



Title	Neuroimaging techniques in epilepsy
Author(s)	Lai, V; Mak, HKF; Yung, AWY; Ho, WY; Hung, KN
Citation	Hong Kong Medical Journal, 2010, v. 16 n. 4, p. 292-298
Issued Date	2010
URL	http://hdl.handle.net/10722/129148
Rights	Hong Kong Medical Journal. Copyright © Hong Kong Academy of medicine press.

Vincent Lai 黎永信
Henry KF Mak 麥嘉豐
Ada WY Yung 楊穎欣
WY Ho 何偉然
KN Hung 洪君毅

Objective	To review state-of-the-art neuroimaging modalities in epilepsy and their clinical applications.
Data sources and study selection	PubMed literature searches to March 2010, using the following key words: 'epilepsy'; 'positron emission tomography (PET)'; 'single photon emission computed tomography (SPECT)'; 'MR volumetry'; 'diffusion tensor imaging'; and 'functional MR imaging'.
Data extraction	All articles including neuroimaging techniques in epilepsy were included in the review.
Data synthesis	High-field magnetic resonance imaging is fundamental for high-resolution structural imaging. Functional radionuclide imaging (positron emission tomography/single-photon emission computed tomography) can provide additional information to improve overall accuracy, and show good results with high concordance rates in temporal lobe epilepsy. Magnetic resonance spectroscopy is a useful adjunct consistently demonstrating changing metabolites in the epileptogenic region. Magnetic resonance volumetric imaging shows excellent sensitivity and specificity for temporal lobe epilepsy but thus far it has been inconsistent for extratemporal epilepsy. Diffusion tensor imaging with tractography allows visualisation of specific tracts such as connections with the language and visual cortex to enhance preoperative evaluation. Functional magnetic resonance imaging using blood oxygen level-dependent activation techniques is mainly used in presurgical planning for the high-sensitivity mapping of the eloquent cortex. Both contrast-bolus and arterial spin labelling magnetic resonance perfusion imaging show good correlation with clinical lateralisation of seizure disorder.
Conclusion	Structural imaging is essential in localisation and lateralisation of the seizure focus. Functional radionuclide imaging or advanced magnetic resonance imaging techniques can provide complementary information when an epileptogenic substrate is not identified or in the presence of non-concordant clinical and structural findings.

Key words

Fluorodeoxyglucose F18; Magnetic resonance imaging; Magnetic resonance spectroscopy; Positron-emission tomography; Tomography, emission-computed, single-photon

Hong Kong Med J 2010;16:292-8

Department of Radiology, Tuen Mun Hospital, Hong Kong

V Lai, FHKCR, FHKAM (Radiology)

Department of Diagnostic Radiology, The University of Hong Kong, Hong Kong

HKF Mak, FHKCR, FHKAM (Radiology)

Queen Mary Hospital, Hong Kong:

Department of Paediatrics and Adolescent Medicine

AWY Yung, FHKCPaed, FHKAM (Paediatrics)

Department of Radiology

WY Ho, FHKCR, FHKAM (Radiology)

Department of Neurosurgery

KN Hung, FCSHK, FHKAM (Surgery)

Correspondence to: Dr V Lai, Dr HKF Mak

Emails: vincentlai@hkcr.org,

makkf@hkucc.hku.hk

Introduction

Epilepsy is a common disorder worldwide, with a prevalence of 4.5/1000 (0.45%) for children and adolescents,¹ and 1.54/1000 (0.15%) for the adult Chinese population in Hong Kong.² It has been estimated that about 7 to 8% of the population experience at least one seizure during their lifetime. Epilepsy is characterised by recurrent seizures unprovoked by an acute systemic or neurologic insult.

Prior to possible surgical cure, neuroimaging becomes important and mandatory in the work-up of epilepsy localisation and the lateralisation of seizure foci. Magnetic resonance (MR) imaging has become the technique of choice and is fundamental for high-resolution structural imaging in epilepsy. This is due to its ability to achieve superior soft tissue contrast, multiplanar imaging capability, and lack of beam-hardening artifacts, which allows visualisation of epileptogenic substrates with greater sensitivity and accuracy. Optimised and dedicated protocols are necessary for evaluation of the hippocampus and temporal lobe for atrophy and subtle signal intensity alterations, as well as for detecting certain structural abnormalities such as cortical dysplasias (Fig 1) or other developmental abnormalities. With the development of MR imaging, it has become more sensitive with

high-field technology, newer hardware, as well as special acquisition and post-processing methods. Yet, up to 15% of patients with epilepsy can still escape detection of any structural lesion. In addition, the structural lesions detected on structural MR images may not reflect the true extent and functional status of the abnormalities, especially with respect to malformations of cortical development.³ Therefore, other neuroimaging techniques become useful and can provide additional information on the location of the seizure focus so as to improve overall accuracy. This is important to achieving a successful and ideally seizure-free surgical outcome. In this article, we review and discuss the feasibility of various other neuroimaging techniques.

