I will have a seizure". Approximately one and a half hours after stimulation she had a non typical seizure.

Preoperative Neurophychological evaluation

Low average verbal and nonverbal reasoning abilities were found. Performance was severely impaired on a measure of executive function requiring abstract problem-solving and mental flexibility. In contrast, she demonstrated intact working memory, processing speed, and language skills. She also demonstrated good learning and recall of both verbal and visual information. She did not report symptoms of depression on interview.

In conclusion, poor performance on a test of problem-solving and mental flexibility was consistent with a right fronto-temporal seizure focus, as evidenced by prior video-EEG monitoring. She appeared to be at an increased risk for visual memory decline following surgery.

Preoperative WADA test

Expressive and receptive language skills appeared to be fully mediated by the left cerebral hemisphere. Verbal and visual memory abilities also appeared to be mediated by the left hemisphere. Therefore, the available data suggested that the patient would appear to be at a relatively lower risk for memory decline following resection of right temporal lobe structures.

Operation

On 9th day after admission she had been done temporal lobectomy, amygdalohippocampectomy and resection of orbitofrontal cortex and then was transferred to NSICU for post-operative care.

Post Operative course

She had increased lethargy so computed tomography (CT) was performed which showed increasing midline shift and mildly dilated lateral ventricles. External ventricular drain (EVD) was placed on one day after resective surgery. Hospitalization was complicated with fever of 102-103°F. Abnormal Cerebrospinal fluid (CSF) was found concerning for meningitis. CSF culture didn't grow any bacteria, and the patient was treated for presumed culture negative meningitis with Vancomycin, cefepime and metronidazole for 3 weeks. She continued to improve and her EVD was pulled after 2 days.

Patient continued to do well clinically. She remained afebrile and no seizures noted post-operatively. After 10 days of resective surgery she was transferred to the Rehabilitation Center.

Postoperative MRI Brain without and with IV contrast

There was a wedge-shaped infarction of the right parietal and occipital lobe, and areas of infarction with gyral enhancement in the inferior frontal lobe in the right middle cerebral artery distribution adjacent to the excised temporal lobe. There were regions of dural and leptomeningeal enhancement over the right frontal, parietal and occipital areas possibly due to postsurgical change. There was a small area of encephalomalacia in the right superior frontal lobe.

Postoperative Neurological Examination

Patient was alert and oriented. Speech and comprehension was intact. No changes were found in the right eye blindness and mild left hemiparesis that were present before the surgical resection. Left hemianopsia was noted as a new abnormal finding related to the surgery. No other new abnormalities were found.

Postoperative neuropsychological evaluation

We did neuropsychological evaluation after a week of surgery and then on every office visit. From the emotional functioning standpoint, she described her mood as happy most of the time. She reported good appetite and sleep and no other symptoms of depression, including suicidal ideation. Neuropsychologically she performed slightly worse on some measures of memory but not likely to a clinically significant degree. Some aspects of her executive functioning had improved (in particular, problem-solving). She was otherwise stable in all cognitive domains assessed.

Seizure Outcome

The patient had no seizures after resection. She was taking levetiracetam 1500mg BID and phenytoin 300mg QHS postoperative. After the two years of follow up, cVEEG was performed and no electrographic or clinical seizures were noted. Phenytoin was discontinued after 2 year postoperatively. The patient is now not experiencing the typical seizure she used to have and neither is she experiencing the auras. Patient continues to be Engel 1A after 3.5 years of the resective surgery.

Pathological Specimen

The laminar architecture of the cortex was preserved. Extensive astrogliosis was noted in the subpial region, molecular layer, all cortical layers and white matter. These findings were highlighted by the GFAP immunostaining. The cytoarchitecture of amygdala and hippocampus was not present.

Discussion and conclusion

Interlobar connections may have a more important role than just one isolated area in the seizure onset in some patients and may not necessarily overlap the epileptogenic lesion[7]. RISCOM allows identifying a more complex network and extended ictal onset zone than SISCOM. In this study we demonstrated the feasibility and usefulness of a new SPECT processing technique during presurgical evaluation. InSpira scanner for SPECT provides better resolution and may be optimal for RISCOM raw SPECTS scan.

