

**Seizures and Epilepsy**  
**EVIDENCE TABLE**

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
1. Banerjee PN, Filippi D, Allen Hauser W. The descriptive epidemiology of epilepsy—a review. <i>Epilepsy Res.</i> 2009;85(1):31-45.	Review/Other-Dx	68 studies; 48 prevalence and 20 incidence	Review prevalence and incidence studies of epilepsy to provide a clear definition of epilepsy.	A higher proportion of epilepsy characterized by generalized seizures was reported in most prevalence studies. Epilepsy characterized by partial seizures accounted for 20%–66% of incident epilepsies. Virtually all prevalence and incidence studies report a preponderance of seizures of unknown cause.	4
2. Hirtz D, Thurman DJ, Gwinn-Hardy K, Mohamed M, Chaudhuri AR, Zalutsky R. How common are the "common" neurologic disorders? <i>Neurology.</i> 2007;68(5):326-337.	Review/Other-Dx	N/A	To estimate the current incidence and prevalence in the United States of 12 neurologic disorders.	For some disorders, prevalence is a better descriptor of impact; for others, incidence is preferable. Per 1,000 children, estimated prevalence was 5.8 for autism spectrum disorder and 2.4 for cerebral palsy; for Tourette syndrome, the data were insufficient. In the general population, per 1,000, the 1-year prevalence for migraine was 121, 7.1 for epilepsy, and 0.9 for multiple sclerosis. Among the elderly, the prevalence of Alzheimer disease was 67 and that of Parkinson disease was 9.5. For diseases best described by annual incidence per 100,000, the rate for stroke was 183, 101 for major TBI, 4.5 for spinal cord injury, and 1.6 for ALS.	4
3. So EL. Classifications and epidemiologic considerations of epileptic seizures and epilepsy. <i>Neuroimaging Clin N Am.</i> 1995;5(4):513-526.	Review/Other-Dx	N/A	Review classifications and epidemiologic considerations of epileptic disorders.	Overview of the epidemiology of epileptic disorders shows they are primarily disorders of childhood; age-specific incidence rates of first unprovoked seizure and of epilepsy are highest in the elderly. An appreciation of the epidemiology of seizure disorders is essential in their clinical and laboratory evaluation.	4
4. Berg AT, Berkovic SF, Brodie MJ, et al. Revised terminology and concepts for organization of seizures and epilepsies: report of the ILAE Commission on Classification and Terminology, 2005-2009. <i>Epilepsia.</i> 2010;51(4):676-685.	Review/Other-Dx	N/A	Revised concepts, terminology, and approaches for classifying seizures and forms of epilepsy by the International League Against Epilepsy Commission on Classification and Terminology.	Natural classes or pragmatic groupings may serve as the basis for organizing knowledge about recognized forms of epilepsy and facilitate identification of new forms.	4
5. Blume WT, Luders HO, Mizrahi E, Tassinari C, van Emde Boas W, Engel J, Jr. Glossary of descriptive terminology for ictal semiology: report of the ILAE task force on classification and terminology. <i>Epilepsia.</i> 2001;42(9):1212-1218.	Review/Other-Dx	N/A	Glossary of descriptive terminology for ictal semiology.	N/A	4

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6. Kim JH. Pathology of seizure disorders. <i>Neuroimaging Clin N Am</i> . 1995;5(4):527-545.	Review/Other-Dx	N/A	Review different pathologic lesions associated with seizures.	Remarkable progress has been made in the early detection, resection, and characterization of previously poorly defined pathologic processes.	4
7. Jackson GD, Kuzniecky RI. Chapter 79: Structural Neuroimaging. In: Engel J, Pedley TA, eds. <i>Epilepsy: A Comprehensive Textbook</i> . 2 ed. Philadelphia PA: Wolters Kluwer/Lippincott Williams & Wilkins; 2008.	Review/Other-Dx	N/A	Book chapter.	N/A	4
8. Toh KH. Clinical applications of magnetic resonance imaging in the central nervous system. <i>Ann Acad Med Singapore</i> . 1993;22(5):785-793.	Review/Other-Dx	N/A	Review comparative studies of CT and MRI in the central nervous system. Article also gives a suggested guideline of the clinical applications of MRI as a primary or complementary imaging modality.	Distinct advantage of MRI over CT in the posterior fossa, the perisellar region and diseases involving the leptomeninges and white matter. Cranial nerves (usually not seen on CT), are much better appreciated on MRI. CT is able to show calcification, subarachnoid hemorrhage and acute hematoma better than MRI. CT is more useful than MRI in acutely-ill patients with cerebrovascular accident and head trauma.	4
9. Goffin K, Dedeurwaerdere S, Van Laere K, Van Paesschen W. Neuronuclear assessment of patients with epilepsy. <i>Semin Nucl Med</i> . 2008;38(4):227-239.	Review/Other-Dx	N/A	To review the role of radionuclide functional imaging techniques incorporating SPECT and PET in localizing the ictal onset zone, seizure propagation pathways, and functional deficit zone in patients with intractable partial epilepsy who are candidates for epilepsy surgery.	Ictal perfusion SPECT and interictal FDG-PET imaging remain important tools in the localization of the ictal onset zone, seizure propagation pathways, and the functional deficit zone in the presurgical evaluation of patients with refractory partial epilepsy.	4
10. Schwartz ES, Dlugos DJ, Storm PB, et al. Magnetoencephalography for pediatric epilepsy: how we do it. <i>AJNR Am J Neuroradiol</i> . 2008;29(5):832-837.	Review/Other-Dx	10 patients	To examine value of MEG in pediatric patients with epilepsy. Study was based on authors' clinical experience.	MEG findings have impacted patient management in nearly every case and have been universally accepted by the clinics pediatric neurologists and pediatric neurosurgeon as beneficial for their patients.	4