Methods

A PubMed search of literatures up to March 2010 was conducted using the following key words: 'epilepsy', 'positron emission tomography (PET)', 'single photon emission computed tomography (SPECT)', 'MR volumetry', 'diffusion tensor imaging', and 'functional MR imaging'. A total of 86 articles were retrieved. Only those concerning neuroimaging techniques related to epilepsy published in or after 1995 were included. During article selection, prospective studies had a higher ranking than retrospective studies, while case reports were not included. For articles on the same or related topics, those published at later or more recent dates were selected. In all, 52 articles were included and formed the basis of our review.

癲癇的神經影像技術

目的 探討診斷癲癇最高技術水平的神經影像技術及其臨床應用。

資料來源及研究選取 使用以下關鍵詞搜索至2010年3月於PubMed發表的文獻：「癲癇」、「正子斷層掃描 (PET)」、「單光子發射斷層成像 (SPECT)」、「MR容積術」、「張力擴散磁共振造影」、和「MR功能成像」。

資料選取 所有關於癲癇的神經影像技術都被納入研究範圍。

資料綜合 高磁場磁共振造影是高解像結構成像的基礎。放射性核素功能顯像 (PET/SPECT) 可提供額外資料以增加準確度，它與顳葉癲癇的一致性也非常高。磁共振光譜分析能穩定顯示癲癇源頭代謝物的變化，是一種有用的輔助方法。磁共振容積成像在顳葉癲癇方面有相當高敏感性和特異性，但至今在顳葉外癲癇的診斷並未達一致性。結合纖維追蹤技術張力擴散磁共振造影可以視化如與語言和視覺皮質聯繫的路徑，有助加強術前評估。利用血氧水平依賴性活化技術的磁共振功能成像主要用作腦功能區皮質高感成像的術前準備。顯影劑和動脈自旋標記技術在磁共振灌注成像方面與癲癇在臨床定邊方面高度相關。

結論 結構成像對於癲癇發作的定位及定邊很重要。如果未能確定癲癇發生的源頭或臨床及結構資料沒有協同性，放射性核素功能顯像或先進的磁共振影像技術都可以提供有用的資料。

Functional radionuclide imaging

Positron emission tomography and PET-computed

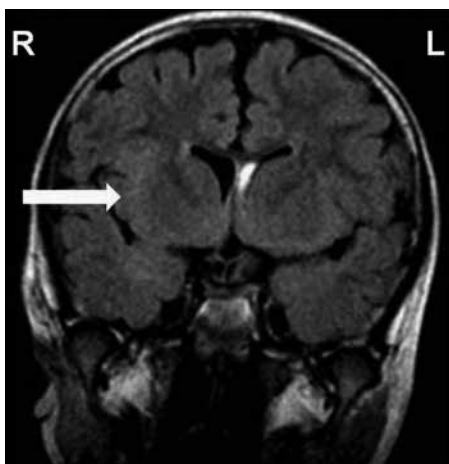


FIG 1. Focal cortical dysplasia in a 5-year-old girl
Non-contrast coronal T2-weighted fluid-attenuated inversion recovery magnetic resonance image of the brain reveals right frontal/insular cortical thickening (arrow)

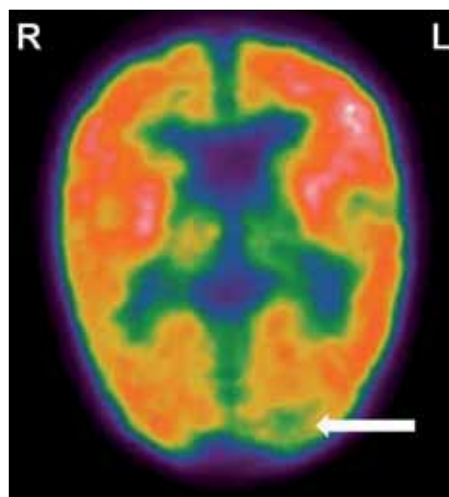


FIG 2. Temporo-parieto-occipital syndrome or posterior quadratic dysplasia or hemihemimegalencephaly in a 3-month-old boy
Interictal positron emission tomography-computed tomography axial image shows hypoperfusion (arrow) in the cortical and subcortical areas of the left occipital lobe and adjacent left posterior parietal lobe, which is highly suggestive of the epileptogenic focus

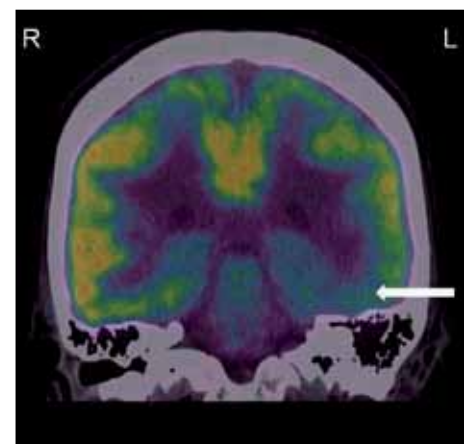


FIG 3. Magnetic resonance image-negative temporal lobe epilepsy in a 17-year-old male
Interictal positron emission tomography coronal image shows hypoperfusion in the left mesial temporal region (arrow)

tomography make use of glucose metabolism (^{18}F -fluorodeoxyglucose [^{18}F -FDG]) for imaging of cerebral metabolism. An epileptogenic focus will typically manifest as an area of hypometabolism on interictal scans (Figs 2 and 3) and an area of hypermetabolism on ictal scans. Its unique ability to image cerebral metabolism is virtually limited to the interictal state due to the long uptake time for the radiotracer (cerebral uptake occurs over 40 minutes after injection).⁴ Ictal scans can occasionally be performed in cases with long duration of epilepsy, refractory epilepsy, or status epilepticus but are of limited clinical use.