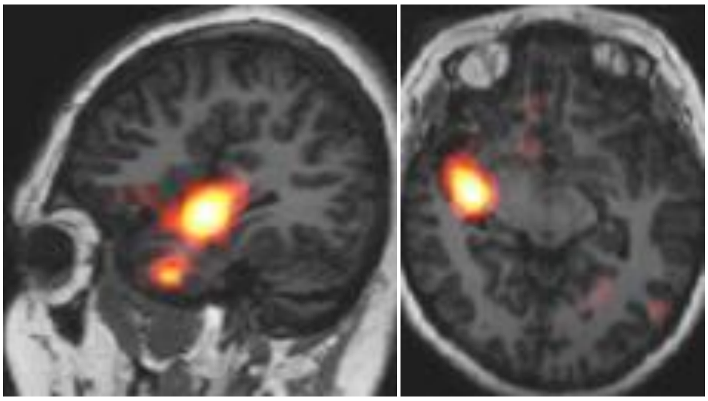

Fig.1(a). SISCOM (Seimens) images both saggital and axial are showing increased signal only within right temporal region.

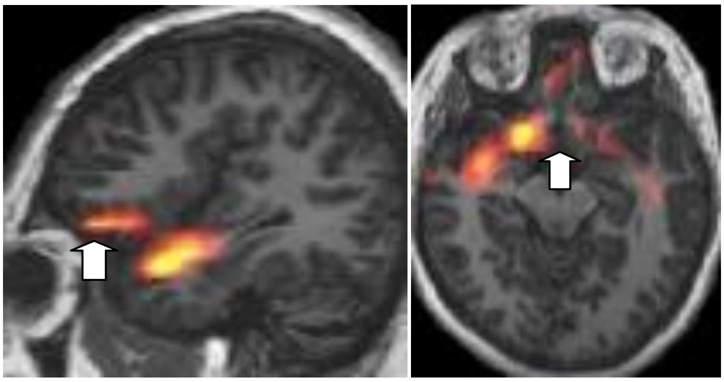

Fig.1(b). RISCOM (InSpira) images both saggital and axial are showing increased signal within right temporal region with ipsilateral orbitofrontal activity (arrow).

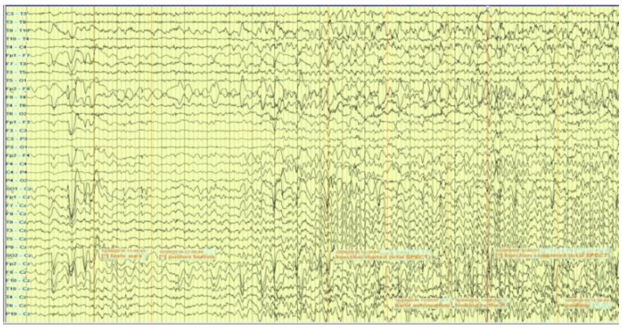

Fig.2. Relation between time of injection for ictal SPECT and clinical onset (aura) of seizure on EEG chart.