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11. Caruso PA, Johnson J, Thibert R, Rapalino O, Rincon S, Ratai EM. The use of magnetic resonance spectroscopy in the evaluation of epilepsy. <i>Neuroimaging Clin N Am.</i> 2013;23(3):407-424.	Review/Other-Dx	N/A	To evaluate the use of 1H-MRS in the evaluation of the patient with epilepsy.	MRS is indicated in the imaging protocol of the patient with epilepsy to screen for metabolic derangements such as inborn errors of metabolism and to characterize masses that may be equivocal on conventional MRI for dysplasia vs neoplasia. Single-voxel MRS with an echo time of 35 milliseconds may be used for this purpose as a quick screening tool in the epilepsy imaging protocol. MRS is useful in the evaluation of both focal and generalized epilepsy.	4
12. Jackson GD. New techniques in magnetic resonance and epilepsy. <i>Epilepsia.</i> 1994;35 Suppl 6:S2-13.	Review/Other-Dx	N/A	Review new techniques in MRI and epilepsy.	New MRI techniques show the structure of the brain in fine detail (especially the hippocampus), provide information about the underlying metabolism of brain regions, and demonstrate functional activity of the brain with high spatial and temporal resolution.	4
13. Bogdanoff BM, Stafford CR, Green L, Gonzalez CF. Computerized transaxial tomography in the evaluation of patients with focal epilepsy. <i>Neurology.</i> 1975;25(11):1013-1017.	Review/Other-Dx	50 consecutive unselected patients	To examine the role of CTAT in the evaluation of patients with focal epilepsy.	CTAT is useful in the evaluation and follow-up of patients with focal seizure disorders.	4
14. Gastaut H, Gastaut JL. Computerized transverse axial tomography in epilepsy. <i>Epilepsia.</i> 1976;17(3):325-336.	Review/Other-Dx	401 patients	Report findings with CTAT in patients with epilepsy. Findings on CTAT were correlated with the electroclinical form of epilepsy and with etiology.	CTAT is useful in the evaluation of epilepsy. In 81/401 patients, CTAT revealed a cerebral lesion which had been missed in the other examinations and which had merely been suspected from the history.	4
15. Bergen D, Bleck T, Ramsey R, et al. Magnetic resonance imaging as a sensitive and specific predictor of neoplasms removed for intractable epilepsy. <i>Epilepsia.</i> 1989;30(3):318-321.	Review/Other-Dx	23 patients had MRI and CT	To compare MRI and CT in intractable epilepsy.	11 patients had neoplasm. 6/11 tumors seen on CT. All 11 tumors were detected by MRI. MRI accurate and superior to CT in intractable epilepsy.	4
16. Brooks BS, King DW, el Gammal T, et al. MR imaging in patients with intractable complex partial epileptic seizures. <i>AJNR Am J Neuroradiol.</i> 1990;11(1):93-99.	Observational-Dx	53 patients	To compare neurologic studies, MRI and CT in patients with intractable complex partial seizures who had surgical treatment for epilepsy.	MRI was accurate in the preoperative diagnosis of structural lesions. MRI provided useful information in 28% of patients who underwent surgery for refractory complex partial epilepsy. MRI obviated invasive EEG monitoring in 93% of the patients with structural lesions. MRI was useful in only 8% of the patients with pathologic changes of mesial temporal gliosis.	2

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17. Gerard G, Shabas D, Rossi D. MRI in epilepsy. <i>Comput Radiol.</i> 1987;11(5-6):223-227.	Observational-Dx	267 consecutive patients	Retrospective study in which MRI and CT scans of patients with seizures were compared.	21% (57/267) of the MRI scans were abnormal. The CT scan was normal in 28% of these MRI documented abnormal cases. In an additional 10% of these cases, MRI was more specific than CT scan. CT was more specific in cases of calcification and abscess (7%). MRI is more sensitive than CT in noting central nervous system pathology and lesions of potential therapeutic significance in patients with seizures.	3
18. Heinz ER, Heinz TR, Radtke R, et al. Efficacy of MR vs CT in epilepsy. <i>AJR Am J Roentgenol.</i> 1989;152(2):347-352.	Observational-Dx	59 seizure patients	To compare and determine the efficacy of CT, MRI and EEG in the detection of an epileptogenic focus.	EEG was most sensitive (67%), MRI was next (53%), and CT was least sensitive (42%). In the complex partial seizure subgroup of 34 patients, MRI was positive in 44%, CT was positive in 29%, and EEG was positive in 80%. MRI is considered the imaging procedure of choice for the detection of an epileptogenic focus in seizure patients. When indicated, CT may be performed as a second procedure to try to distinguish neoplasm from thrombosed vascular malformations and other lesions.	3
19. Kilpatrick CJ, Tress BM, O'Donnell C, Rossiter SC, Hopper JL. Magnetic resonance imaging and late-onset epilepsy. <i>Epilepsia.</i> 1991;32(3):358-364.	Observational-Dx	50 patients normal CT scan (32), no definitive diagnosis (12), irrelevant lesions (6)	To prospectively evaluate the value of MRI in patients with late-onset epilepsy in whom a CT scan was normal, did not allow a definitive diagnosis to be made, or showed irrelevant lesions. MRI was compared to CT.	MRI was diagnostic in 32% of the patients with partial seizures and/or focal EEG findings, as compared with 0% of patients without focal features (P<0.01). MRI is useful in investigation of patients with late-onset epilepsy with focal features.	2
20. Maxwell RE, Gates JR, McGeachie R. Magnetic resonance imaging in the assessment and surgical management of epilepsy and functional neurological disorders. <i>Appl Neurophysiol.</i> 1987;50(1-6):369-373.	Review/Other-Dx	40 patients 20 had postoperative MRI scans	To examine utility of MRI, CT, EEG in the surgical management of epilepsy.	MRI superior to CT in pre and post surgical evaluation of epilepsy patients.	4