Single-photon emission computed tomography is complementary in defining an epileptogenic zone. It entails use of $^{99\text{m}}\text{Tc}$ -HMPAO (technetium-99m hexamethylpropylene amine oxime) or $^{99\text{m}}\text{Tc}$ -ECD (technetium-99m-ethyl cysteinate diethylester) as substrate to assess regional cerebral blood flow changes during both the ictal and interictal periods. The epileptogenic focus will typically manifest as area of hypoperfusion in the interictal stage, and hyperperfusion in the ictal stage (Fig 4). Ictal SPECT has a higher rate of correct localisation⁵ but often proves difficult, as the agent has to be injected within 90 seconds of seizure onset to demonstrate the expected localised increase in cerebral perfusion.

Past studies in temporal lobe epilepsy have shown that the correct localisation rates of MR imaging, interictal PET and ictal SPECT were 64%, 87%, and 81%, respectively. Corresponding rates in non-temporal lobe epilepsy were 57%, 71%, and 64%, respectively.⁶ A more recently reported study by Kim et al⁷ revealed the correct localisation rates of MR imaging, interictal PET, and ictal SPECT were 83%, 73%, and 67%, respectively for temporal lobe epilepsy. Whilst for non-temporal lobe epilepsy, the respective rates were 84%, 68%, and 85%. The discrepancy in results illustrates the difficulty in detecting epileptogenic foci, especially in non-temporal lobe/neocortical group. Nevertheless, for interictal PET and ictal SPECT for temporal lesions, concordance rates are remarkably high (96% and 100%, respectively) and for extratemporal lesions respective rates were 68% and 92%.⁷ This finding supports their complementary usefulness in instances of non-concordance between ictal electroencephalography (EEG) and MR imaging. The superior results of PET in temporal lobe epilepsy have led to improved positive and negative predictive values,⁸ and allowed more precise presurgical evaluation. On the contrary, the inferior results for non-temporal lobe lesion detection reflect the relative insensitivity of structural and functional imaging for neuronal migration disorders, which constitute majority of the cases,⁶ especially those with mild dysplasia only. The relatively poor results with PET scans may be attributed to the mixed

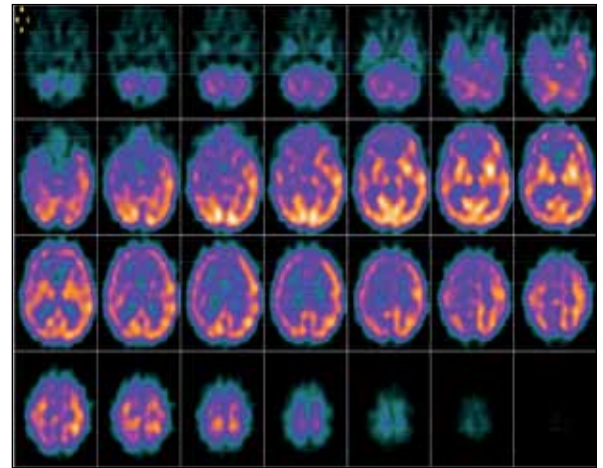


FIG 4. Left temporo-parieto-occipital syndrome in a 3-year-old boy

Ictal single-photon emission computed tomography axial images demonstrate left cerebral hyperperfusion, maximal over the left posterior temporal and parietal lobes

responses from various types of malformations. Such responses include: decreased uptake in most cases of focal cortical malformations, normal-to-increased uptake in band heterotopias, as well as increased uptake in focal subcortical heterotopia and lobar dysplasia.⁹ Coregistration of MR imaging with PET/SPECT has been used for precise lesion localisation in the preoperative evaluation for such patients, even though the results to date have been inconsistent.^{1,10-13}

Non-lesional epilepsy (including patients with negative MR imaging findings) poses a major problem. In general, ^{18}F -FDG PET has shown relatively constant congruent hypometabolism with EEG lateralisation, and can sometimes lateralise hypometabolism in patients in bitemporal seizure onset as depicted by Liew et al.¹⁴ They even reported the use of ^{18}F -FCWAY (^{18}F -trans-4-fluoro-N-2-[4-(2-methoxyphenyl)piperazin-1-yl]ethyl-N-(2-pyridyl)cyclohexane carboxamide) PET as a superior and more accurate modality to detect epileptic foci and lateralisation of MR imaging-negative mesial temporal lobe epilepsy. This entailed more specific 5-HT(1A)-receptor binding reduction in seizure initiation than propagation regions.¹⁴ Yet this would require a larger study to validate its use and accuracy. Recently, Akman et al¹⁵ reported the use of statistical parametric mapping to quantify the duration of epilepsy in PET scans of patients with temporal lobe epilepsy. They found that temporal lobe (parahippocampal gyrus, uncus, middle, and superior temporal gyri) hypometabolism was consistently present in patients with longer-duration epilepsy (10 years, $P < 0.05$ corrected), the two being inversely correlated. Buch et al¹⁶ also reported the use of statistical parametric mapping to create a functional image by spatially registering the PET and SPECT images, allowing the calculation of perfusion-

to-metabolism ratio. In their study of 21 patients with lesional temporal lobe epilepsy, the ratio-images demonstrated a correct hemispheric localisation rate, sensitivity, and specificity of 83%, 68% and 96% respectively, as compared with 70%, 63% and 96% with PET images only, revealing a significantly improved hemispheric localisation. This would also be beneficial in cases of non-lesional temporal lobe epilepsy.