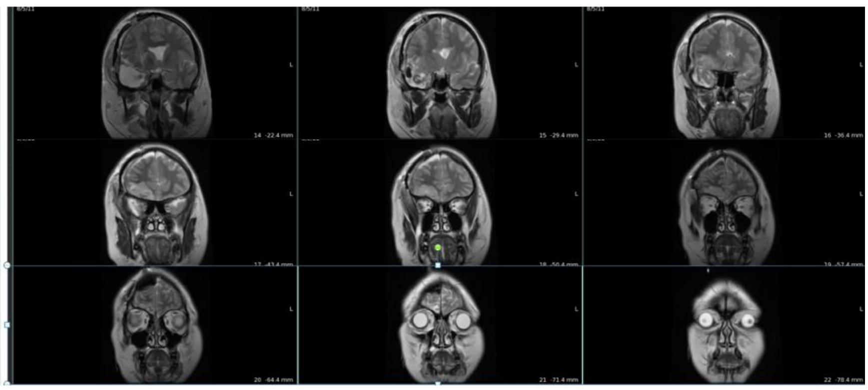

Fig.3. MRI Stealth T2 after craniotomy

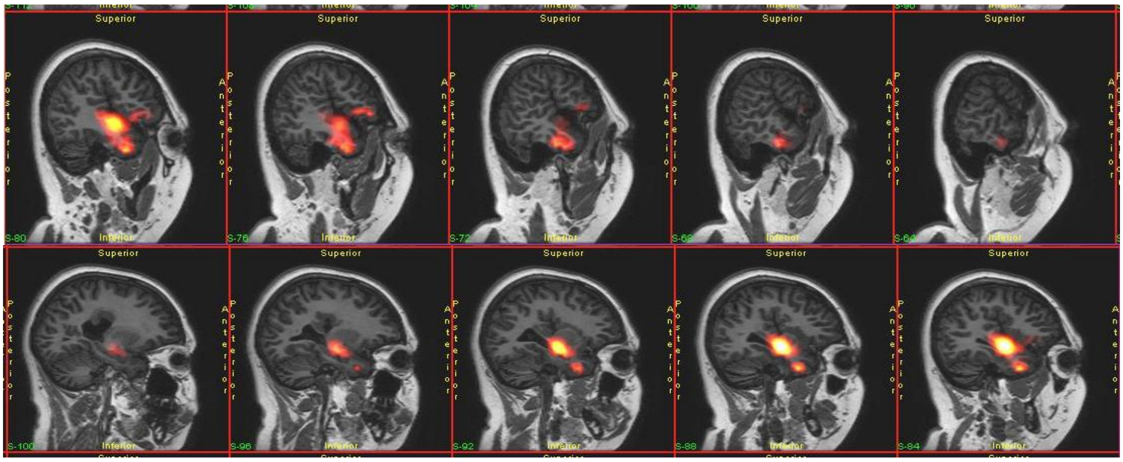

Fig.4. SISCOM (Seimens)

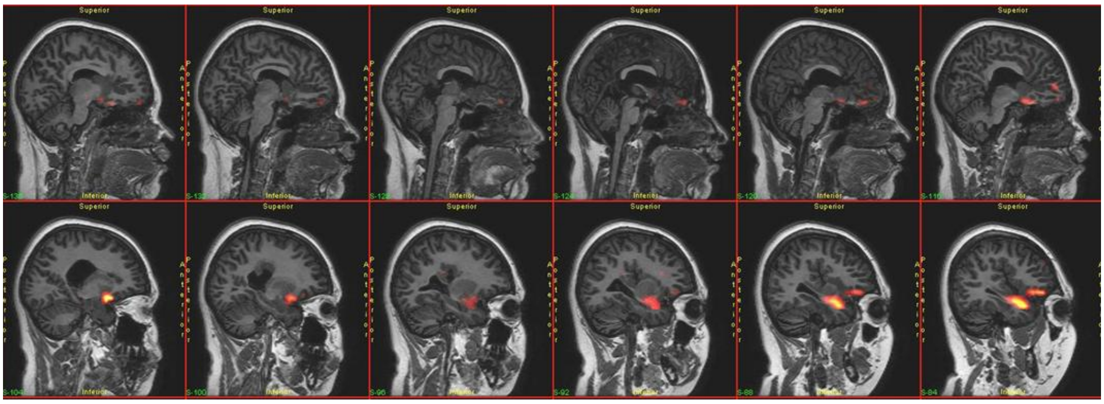

Fig.5. Perfusion Neuroimaging RISCOM (Inspira)

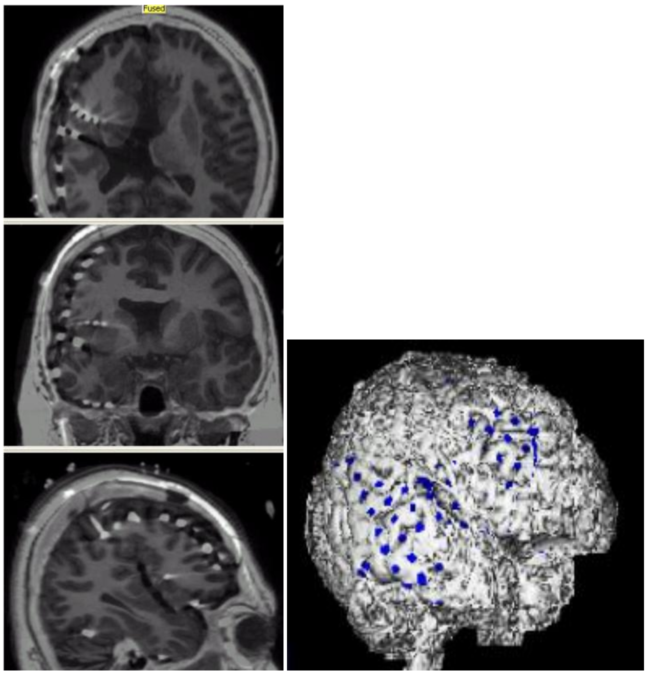

Fig.6. Postoperative CT/MRI showing electrode placement

Fig.7. Intra operative ECoG picture showing the electrodes under scalp

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