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21. Cascino GD, Jack CR, Jr., Parisi JE, et al. MRI in the presurgical evaluation of patients with frontal lobe epilepsy and children with temporal lobe epilepsy: pathologic correlation and prognostic importance. <i>Epilepsy Res.</i> 1992;11(1):51-59.	Observational-Dx	2 series of 53 patients	First study – pathologic correlation and prognostic importance of an MRI-identified lesion in the frontal lobe were assessed. Second study – sensitivity and specificity of MRI-based hippocampal volumetry was determined in pediatric patients with partial epilepsy of temporal lobe origin unrelated to foreign-tissue pathology.	First study – 25% of the patients with negative MRI studies and 67% of patients with neuroimaging abnormalities restricted to the frontal lobe, were seizure-free at a minimum duration of follow-up of 1 year. Second study - Hippocampal formation atrophy in the epileptic temporal lobe was identified in 63% of patients. The sensitivity and specificity of hippocampal volumetry was 100% in patients with mesial temporal sclerosis. The presence of an MRI-detected epileptogenic lesion in the frontal lobe and hippocampal formation atrophy in the temporal lobe may correlate with the underlying pathology and affect the identification of potential candidates for epilepsy surgery.	2
22. Cross JH, Jackson GD, Neville BG, et al. Early detection of abnormalities in partial epilepsy using magnetic resonance. <i>Arch Dis Child.</i> 1993;69(1):104-109.	Review/Other-Dx	30 consecutive children	To examine the incidence of brain abnormalities determined by MRI in children presenting with intractable complex partial seizures.	Identification of focal brain abnormalities using optimized MRI enables early noninvasive assessment of children with intractable seizure disorders and the identification of patients for whom epilepsy surgery may be appropriate. It may also lead to a better understanding of the structural basis of intractable epilepsy, and thereby contribute to early treatment decisions.	4
23. Spencer SS. The relative contributions of MRI, SPECT, and PET imaging in epilepsy. <i>Epilepsia.</i> 1994;35 Suppl 6:S72-89.	Review/Other-Dx	N/A	Review roles of MRI, SPECT, and PET imaging in epilepsy.	Functional imaging by PET or SPECT provides complementary information. Ideally these techniques should be used and interpreted together to improve the localization and understanding of epileptic brain.	4
24. Van Paesschen W, Sisodiya S, Connelly A, et al. Quantitative hippocampal MRI and intractable temporal lobe epilepsy. <i>Neurology.</i> 1995;45(12):2233-2240.	Observational-Dx	40 patients had presurgical evaluation and subsequent temporal lobe surgery	To evaluate and compare T2 relaxometry and volumetrics of hippocampus in the presurgical evaluation of patients with intractable TLE and to correlate these quantitative MRI measures with the pathology of the resected hippocampus.	Hippocampal volume asymmetry could be reliably detected on visual inspection of the MRI with an hippocampal volume ratio of 0.85 or less, and an increase of hippocampal T2 with a T2 of 115 msec or higher. Quantitative MRI (volumetric and T2 relaxometry assessment) reliable for detection of hippocampal sclerosis.	2

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25. Wieshmann UC. Clinical application of neuroimaging in epilepsy. <i>J Neurol Neurosurg Psychiatry</i> . 2003;74(4):466-470.	Review/Other-Dx	919 outpatients 528 patients had scan, results not available in 33, 163 had x-ray CT only, 178 had standard MRI, and 154 had high resolution MRI	To examine the use of neuroimaging in clinical practice and to assess the prevalence of detected structural abnormalities in epilepsy patients in a clinical set-up.	Abnormalities detected in more than half of all patients with localization related epilepsy, and in about 1/5 patients with single seizures or epilepsy in remission. Many patients had no scan or only CT or standard MRI. The true prevalence of structural abnormalities may have been higher. Scanning did not add any information in patients with idiopathic generalized epilepsy or nonepileptic attacks.	4
26. Coan AC, Kubota B, Bergo FP, Campos BM, Cendes F. 3T MRI Quantification of Hippocampal Volume and Signal in Mesial Temporal Lobe Epilepsy Improves Detection of Hippocampal Sclerosis. <i>AJNR Am J Neuroradiol</i> . 2013.	Observational-Dx	203 patients	To compare visual analysis, volumetry, and signal quantification of the hippocampus for detecting hippocampal sclerosis in 3T MRI.	Visual analysis classified 125 patients (62%) as having signs of hippocampal sclerosis and 78 (38%) as having normal MRI findings. Automatic volumetry detected atrophy in 119 (95%) patients with visually detected hippocampal sclerosis and in 10 (13%) with visually normal MRI findings. Relaxometry analysis detected hyperintense T2 signal in 103 (82%) patients with visually detected hippocampal sclerosis and in 15 (19%) with visually normal MRI findings. Considered together, volumetry plus relaxometry detected signs of hippocampal sclerosis in all except 1 (99%) patient with visually detected hippocampal sclerosis and in 22 (28%) with visually normal MRI findings.	3

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27. Farid N, Girard HM, Kemmotsu N, et al. Temporal lobe epilepsy: quantitative MR volumetry in detection of hippocampal atrophy. <i>Radiology</i> . 2012;264(2):542-550.	Observational-Dx	34 patients and 116 control subjects	To determine the ability of fully automated volumetric MRI to depict hippocampal atrophy and to help correctly lateralize the seizure focus in patients with TLE.	Quantitative MRI-derived hippocampal asymmetries discriminated patients with TLE from control subjects with high sensitivity (86.7%–89.5%) and specificity (92.2%–94.1%). When a linear classifier was used to discriminate left vs right TLE, hippocampal asymmetry achieved 94% classification accuracy. Volumetric asymmetries of other subcortical structures did not improve classification. Compared with invasive video electroencephalographic recordings, lateralization accuracy was 88% with quantitative MRI and 85% with visual inspection of volumetric MRI studies but only 76% with visual inspection of clinical MRI studies.	2
28. Adams C, Hwang PA, Gilday DL, Armstrong DC, Becker LE, Hoffman HJ. Comparison of SPECT, EEG, CT, MRI, and pathology in partial epilepsy. <i>Pediatr Neurol</i> . 1992;8(2):97-103.	Review/Other-Dx	20 children total: Path site (n=20); Interictal EEG (n=20); Ictal EEG (n=9); CT (n=20); MRI (n=14)	To compare roles of SPECT, EEG, CT, MRI, and pathology in children with partial epilepsy.	SPECT adds evidence useful for localization of seizure foci.	4
29. Jackson GD, Connelly A, Cross JH, Gordon I, Gadian DG. Functional magnetic resonance imaging of focal seizures. <i>Neurology</i> . 1994;44(5):850-856.	Review/Other-Dx	1	To determine whether MRI could map the cortical activation that occurs during focal seizures. Conventional 1.5-T clinical MRI system was used in a 4-year-old boy suffering from frequent partial motor seizures of his right side.	fMRI revealed sequential activation associated with specific gyri within the left hemisphere with each of five consecutive clinical seizures, and also during a period that was not associated with a detectable clinical seizure. fMRI can provide new insights into the dynamic events that occur in the epileptic brain and their relationship to brain structure.	4
30. Kuzniecky R, Elgavish GA, Hetherington HP, Evanochko WT, Pohost GM. In vivo 31P nuclear magnetic resonance spectroscopy of human temporal lobe epilepsy. <i>Neurology</i> . 1992;42(8):1586-1590.	Observational-Dx	12 individuals: 5 healthy volunteers and 7 patients	To examine the use of P nuclear MRS in patients with intractable temporal lobe seizures.	P nuclear MRS yields a distinct interictal metabolic profile in TLE and may allow noninvasive lateralizing evidence of the seizure focus.	3