Advanced magnetic resonance imaging techniques

These include proton spectroscopy (MR spectroscopy), MR volumetry, diffusion tensor imaging (DTI), MR perfusion, and functional MR imaging (fMRI) with blood oxygen level-dependent (BOLD) activation. The widespread application of most of these techniques in clinical practice depends on the availability of high-performance MR imagers capable of performing fast echo-planar pulse sequences (echo-planar imaging), as well as substantial data processing capabilities.

Single-voxel proton MR spectroscopy is a non-invasive technique that depicts the anatomic distribution of metabolite signals, including those of compounds containing N-acetylaspartate (NAA), creatine and phosphocreatine (Cr), and choline (Cho). It has consistently demonstrated metabolite changes in the epileptogenic region of the brain.¹⁷ Patients with mesial temporal lobe epilepsy typically demonstrate extensive reduction in NAA in the temporal lobe and insular cortex, whereas symmetrical generalised reduction of NAA (Fig 5) can occur in both cerebral hemispheres as demonstrated on multi-voxel MR spectroscopy, and probably reflects metabolic impairment due to repeated seizures. Therefore NAA asymmetry in the temporal lobe and insular cortex robustly lateralises the seizure focus.¹⁸ Achten et al¹⁹ even postulated an asymmetry index (NAA/Cho+Cr) of more than 0.05 to 0.10 that would point to the diseased side. Chernov et al²⁰ also found frequent presence of lactate on the side of epileptogenic zone in addition to decrease in NAA. They continued to postulate a decrease of NAA content below 0.75 and/or unilateral presence of lactate would provide 86% (95% confidence interval, 68-100%) lateralisation accuracy. Hence, MR spectroscopy is a useful adjunctive presurgical test for localising seizure foci, particularly in temporal lobe epilepsy, and has the potential to reduce the need for intracranial-depth electrode EEG recordings. Multi-voxel MR spectroscopy can achieve higher sensitivity and better spectral quality, improving lateralisation of the seizure focus.¹⁸

Magnetic resonance volumetric imaging can detect decreases in volumes of structures functionally connected to the hippocampus, such as the amygdala,

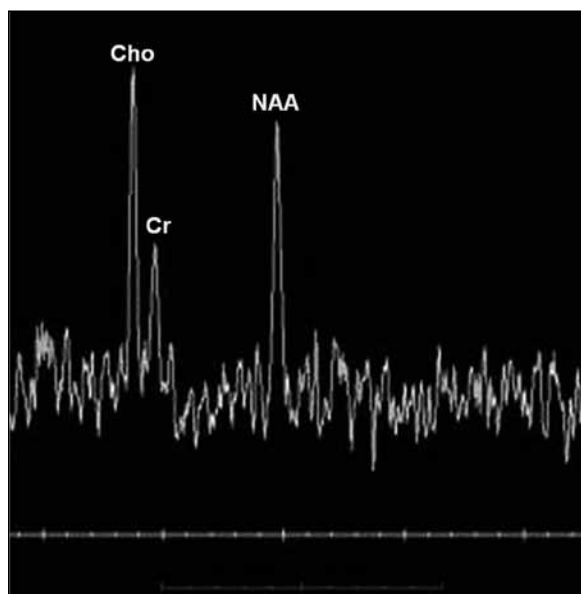


FIG 5. Focal cortical dysplasia in a 5-year-old girl
Magnetic resonance spectroscopy reveals mild reduction in N-acetylaspartate (NAA) and marked elevation in choline (Cho); Cr denotes creatine and phosphocreatine

entorhinal cortex, fornix, mamillary body and thalamus, and to a far lesser degree, in more remotely connected structures such as striatum and cerebellar hemispheres. It is still unclear to what extent the volume loss is related to a pre-existent injury or the result of recurrent seizure, but several cross-sectional volumetric studies have shown a definite relation to the duration of epilepsy.²¹ This was probably due to a combination of neurodevelopmental and progressive effects, characterised by a prominent disruption in the ipsilateral hippocampus and neural connectivity (white matter volume loss) that extended beyond the temporal lobe, and affected both ipsilateral and contralateral hemispheres.²² It has shown excellent sensitivity, ranging from 75 to 92%, and with specificities of 64 to 100% for temporal lobe seizure foci.^{5,23} Thalamic volume loss is typically bilateral, but in the presence of asymmetry, the smaller side correlates strongly with the onset and duration of epilepsy.²¹ This reflects either a remote acute injury in the setting of status epilepticus or chronic injury due to seizure propagation. The results of MR volumetry in the evaluation of extratemporal epilepsy have been inconsistent so far. Bearing in mind the variation of total cerebral brain volume across different ages, genders, and congenital insults, potential errors can occur. Several authors have even advocated scaled measurements in relation to total brain volume or direct measurements in a stereotaxic space.²⁴⁻²⁶ Nevertheless, volume measurement generally indicates a later stage of the disease process.