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31. Warach S, Levin JM, Schomer DL, Holman BL, Edelman RR. Hyperperfusion of ictal seizure focus demonstrated by MR perfusion imaging. <i>AJNR Am J Neuroradiol.</i> 1994;15(5):965-968.	Review/Other-Dx	1	To examine utilization of contrast augmented perfusion activation fMRI in epilepsy evaluation. Comparison with SPECT, EEG.	Activation fMRI potentially useful in epilepsy.	4
32. Chernov MF, Ochiai T, Ono Y, et al. Role of proton magnetic resonance spectroscopy in preoperative evaluation of patients with mesial temporal lobe epilepsy. <i>J Neurol Sci.</i> 2009;285(1-2):212-219.	Observational-Dx	18 patients	To evaluate of the role of single-voxel 1H-MRS in preoperative investigation of patients with mesial temporal lobe epilepsy.	The length of follow-up varied from 24 to 71 months (median, 35 months). Before surgery, 1H-MRS disclosed decrease of N-acetylaspartate content (P=0.01) and more frequent (P=0.07) presence of lactate on the side of the epileptogenic zone. Decrease of N-acetylaspartate content below 0.75 and/or unilateral presence of lactate provided 86% (95% CI, 68%–100%) lateralization accuracy. Metabolic parameters did not differ in subgroups with hippocampal sclerosis and brain tumors. On the long-term follow-up 12 patients (67%) were free of disabling seizures. There was a trend (P=0.05) for worse seizure outcome in cases with significant bilateral metabolic alterations characterized by predominance of choline-containing compounds' peak on 1H-MRS on both sides. In conclusion, 1H-MRS-detected reduction of N-acetylaspartate content and unilateral presence of lactate in the mesial temporal lobe structures may serve as additional diagnostic clues for lateralization of the epileptogenic zone in mesial temporal lobe epilepsy. Metabolic imaging has limited usefulness for differentiation of the hippocampal sclerosis and low-grade intraaxial brain tumor. Presence of significant bilateral metabolic alterations in the mesial temporal lobe structures is associated with worse postoperative seizure control.	3



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33. Krsek P, Hajek M, Dezortova M, et al. (1)H MR spectroscopic imaging in patients with MRI-negative extratemporal epilepsy: correlation with ictal onset zone and histopathology. <i>Eur Radiol.</i> 2007;17(8):2126-2135.	Observational-Dx	7 patients	To verify how 1H-MRS could help in localizing the epileptogenic zone in patients with MRI-negative extratemporal epilepsy.	MRS detected lateralization in all patients and was able to localize pathology in 5. The most frequent findings were decreased ratios of N-acetylaspartate to choline compounds characterized by increasing choline concentration. The localization of the 1H-MRS abnormality correlated well with ictal SPECT and subdural mapping. In all cases, histopathological analysis revealed MRI-undetected focal cortical dysplasias. 1H-MRS could be more sensitive for the detection of discrete malformations of cortical development than conventional MRI. It is valuable in the presurgical evaluation of patients without MRI-apparent lesions.	3
34. Willmann O, Wennberg R, May T, Woermann FG, Pohlmann-Eden B. The contribution of 18F-FDG PET in preoperative epilepsy surgery evaluation for patients with temporal lobe epilepsy A meta-analysis. <i>Seizure.</i> 2007;16(6):509-520.	Review/Other-Dx	46 studies	To assess the predictive diagnostic added value of PET in preoperative epilepsy surgery evaluation for patients with TLE.	The analyses were complicated by significant differences in study design and often by lack of precise patient data. Ipsilateral PET hypometabolism showed a predictive value of 86% for good outcome. The predictive value was 80% in patients with normal MRI and 72% in patients with nonlocalized ictal scalp EEG. In a selected population of 153 TLE patients with a follow-up of >12 months PET correlated well with other noninvasive diagnostic tests, but none of the odds ratios of any test combination was significant.	4
35. Siegel A, Lewis P, Siegel AM. The value of interictal brain SPECT in epilepsy patients without mesial-temporal sclerosis. <i>Clin Nucl Med.</i> 2002;27(10):716-720.	Review/Other-Dx	84 patients evaluated with 95 interictal SPECT scans and MRI	To determine the utility of interictal SPECT in patients with neocortical epilepsy.	54% of studies with normal MRI findings had SPECT images without regions of hypoperfusion. 61% of patients with abnormal MRI results had matching defects visible on SPECT images. 14 scans (only 24%) had focal hypoperfusion by SPECT and no obvious matching MRI finding. Interictal SPECT, without a comparison ictal study, is of potentially limited value in localizing neocortical seizure foci. SPECT findings usually match MRI findings.	4

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36. So EL, O'Brien TJ, Brinkmann BH, Mullan BP. The EEG evaluation of single photon emission computed tomography abnormalities in epilepsy. <i>J Clin Neurophysiol.</i> 2000;17(1):10-28.	Review/Other-Dx	N/A	To review the current role of SPECT in the evaluation of patients for epilepsy surgery, especially as it relates to other clinical and laboratory data used in presurgical evaluation.	Techniques such as SISCOM and computer image-guided surgery have great potential in enhancing the clinical electrophysiologic evaluation of SPECT-detected abnormalities in epilepsy. These techniques permit accurate spatial correlation between ICEEG activity and SPECT perfusion patterns. Need both animal and human studies to advance knowledge of the electrophysiology associated with the various SPECT perfusion patterns.	4
37. Desai A, Bekelis K, Thadani VM, et al. Interictal PET and ictal subtraction SPECT: sensitivity in the detection of seizure foci in patients with medically intractable epilepsy. <i>Epilepsia.</i> 2013;54(2):341-350.	Observational-Dx	53 patients	To determine the relative utility of interictal PET and ictal subtraction SPECT in the localization of seizure foci, the authors compared interictal PET and ictal subtraction SPECT to subdural and depth electrode recordings in patients with medically intractable epilepsy.	53 patients underwent ICEEG monitoring with preoperative interictal PET and ictal subtraction SPECT scans. The average patient age was 32.7 years (median 32 years, range 1-60 years). 27 patients had findings of reduced metabolism on interictal PET scan, whereas all 53 patients studied demonstrated a region of relative hyperperfusion on ictal subtraction SPECT suggestive of an epileptogenic zone. ICEEG monitoring identified a single seizure focus in 45 patients, with 39 eventually undergoing resective surgery. Of the 45 patients in whom a seizure focus was localized, PET scan identified the same region in 25 cases (56% sensitivity) and SPECT in 39 cases (87% sensitivity). ICEEG was concordant with at least one study in 41 cases (91%) and both studies in 23 cases (51%). In 16 (80%) of 20 cases where PET did not correlate with ICEEG, the SPECT study was concordant. Conversely, PET and ICEEG were concordant in 2 (33%) of the 6 cases where the SPECT did not demonstrate the seizure focus outlined by ICEEG. 33 patients had surgical resection and >2 years of follow-up, and 21 of these (64%) had Engel class 1 outcome. No significant effect of imaging concordance on seizure outcome was seen.	3

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38. Avery RA, Zubal IG, Stokking R, et al. Decreased cerebral blood flow during seizures with ictal SPECT injections. <i>Epilepsy Res.</i> 2000;40(1):53-61.	Review/Other-Dx	21 patients had ictal and interictal HMPAO SPECT scans	To determine whether ictal SPECT injections demonstrate a similar change in regional cerebral blood flow around 100 s from seizure onset.	By examining ictal SPECT injections made 90 s after seizure onset, evidence was found that reduced regional cerebral blood flow may exist during ictus. Change in regional cerebral blood flow around 90 s is also observed in postictal injections, suggesting a common metabolic mechanism may be responsible.	4
39. Medina LS, Bernal B, Dunoyer C, et al. Seizure disorders: functional MR imaging for diagnostic evaluation and surgical treatment--prospective study. <i>Radiology.</i> 2005;236(1):247-253.	Observational-Dx	60 patients	To prospectively evaluate effect of fMRI on diagnostic workup and treatment planning in patients with seizure disorders who are candidates for surgical treatment.	In 53 patients, language mapping was performed; in 33, motor mapping; and in 7, visual mapping. The study revealed change in anatomic location or lateralization of language-receptive (Wernicke) (28% of patients) and language-expressive (Broca) (21% of patients) areas. Statistically significant increases were found in confidence levels after fMRI in regard to motor and visual cortical function evaluation. In 35 (58%) of 60 patients, the seizure team thought that fMRI results altered patient and family counseling. In 38 (63%) of 60 patients, fMRI results helped to avoid further studies, including Wada test. In 31 (52%) and 25 (42%) of 60 patients, intraoperative mapping and surgical plans, respectively, were altered because of fMRI results. In 5 (8%) patients, two-stage surgery with extra-operative direct electrical stimulation mapping was averted, and resection was accomplished in one stage. In 4 (7%) patients, extent of surgical resection was altered because eloquent areas were identified close to seizure focus.	4
40. Lau M, Yam D, Burneo JG. A systematic review on MEG and its use in the presurgical evaluation of localization-related epilepsy. <i>Epilepsy Res.</i> 2008;79(2-3):97-104.	Review/Other-Dx	17 articles analyzed 3 reviewers	Systematic review to determine the effectiveness of MEG in the presurgical evaluation of localization-related epilepsies.	Sensitivity (range: 0.20-1.0) values for all articles, and specificity (0.06-1.00) values, positive likelihood ratios (0.67-2.0) and negative likelihood ratios (0.40-2.13) for some articles. There is insufficient evidence in the current literature to support the relationship between the use of MEG in surgical planning and seizure-free outcome after epilepsy surgery. Additional studies needed.	4

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41. Sutherling WW, Mamelak AN, Thyerlei D, et al. Influence of magnetic source imaging for planning intracranial EEG in epilepsy. <i>Neurology</i> . 2008;71(13):990-996.	Review/Other-Dx	69 patients	Prospective, blinded, crossover-controlled, single-treatment, observational case series to determine the influence of MSI for planning ICEEG in epilepsy.	MSI provided nonredundant information in 33% of patients. In those who have undergone surgery to date, MSI added useful information that changed treatment in 6 (9%), without increasing complications. MSI has benefited 21% who have gone to surgery.	4
42. Knowlton RC. Can magnetoencephalography aid epilepsy surgery? <i>Epilepsy Curr</i> . 2008;8(1):1-5.	Review/Other-Dx	N/A	Review article to determine whether MEG can help in epilepsy surgery.	Evidence exist to support the current use of MEG spike source localization in any patient for whom the question of seizure localization remains after EEG with video recording of habitual seizures and for whom strong clinical suspicion continues for unifocal epilepsy that may be treated surgically.	4
43. Knowlton RC, Elgavish RA, Bartolucci A, et al. Functional imaging: II. Prediction of epilepsy surgery outcome. <i>Ann Neurol</i> . 2008;64(1):35-41.	Observational-Dx	160 patients enrolled; 62 completed ICEEG and subsequent surgical resection	To gain information on the value of MSI, FDG-PET, and ictal SPECT to predict seizure-free outcome following epilepsy surgery in patients who require ICEEG.	MSI sensitivity for a conclusively localized study was 55% with PPV of 78%. Eliminating nondiagnostic MSI cases (no spikes captured during recording) yielded a corrected NPV of 64%. The OR (adjusted for epilepsy and MRI classification) for MSI prediction of seizure-free outcome was 4.4 (P=0.01). In cases with both PET and MSI, the adjusted OR for PET was 7.1 (P<0.01) and for MSI was 6.4 (P=0.01). In the cases with all three tests (n = 27), ictal SPECT had the highest OR of 9.1 (P=0.05). MSI, FDG-PET, and ictal SPECT each have clinical value in predicting seizure-free surgical outcome in epilepsy surgery candidates who typically require ICEEG.	3