A new imaging technique, DTI, makes use

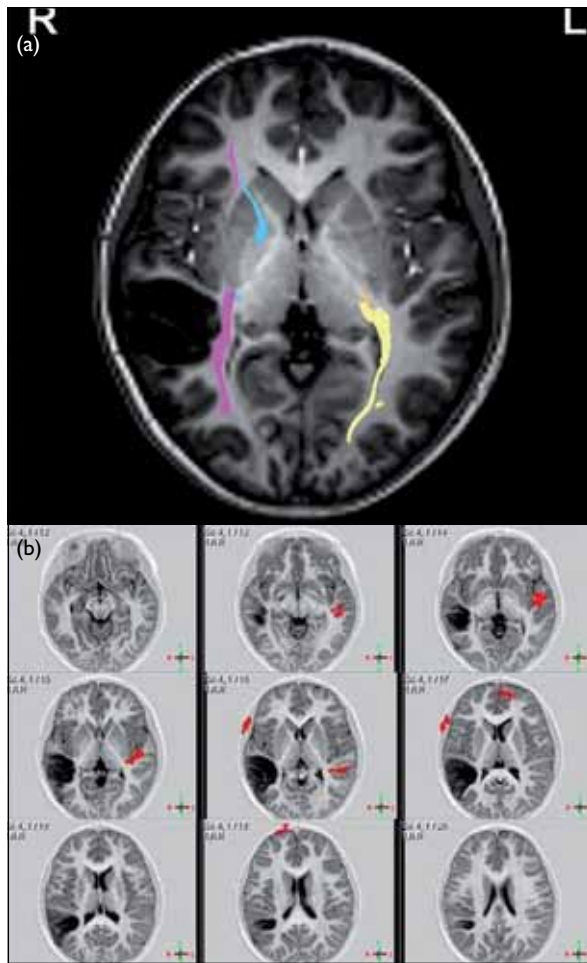


FIG 6. Right temporal lobe dysembryoplastic neuroepithelial tumour in an 8-year-old boy

(a) Diffusion tensor imaging with tractography in the axial plane showing an inferior longitudinal fasciculus (pink fibres) on the right side being displaced by the tumour medially. (b) Functional magnetic resonance images with receptive language task (listening to words) reveal activation in the left superior temporal and transverse temporal gyri (auditory cortex), suggesting left dominance

of the anisotropic diffusion of water to delineate microstructural tissue organisation, allowing axonal fibre delineation based on the observation that the diffusion of water in white matter is greater in directions parallel to fibre tracts but more limited in other directions. Thereby it differentiates pathologic from normal tissue.²⁷ Data can be displayed in a three-dimensional format referred to as fibre tractography (Fig 6a), which allows illustration and visualisation of specific tracts such as connections with the language cortex.²⁸ It has been shown useful in studying cerebral ischaemia, acute stroke, multiple sclerosis, schizophrenia, and more recently in epilepsy. In general, increased mean diffusivity and decreased fractional anisotropy are observed at the seizure focus. The former is more sensitive, whilst a left-right diffusivity index/difference can be

established to lateralise the epileptogenic focus.²⁹ It is of proven value in the evaluation of language connectivity areas in patients undergoing dominant hemisphere anterior temporal lobe resection. Greater lateralisation of tracts to the dominant hemisphere was associated with greater decline in naming function,³⁰ hence the potential to predict language deficits in such patients. Visualisation of the optic radiation is another useful preoperative imaging technique in patients undergoing temporal lobe resection, by helping to predict visual field defects (superior homonymous quadrantanopia) due to disruption of the Meyer loop.³¹ Temporal lobe epilepsy has attracted much attention. Past studies reported substantial white matter abnormalities but with limited data on the extent of such abnormalities and their association with clinical factors. Riley et al³² identified important cognitive and clinical consequences associated with widespread disturbances in white matter tracts, including positive correlation of mean fractional anisotropy with delayed memory related to the anterior temporal lobe, and immediate memory impairment linked to the mesial temporal lobe. Lower fractional anisotropy values in the posterior region of corpus callosum were also related to earlier age of seizure onset.