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44. Knowlton RC, Elgavish RA, Limdi N, et al. Functional imaging: I. Relative predictive value of intracranial electroencephalography. <i>Ann Neurol</i> . 2008;64(1):25-34.	Observational-Dx	160 patients enrolled; 77 completed ICEEG seizure monitoring	To gain information on the predictive and prognostic value of MSI, FDG-PET, and ictal SPECT as compared with ICEEG localization in epilepsy surgery.	Of 72 diagnostic ICEEG studies, seizure localization results were 74% localized, 10% multifocal, and 17% nonlocalized. Depending on patient subgroup pairs, sensitivity ranged from 58%–64% (MSI), 22%–40% (PET), and 39%–48% (SPECT); specificity ranges were 79%–88% (MSI), 53%–63% (PET), and 44%–50% (SPECT). Gains in diagnostic yield were seen only with the combination of MSI and PET or MSI and ictal SPECT. Localization concordance with ICEEG was greatest with MSI, but a significant difference was demonstrated only between MSI and PET. Moderate redundancy was seen between PET and ictal SPECT (kappa = 0.452; P=0.011). Conclusively positive MSI has a high predictive value for seizures localized with ICEEG.	3
45. Knowlton RC, Razdan SN, Limdi N, et al. Effect of epilepsy magnetic source imaging on intracranial electrode placement. <i>Ann Neurol</i> . 2009;65(6):716-723.	Observational-Dx	160 patients enrolled, 77 had ICEEG recordings	Prospective observational study to determine whether MSI can supplement ICEEG electrode implantation such that epilepsy localization yield, and ultimately surgical decision-making, may be improved.	MSI indicated additional electrode coverage in 18/77 (23%) ICEEG cases. In 39% (95% CI, 16.4-61.4), seizure-onset ICEEG patterns involved the additional electrodes indicated by MSI. 62 patients underwent surgical resection based on ICEEG recording of seizures. Highly localized MSI was significantly associated with seizure-free outcome (mean, 3.4 years; minimum, >1 year) for the entire surgical population (n = 62).	3

**Seizures and Epilepsy  
EVIDENCE TABLE**

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
46. Harden CL, Huff JS, Schwartz TH, et al. Reassessment: neuroimaging in the emergency patient presenting with seizure (an evidence-based review): report of the Therapeutics and Technology Assessment Subcommittee of the American Academy of Neurology. <i>Neurology</i> . 2007;69(18):1772-1780.	Review/Other-Dx	15 articles	To reassess the value of neuroimaging of the emergency patient presenting with seizure as a screening procedure for providing information that will change acute management, and to reassess clinical and historical features associated with an abnormal neuroimaging study in these patients.	The 15 articles meeting criteria were Class II or III evidence since interpretation was not masked to the patient's clinical presentation; most were series including 22 to 875 patients. There is evidence that for adults with first seizure, cranial CT will change acute management in 9%–17% of patients. CT in the emergency department for children presenting with first seizure will change acute management in approximately 3%–8%. There is no clear difference between rates of abnormal emergent CT for patients with chronic seizures vs first. Children <6 months presenting with seizures have clinically relevant abnormalities on CT scans 50% of the time. Persons with AIDS and first seizure have high rates of abnormalities, and central nervous system toxoplasmosis is frequently found. Abnormal neurologic examination, predisposing history, or focal seizure onset are probably predictive of an abnormal CT study in this context.	4
47. Jagoda A, Gupta K. The emergency department evaluation of the adult patient who presents with a first-time seizure. <i>Emerg Med Clin North Am</i> . 2011;29(1):41-49.	Review/Other-Dx	N/A	A review on the emergency department evaluation of the adult patient who presents with a first-time seizure.	In the evaluation of a first seizure, determination of serum glucose and electrolytes is recommended, as is a pregnancy test in women of child-bearing age. A head CT should be obtained in the emergency department whenever feasible, but when reliable follow-up is available, it is acceptable to discharge the stable patient with no comorbidities for deferred outpatient evaluation.	4

**Seizures and Epilepsy  
EVIDENCE TABLE**

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
48. Krumholz A, Wiebe S, Gronseth G, et al. Practice Parameter: evaluating an apparent unprovoked first seizure in adults (an evidence-based review): report of the Quality Standards Subcommittee of the American Academy of Neurology and the American Epilepsy Society. <i>Neurology</i> . 2007;69(21):1996-2007.	Review/Other-Dx	N/A	Practice parameter developed Quality Standards Subcommittee of the American Academy of Neurology and the American Epilepsy Society. The authors reviewed available evidence relevant to evaluating adults presenting with an apparent unprovoked first seizure.	For adults presenting with a first seizure, a routine EEG revealed epileptiform abnormalities in approximately 23% of patients, and these were predictive of seizure recurrence. A brain imaging study (CT or MRI) was significantly abnormal in 10% of patients, indicating a possible seizure etiology. Laboratory tests such as blood counts, blood glucose, and electrolyte panels were abnormal in up to 15% of individuals, but abnormalities were minor and did not cause the seizure. Overt clinical signs of infection such as fever typically predicted significant CSF abnormalities on lumbar puncture. Toxicology screening studies were limited, but report some positive tests.	4
49. Clinical policy: Critical issues in the evaluation and management of adult patients presenting to the emergency department with seizures. <i>Ann Emerg Med</i> . 2004;43(5):605-625.	Review/Other-Dx	N/A	Guidelines document to address critical issues in the evaluation and management of adult patients with seizures.	N/A	4
50. Earnest MP, Feldman H, Marx JA, Harris JA, Bilech M, Sullivan LP. Intracranial lesions shown by CT scans in 259 cases of first alcohol-related seizures. <i>Neurology</i> . 1988;38(10):1561-1565.	Observational-Dx	259 patients	To evaluate CTs in patients with a first alcohol-related convulsion.	16 patients (6.2%) had intracranial lesions on CT. 8 had subdural hematomas or hygromas, 2 had vascular malformations, 2 had neurocysticercosis, and 1 each showed a Berry aneurysm, possible tumor, skull fracture with subarachnoid hemorrhage, and probable cerebral infarction. In 10 cases (3.9%), clinical management was altered because of the CT result. History or signs of minor head trauma, headache, level of consciousness, or focal neurologic signs did not significantly correlate with CT abnormality.	3
51. Mower WR, Biros MH, Talan DA, Moran GJ, Ong S. Selective tomographic imaging of patients with new-onset seizure disorders. <i>Acad Emerg Med</i> . 2002;9(1):43-47.	Observational-Dx	875 patients	To determine whether a reliable decision rule could be developed using a limited number of clinical and demographic characteristics.	A decision rule using age ≥65 years, lateralizing neurologic findings, altered mentation, high risk or known HIV infection, history of cysticercosis, and Hispanic ethnicity showed a sensitivity of 91.9% [95% CI, 88.8%–94.9%] in detecting individuals who had any tomographic finding. This rule had a sensitivity of 90.1% (95% CI, 83.4%–96.7%) in detecting individuals with emergent tomographic findings.	3