Functional MR imaging using the BOLD technique has been assessed as a mean of non-invasive mapping of the eloquent cortex (Fig 6b) and for assessing memory function in temporal lobe structures.³³ This was in contrast to the invasive intra-operative electrocortical stimulation and intracarotid amobarbital procedure (Wada test), mainly used in presurgical planning and shown to influence diagnostic and therapeutic decisions.³³ Being based on the magnetic property of blood (oxygenation state of haemoglobin) to measure haemodynamic changes as major determination of BOLD signals, any consequent increase in local blood oxygenation leads to an increase of the resulting MR signal.³⁴ Mapping of motor cortex has shown consistently good results, as motor paradigms to activate the cortex are simple and robust.³⁵ Functional MR imaging in mapping language centres, however, yields variable results as language tasks show greater variability and difficulty. Nevertheless, it can help determine the dominant hemisphere in both epilepsy and non-epilepsy populations³⁶ and can also act as a predictor of deficits resulting from temporal lobe resection.²⁸ This is of particular importance in patients with temporal lobe epilepsy as reorganisation of language functions with structural fibre tract distortion and greater involvement of the non-dominant hemisphere had been demonstrated.³⁷ Even so, its clinical application is still debatable as it is generally considered inferior to intra-operative electrocortical stimulation, largely because of technical and conceptual problems.³⁸

Moreover, it shows poor concordance with Wada tests, especially in patients with left-sided temporal lobe epilepsy.³⁹ Gartus et al⁴⁰ developed a clinical fMRI overt language design at the sentential level, so as to optimise sensitivity for language-related areas of the brain. This included the application of semantic and syntactic error-detection tasks (constructed to represent the most relevant aspects of everyday language demands). These are believed to integrate relevant aspects of everyday language demands and enable robust localisation of core language areas. Task-free paradigm fMRI has been explored by Liu et al.⁴¹ It uses low-frequency components of spontaneous MR signals to provide information about the intrinsic functional and anatomical organisation of the brain. Liu et al⁴¹ were able to demonstrate comparable results in motor function mapping to those obtained by actual movement tasks and cortical stimulation. This provided a powerful approach to mapping the functional anatomy in patients lacking task compliance. Mapping memory, however, is more challenging, as different sites of activation have been demonstrated for different memory processing tasks and it is difficult to separate brain activity related to memory from other cognitive processes.⁴² In patients with temporal lobe epilepsy, it appeared useful in studying lateralisation of memory encoding processes (patterns, faces, scenes, and words) within the mesial temporal lobe.^{43,44} It was also shown to predict postoperative memory deficits following anterior temporal lobe resection; increased activation ipsilateral to the seizure focus being associated with greater memory decline.^{45,46} Apart from the mapping of motor, language and memory cortexes, a study involving correlations with EEGs by Patel et al⁴⁷ showed that it could yield a sensitivity of 90% in identifying sites of cerebral activation corresponding to sites of potential epileptogenesis. Several confounding factors remain unresolved however, and possibly explain the variable responses to BOLD activation.

Arterial spin labelling (ASL) is another non-

invasive technique for quantitative perfusion MR imaging.⁴⁸ Relative mesial temporal hypoperfusion demonstrated by continuous ASL perfusion MR imaging correlated well with clinical lateralisation of the seizure side, as well as with ¹⁸F-DG-PET hypometabolism⁴⁹ and hippocampal volume loss.⁵⁰ Similar findings were reported using a contrast-bolus MR perfusion technique, measuring interictal relative cerebral blood volume in patients with temporal lobe epilepsy.⁵¹ The continuous ASL technique has the advantage of providing a diffusible tracer and therefore measures classical tissue perfusion.⁵⁰ A previous study combining contrast-enhanced MR perfusion and diffusion-weighted imaging also provided lateralising information in non-lesional temporal lobe epilepsy; lower cerebral blood flow and a larger apparent diffusion coefficient in the lesional side.⁵² Since there is coupling of cerebral blood flow and metabolism, MR perfusion can act as a surrogate marker of metabolism as measured by PET. Magnetic resonance perfusion holds promise as a better alternative since it is less expensive, does not involve ionising radiation, and is more readily available. Yet more and larger clinical trials are needed to validate its use, and determine whether these techniques provide independent data to established MR quantitative measures. Nevertheless, such techniques are expected to continue evolving and provide a means of determining the exact site of origin and propagation pathways for seizures.

Conclusion

Both structural and functional neuroimaging play essential roles in non-invasive localisation of epileptogenic foci. Both functional radionuclide and advanced MR techniques can provide complementary information to structural MR imaging whenever an epileptogenic substrate is not identified or is non-concordant clinically (ictal EEG and semiology) or structurally.

References

1. Wong V. Study of seizure and epilepsy in Chinese children in Hong Kong: period prevalence and patterns. *J Child Neurol* 2004;19:19-25.
2. Fong GC, Mak W, Cheng TS, Chan KH, Fong JK, Ho SL. A prevalence study of epilepsy in Hong Kong. *Hong Kong Med J* 2003;9:252-7.
3. Pillai JJ, Hessler RB, Allison JD, Park YD, Lee MR, Lavin T. Advanced MR imaging of cortical dysplasia with or without neoplasm: a report of two cases. *AJNR Am J Neuroradiol* 2002;23:1686-91.
4. Saneto RP, Wyllie E. Surgically treatable epilepsy syndromes in infancy and childhood. In: Miller JW, Silbergeld DL, editors. *Epilepsy surgery: principles and controversies*. New York: Taylor and Francis; 2006: 121-41.
5. Helveston W, Gilmore R, Roper S, et al. Intractable temporal lobe epilepsy: comparison of positron emission tomography with qualitative and quantitative MR. *AJNR Am J Neuroradiol* 1996;17:1515-21.
6. Hwang S, Kim JH, Park SW, et al. Comparative analysis of MR imaging, positron emission tomography, and ictal single-photon emission CT in patients with neocortical epilepsy. *AJNR Am J Neuroradiol* 2001;22:937-46.
7. Kim JT, Bai SJ, Choi KO, et al. Comparison of various imaging modalities in localization of epileptogenic lesion using epilepsy surgery outcome in pediatric patients. *Seizure* 2009;18:504-10.
8. Uijl SG, Leijten FS, Arends JB, Parra J, van Huffelen AC, Moons KG. The added value of [18F]-fluoro-D-deoxyglucose positron emission tomography in screening for temporal lobe epilepsy surgery. *Epilepsia* 2007;48:2121-9.