\* See Last Page for Key

**Seizures and Epilepsy  
EVIDENCE TABLE**

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
52. Schoenenberger RA, Heim SM. Indication for computed tomography of the brain in patients with first uncomplicated generalised seizure. <i>BMJ</i> . 1994;309(6960):986-989.	Observational-Dx	119 patients	To assess the yield of emergency CT of the brain in patients with a first generalized epileptic seizure and to evaluate a 4 item screening questionnaire on alcohol misuse (CAGE questionnaire) as a triage tool to avoid unnecessary scans in cases of seizures related to withdrawal from alcohol.	CT showed a focal, structural lesion of the brain in 40 patients (34% (95% CI, 25%–42%)). In 20 patients (17% (10%–24%)) an important therapeutic intervention resulted. The presence of a focal neurological deficit had a sensitivity of 50% and a specificity of 89% in predicting focal lesions on CT. Answering "yes" to fewer than two CAGE questions had a sensitivity of 90% and specificity of 44% in identifying patients with focal CT lesions. Focal lesions were not detected on CT in any of the 35 patients (0% (0%–10%)) who showed no focal neurological symptoms and answered "yes" to two or more CAGE questions.	3
53. Sempere AP, Villaverde FJ, Martinez-Menendez B, Cabeza C, Pena P, Tejerina JA. First seizure in adults: a prospective study from the emergency department. <i>Acta Neurol Scand</i> . 1992;86(2):134-138.	Observational-Dx	98 patients	To prospectively study adults with a first seizure to determine the most important etiological factors and the optimum diagnostics.	27 were thought to have cryptogenic seizures. Main causes of symptomatic seizures were: cerebral infarction, alcohol-withdrawal, central nervous system infections, tumors, vascular malformations, traumatism and miscellanea. 8 were infected by HIV-1 representing 8.2% of all the patients with a first seizure and 20% of the 15-45-year age group. CT disclosed structural lesions in 33 cases. MRI in those with normal CT and no other explanation of seizure revealed additional lesions in 22.2%, but did not change management in any.	3



**Seizures and Epilepsy  
EVIDENCE TABLE**

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
54. King MA, Newton MR, Jackson GD, et al. Epileptology of the first-seizure presentation: a clinical, electroencephalographic, and magnetic resonance imaging study of 300 consecutive patients. <i>Lancet</i> . 1998;352(9133):1007-1011.	Observational-Dx	300 consecutive adults and children	To determine whether it is possible to diagnose specific epilepsy syndromes promptly by use of standard clinical methods, EEG and MRI.	A generalized or partial epilepsy syndrome was clinically diagnosed in 141 (47%) patients. Subsequent analysis showed that only 3 of these clinical diagnoses were incorrect. Addition of the EEG data enabled authors to diagnose an epilepsy syndrome in 232 (77%) patients. EEG within 24 hours was more useful in diagnosis of epileptiform abnormalities than later EEG (51% vs 34%). Neuroimaging showed 38 epileptogenic lesions, including 17 tumors. There were no lesions in patients for whom generalized epilepsy was confirmed by EEG. Final diagnoses were: generalized epilepsy (23% of patients); partial epilepsy (58%); and unclassified (19%).	2
55. Pugh MJ, Berlowitz DR, Montouris G, et al. What constitutes high quality of care for adults with epilepsy? <i>Neurology</i> . 2007;69(21):2020-2027.	Review/Other-Dx	N/A	To describe the development of quality indicators for evaluating care of adults with epilepsy.	From the original 37 evidence-based and 10 patient-based quality indicators, the panel identified 24 evidence-based and 5 patient-based indicators as appropriate indicators of quality. Of these, the panel identified 9 that were not necessary for high quality care. There is, at best, a poor understanding of the quality of care provided for adults with epilepsy. These indicators, developed based on published evidence, expert opinion, and patient perceptions, provide a basis to assess and improve the quality of care for this population.	4

**Seizures and Epilepsy  
EVIDENCE TABLE**

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
56. Hauser WA, Annegers JF, Kurland LT. Incidence of epilepsy and unprovoked seizures in Rochester, Minnesota: 1935-1984. <i>Epilepsia</i> . 1993;34(3):453-468.	Review/Other-Dx	N/A	To determine the incidence of epilepsy and of all unprovoked seizures for residents of Rochester, Minnesota U.S.A. from 1935 through 1984.	Age-adjusted incidence of epilepsy was 44 per 100,000 person-years. Incidence in males was significantly higher than in females and was high in the first year of life but highest in persons aged $\geq 75$ years. 60% of new cases had epilepsy manifested by partial seizures, and two thirds had no clearly identified antecedent. Cerebrovascular disease was the most commonly identified antecedent, accounting for 11% of cases. Neurologic deficits from birth, mental retardation and/or cerebral palsy, observed in 8% of cases, was the next most frequently identified preexisting condition. The cumulative incidence of epilepsy through age 74 years was 3.1%. The age-adjusted incidence of all unprovoked seizures was 61 per 100,000 person-years. Age- and gender-specific incidence trends were similar to those of epilepsy, but a higher proportion of cases was of unknown etiology and was characterized by generalized onset seizures. The cumulative incidence of all unprovoked seizures was 4.1% through age 74 years.	4