9. Poduri A, Golja A, Takeoka M, Bourgeois BF, Connolly L, Riviello JJ Jr. Focal cortical malformations can show asymmetrically higher uptake on interictal fluorine-18 fluorodeoxyglucose positron emission tomography (PET). *J Child Neurol* 2007;22:232-7.
10. Doelken MT, Richter G, Stefan H, et al. Multimodal coregistration in patients with temporal lobe epilepsy—results of different imaging modalities in lateralization of the affected hemisphere in MR imaging positive and negative subgroups. *AJNR Am J Neuroradiol* 2007;28:449-54.
11. Chassoux F, Chiron C. Positron emission tomography: which indications, which benefits? [in French]. *Neurochirurgie* 2008;54:219-25.
12. Maehara T. Neuroimaging of epilepsy. *Neuropathology* 2007;27:585-93.
13. Aubert-Broche B, Grova C, Reilhac A, Evans AC, Collins DL. Realistic simulated MRI and SPECT databases. Application to SPECT/MRI registration evaluation. *Med Image Comput Comput Assist Interv* 2006;9:330-7.
14. Liew CJ, Lim YM, Bonwetsch R, et al. 18F-FCWAY and 18F-FDG PET in MRI-negative temporal lobe epilepsy. *Epilepsia* 2009;50:234-9.
15. Akman CL, Ichise M, Olsavsky A, Tikofsky RS, Van Heertum RL, Gilliam F. Epilepsy duration impacts on brain glucose metabolism in temporal lobe epilepsy: results of voxel-based mapping. *Epilepsy Behav* 2010;17:373-80.
16. Buch K, Blumenfeld H, Spencer S, Novotny E, Zubal IG. Evaluating the accuracy of perfusion/metabolism (SPET/PET) ratio in seizure localization. *Eur J Nucl Med Mol Imaging* 2008;35:579-88.
17. Paciorek A, Urbanik A, Paciorek J, et al. The role of magnetic resonance spectroscopy in the diagnosis of temporal lobe epilepsy [in Polish]. *Przegl Lek* 2007;64:956-9.
18. Capizzano AA, Vermathen P, Laxer KD, et al. Multisection proton MR spectroscopy for mesial temporal lobe epilepsy. *AJNR Am J Neuroradiol* 2002;23:1359-68.
19. Achten E, Boon P, Van De Kerckhove T, Caemaert J, De Reuck J, Kunnen M. Value of single-voxel proton MR spectroscopy in temporal lobe epilepsy. *AJNR Am J Neuroradiol* 1997;18:1131-9.
20. Chernov MF, Ochiai T, Ono Y, et al. Role of proton magnetic resonance spectroscopy in preoperative evaluation of patients with mesial temporal lobe epilepsy. *J Neurol Sci* 2009;285:212-9.
21. Szabo CA, Lancaster JL, Lee S, et al. MR imaging volumetry of subcortical structures and cerebellar hemispheres in temporal lobe epilepsy. *AJNR Am J Neuroradiol* 2006;27:2155-60.
22. Seidenberg M, Kelly KG, Parrish J, et al. Ipsilateral and contralateral MRI volumetric abnormalities in chronic unilateral temporal lobe epilepsy and their clinical correlates. *Epilepsia* 2005;46:420-30.
23. Boling WW, Lancaster M, Kraszpulski M, Palade A, Marano G, Puce A. Fluorodeoxyglucose-positron emission tomographic imaging for the diagnosis of mesial temporal lobe epilepsy. *Neurosurgery* 2008;63:1130-8.
24. Bernasconi N, Bernasconi A, Andermann F, Dubeau F, Feindel W, Reutens DC. Entorhinal cortex in temporal lobe epilepsy: a quantitative MRI study. *Neurology* 1999;52:1870-6.
25. Natsume J, Bernasconi N, Andermann F, Bernasconi A. MRI volumetry of the thalamus in temporal, extratemporal, and idiopathic generalized epilepsy. *Neurology* 2003;60:1296-300.
26. Salmenperä T, Kälviäinen R, Partanen K, Pitkänen A. Hippocampal and amygdaloid damage in partial epilepsy: a cross-sectional MRI study of 241 patients. *Epilepsy Res* 2001;46:69-82.
27. Rastogi S, Lee C, Salamon N. Neuroimaging in pediatric epilepsy: a multimodality approach. *Radiographics* 2008;28:1079-95.
28. Duncan J. The current status of neuroimaging for epilepsy. *Curr Opin Neurol* 2009;22:179-84.
29. Assaf BA, Mohamed FB, Abou-Khaled KJ, et al. Diffusion tensor imaging of the hippocampal formation in temporal lobe epilepsy. *AJNR Am J Neuroradiol* 2003;24:1857-62.
30. Powell HW, Parker GJ, Alexander DC, et al. Imaging language pathways predicts postoperative naming deficits. *J Neurol Neurosurg Psychiatry* 2008;79:327-30.
31. Powell HW, Parker GJ, Alexander DC, et al. MR tractography predicts visual field defects following temporal lobe resection. *Neurology* 2005;65:596-9.
32. Riley JD, Franklin DL, Choi V, et al. Altered white matter integrity in temporal lobe epilepsy: association with cognitive and clinical profiles. *Epilepsia* 2010;51:536-45.
33. Medina LS, Bernal B, Dunoyer C, et al. Seizure disorders: functional MR imaging for diagnostic evaluation and surgical treatment—prospective study. *Radiology* 2005;236:247-53.
34. Wang XY, Lam WW. Characterisation of brain disorders and evaluation of therapy by functional and molecular magnetic resonance techniques. *Hong Kong Med J* 2008;14:469-78.
35. Ashtari M, Perrine K, Elbaz R, et al. Mapping the functional anatomy of sentence comprehension and application to presurgical evaluation of patients with brain tumor. *AJNR Am J Neuroradiol* 2005;26:1461-8.
36. Medina LS, Bernal B, Ruiz J. Role of functional MR in determining language dominance in epilepsy and nonepilepsy populations: a Bayesian analysis. *Radiology* 2007;242:94-100.
37. Powell HW, Parker GJ, Alexander DC, et al. Abnormalities of language networks in temporal lobe epilepsy. *Neuroimage* 2007;36:209-21.
38. Munk S, Forchhammer HB, Brennum J, Hansen AE, Larsson HB. Presurgical functional MR imaging in the mapping of language function [in Danish]. *Ugeskr Laeger* 2007;169:3571-4.
39. Deblaere K, Backes WH, Tieleman A, et al. Lateralized anterior mesiotemporal lobe activation: semirandom functional MR imaging encoding paradigm in patients with temporal lobe epilepsy—initial experience. *Radiology* 2005;236:996-1003.
40. Gartus A, Foki T, Geissler A, Beisteiner R. Improvement of clinical language localization with an overt semantic and syntactic language functional MR imaging paradigm. *AJNR Am J Neuroradiol* 2009;30:1977-85.
41. Liu H, Buckner RL, Talukdar T, Tanaka N, Madsen JR, Stufflebeam SM. Task-free presurgical mapping using functional magnetic resonance imaging intrinsic activity. *J Neurosurg* 2009;111:746-54.
42. Kesavadas C, Thomas B. Clinical applications of functional MRI in epilepsy. *Indian J Radiol Imaging* 2008;18:210-7.
43. Jokeit H, Okujava M, Woermann FG. Memory fMRI lateralizes temporal lobe epilepsy. *Neurology* 2001;57:1786-93.
44. Detre JA, Maccotta L, King D, et al. Functional MRI lateralization of memory in temporal lobe epilepsy. *Neurology* 1998;50:926-32.
45. Rabin ML, Narayan VM, Kimberg DY, et al. Functional MRI predicts post-surgical memory following temporal lobectomy. *Brain* 2004;127:2286-98.
46. Powell HW, Richardson MP, Symms MR, et al. Preoperative fMRI predicts memory decline following anterior temporal lobe resection. *J Neurol Neurosurg Psychiatry* 2008;79:686-93.
47. Patel MR, Blum A, Pearlman JD, et al. Echo-planar functional MR imaging of epilepsy with concurrent EEG monitoring. *AJNR Am J Neuroradiol* 1999;20:1916-9.
48. Deibler AR, Pollock JM, Kraft RA, Tan H, Burdette JH, Maldjian JA. Arterial spin-labeling in routine clinical practice, part 1: technique and artifacts. *AJNR Am J Neuroradiol* 2008;29:1228-34.
49. Lim YM, Cho YW, Shamim S, et al. Usefulness of pulsed arterial spin labeling MR imaging in mesial temporal lobe epilepsy. *Epilepsy Res* 2008;82:183-9.
50. Wolf RL, Alsop DC, Levy-Reis I, et al. Detection of mesial temporal lobe hypoperfusion in patients with temporal lobe epilepsy by use of arterial spin labeled perfusion MR imaging. *AJNR Am J Neuroradiol* 2001;22:1334-41.
51. Wu RH, Bruening R, Noachtar S, et al. MR measurement of regional relative cerebral blood volume in epilepsy. *J Magn Reson Imaging* 1999;9:435-40.
52. O'Brien TJ, David EP, Kilpatrick CJ, Desmond P, Tress B. Contrast-enhanced perfusion and diffusion MRI accurately lateralize temporal lobe epilepsy: a pilot study. *J Clin Neurosci* 2007;14:841-9.