**Seizures and Epilepsy  
EVIDENCE TABLE**

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
57. Lee ST, Lui TN. Early seizures after mild closed head injury. <i>J Neurosurg.</i> 1992;76(3):435-439.	Review/Other-Dx	4,232 patients	To review seizure incidence in adult patients with mild closed head injury who did not receive prophylactic anticonvulsant agents.	No definite intracranial pathological findings were detected by CT in 53% of patients with early posttraumatic seizures; 6 patients had intracranial hemorrhage without intracranial parenchymal damage (3 with epidural hematoma and 3 with subarachnoid hemorrhage). The most common positive CT findings in the early post-traumatic-seizure group were intracerebral hemorrhage (24%), followed by acute subdural hematoma with intracerebral hemorrhage (17%). Intracerebral parenchymal damage could be identified on CT scans in 41 (48.8%) of 84 patients with generalized tonic-clonic seizures and 5 (31%) of 16 patients with partial seizures with motor symptoms. The intracerebral parenchymal damage was most commonly detected in the frontal lobe (21%) and the temporal lobe (19%). 7 patients with early post-traumatic seizures received emergency craniotomy to remove an intracranial hematoma (epidural in 3, subdural and intracerebral in 4) because the mass effect resulted in significant midline shift as seen on CT scans.	4
58. Bellamy JL, Molendijk J, Reddy SK, et al. Severe infectious complications following frontal sinus fracture: the impact of operative delay and perioperative antibiotic use. <i>Plast Reconstr Surg.</i> 2013;132(1):154-162.	Review/Other-Dx	242 consecutive patients	To investigate whether a delay in operative management of frontal sinus fractures is associated with increased risk of serious infections.	There were 14 serious infections (5.8 percent). All patients with serious infections had both involvement of the posterior table and nasofrontal outflow tract injury. The cumulative incidence of serious infection in these patients was 10.8%. After adjustments for confounding, multivariable regression showed that operative delay beyond 48 hours was independently associated with a 4.03-fold (P<0.05) increased risk for serious infection; external cerebrospinal fluid drainage catheter use and local soft-tissue infection conferred a 4.09-fold (P<0.05) and 5.10-fold (P<0.001) increased risk, respectively. Antibiotic use beyond 48 hours postoperatively was not associated with fewer infections.	4

**Seizures and Epilepsy  
EVIDENCE TABLE**

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
59. Messori A, Polonara G, Carle F, Gesuita R, Salvolini U. Predicting posttraumatic epilepsy with MRI: prospective longitudinal morphologic study in adults. <i>Epilepsia</i> . 2005;46(9):1472-1481.	Observational-Dx	135 patients	To evaluate morphologic risk factors for post-traumatic epilepsy by using brain MRI in serial assessments $\leq 2$ years after TBI.	In 20 patients, post-traumatic epilepsy developed. Kaplan-Meier curves showed that gliomesenchymal sequelae of focal brain lesions (subdural hematomas/contusions) that required surgical treatment were a post-traumatic epilepsy risk factor ( $P < 0.001$ ), as were sequelae of nonsurgical hemorrhagic contusions with gliosis wall incompletely surrounding hemosiderin degress ( $P = 0.039$ ) and mainly those with time-related changes from incomplete to complete gliosis wall around hemosiderin ( $P = 0.005$ ); those with early hemosiderin completely surrounded by gliosis were not ( $P = 0.821$ ). Cox regression analysis showed that for patients with sequelae of subdural hematomas/contusions, the post-traumatic epilepsy risk was 4.38 ( $P = 0.023$ ) times higher than for those who did not require surgical treatment or underwent surgery because of purely extradural hematoma; for those with hemosiderin degress and incomplete to complete gliosis wall lesions, considered pooled, it was 6.61 times higher ( $P = 0.014$ ) than for those with completely surrounded lesions.	3
60. Gupta RK, Saksena S, Agarwal A, et al. Diffusion tensor imaging in late posttraumatic epilepsy. <i>Epilepsia</i> . 2005;46(9):1465-1471.	Observational-Dx	23 patients and 11 controls	To use diffusion tensor imaging to search and quantify the extent of abnormality beyond the obvious lesions seen on the T2 and fluid-attenuation inversion recovery MRIs in patients with chronic TBI with and without epilepsy.	The mean regional fractional anisotropy ratio was significantly lower, whereas the mean regional mean diffusivity value was higher in patients with TBI compared with controls. The mean regional fractional anisotropy ratio was significantly lower in TBI patients with epilepsy ( $0.57 \pm 0.059$ ) than in those without epilepsy ( $0.68 \pm 0.039$ ). Although the regional mean diffusivity ratio was higher in TBI patients with epilepsy ( $1.15 \pm 0.140$ ) relative to those without epilepsy ( $1.09 \pm 0.141$ ), the difference did not reach statistical significance. The tissue volume with low FA value also was found to be higher in TBI patients with epilepsy than without.	3

## Evidence Table Key

### Study Quality Category Definitions

- *Category 1* The study is well-designed and accounts for common biases.
- *Category 2* The study is moderately well-designed and accounts for most common biases.
- *Category 3* There are important study design limitations.
- *Category 4* The study is not useful as primary evidence. The article may not be a clinical study or the study design is invalid, or conclusions are based on expert consensus. For example:
  - a) the study does not meet the criteria for or is not a hypothesis-based clinical study (e.g., a book chapter or case report or case series description);
  - b) the study may synthesize and draw conclusions about several studies such as a literature review article or book chapter but is not primary evidence;
  - c) the study is an expert opinion or consensus document.

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Dx = Diagnostic

Tx = Treatment

## Abbreviations Key

1H-MRS = Proton magnetic resonance spectroscopy

CI = Confidence interval

CT = Computed tomography

CTAT = Computerized transverse axial tomography

EEG = Electroencephalography

FDG-PET = Fluorine-18-2-fluoro-2-deoxy-D-glucose-positron emission tomography

fMRI = Functional magnetic resonance imaging

HMPAO = 99mTc-Hexamethyl-propyleneamineoxime

ICEEG = Intracranial electroencephalography

MEG = Magnetoencephalography

MRI = Magnetic resonance imaging

MRS = Magnetic resonance spectroscopy

MRSI = Magnetic resonance spectroscopic imaging

MSI = Magnetic source imaging

NPV = Negative predictive value

PET = Positron emission tomography

PPV = Positive predictive value

RR = Relative risk

SISCOM = subtraction ictal single photon emission computed tomography co-registered to magnetic resonance imaging

SPECT = Single photon emission computed tomography

TBI = Traumatic brain injury

TLE = Temporal lobe epilepsy