Original article

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Predictive factors of ictal SPECT findings in paediatric patients with focal cortical dysplasia

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ABSTRACT – *Aims*. To identify variables that influence the extent of ictal single-photon emission computed tomography (SPECT) findings in paediatric patients with focal cortical dysplasia (FCD). *Methods*. We visually evaluated 98 ictal SPECT studies from 67 children treated surgically for intractable epilepsy caused by FCD. SPECT findings were classified as "non-localised", "well-localised", and "extensive" and compared with parameters of injected seizures (seizure type and duration, injection time, and scalp EEG ictal pattern), presence of structural pathology on MRI, type of surgery performed after SPECT study, and histological findings. *Results*. A shorter injection time and duration of injected seizure was associated with more localised SPECT hyperperfusion. SPECT findings were not significantly influenced by type of injected seizure. Widespread ictal scalp EEG patterns were associated with extensive SPECT findings. Larger zones of hyperperfusion were more common in patients with lesional MRI and patients undergoing multilobar resections. SPECT studies demonstrating good localisation were more common in patients with mild malformations of cortical development. *Conclusion*. Early ictal SPECT radiotracer injection is crucial for successful localisation of the epileptogenic zone. Seizure duration, type of scalp EEG findings, and presence of structural pathology on MRI may influence the extent of ictal SPECT hyperperfusion, which was associated with certain types of epilepsy surgery as well as histopathological findings.

Key words: Ictal SPECT, focal cortical dysplasia, epilepsy surgery

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Ictal single photon emission computed tomography (SPECT) is often employed to localise the seizure onset zone in patients with focal epilepsy. Localising studies improve surgical outcome in subjects with focal cortical dysplasia (FCD) by guiding the location and extent of intracranial electrode implantation and resective epilepsy surgery (O'Brien *et al.,* 1998a; O'Brien *et al.,* 2000; Won *et al.,* 1999; So, 2000). When the location of the hyperperfusion zone is concordant with other non-invasive methods, intracranial electrode implantation may not be necessary (Buchhalter and So, 2004; Cascino *et al.,* 2004; Dupont *et al.,* 2006).

Ictal SPECT is based on the localisation of increased cerebral blood flow associated with increased metabolic activity of cerebral tissue involved in epileptogenesis (Stefan *et al.,* 1990; Van Paesschen *et al.,* 2007). Due to the propagation of seizure activity and "postictal switch" (Newton *et al.,* 1992) of blood flow from hyperperfusion to hypoperfusion, early injection of the radiotracer is recognised as being crucial for success and accurate interpretation of ictal SPECT data (O'Brien *et al.,* 1998a; O'Brien *et al.,* 1999a; Buchhalter and So, 2004). Several other variables for injected seizures including seizure duration and type, as well as scalp ictal EEG findings, are reported to influence ictal SPECT findings (Van Paesschen *et al.,* 2007). However, these factors have not been systematically studied and there are no observations based on large cohorts of patients.

The present study aimed to analyse a large number of SPECT studies of paediatric patients with histologically-proven mild malformation of cortical development (mMCD) and FCD, who underwent ictal SPECT prior to resective epilepsy surgery. For ictal SPECT, we presumed that the presence of localised, rather than extensive, hyperperfusion is more informative with regards to epilepsy surgery planning, and thus sought to identify factors that might be predictive of localised ictal SPECT findings. Our ultimate goal is to improve noninvasive presurgical diagnosis as well as surgical treatment of paediatric epilepsy surgery patients. The predictive value of ictal SPECT for outcome after excisional epilepsy surgery is discussed in another study (Krsek *et al.,* 2013).

Methods

Inclusion criteria

Data from 567 children who underwent excisional epilepsy surgery at Miami Children's Hospital from March 1986 to June 2006 were retrospectively reviewed. We selected SPECT findings from patients who had (1) had at least one epilepsy surgical procedure at the Miami Children's Hospital; (2) definitive histological evidence of mMCD/FCD; (3) at least one presurgical ictal SPECT study; and (4) available data on injection time, length, and type, as well as scalp EEG findings, for injected seizures. A total of 173 ictal SPECT studies were performed for 106 patients from this cohort. Data regarding injected seizures were available from 98 studies, corresponding to 67 patients.

Ictal SPECT examination

Periictal radioisotope injections were always performed by specially-trained registered radiology technicians during video-EEG monitoring. The radiotracer 99mTc-HMPAO was used for all patients. Doses of the radiotracer were calculated according to the patient's weight. Injections were administered as soon as either clinical or EEG seizure onset of a habitual seizure was observed. The radiotracer injection was followed by a saline flush. SPECT images were acquired within four hours of the radiotracer injection. The acquisition was performed on a three-headed Multispect 3 Siemens' Medical System machine (Hoffman Estate, Illinois, USA) with the following acquisition parameters: 120-word mode, 360-degree rotations, 40 stops, 120 images, 60-second-per-frame imaging, 1.28-magnification factor, and fan beam collimation. A standard series of axial, coronal, and sagittal images were created. Selected patients underwent a paediatric sedation protocol during image acquisition consisting of orally-administered chloral hydrate (50-75 mg/kg) or pentobarbital (3-6 mg/kg). Continuous monitoring of the airway and pulse oximetry was performed by a trained registered nurse.

Review of ictal SPECT images

In order to localise a region of greatest increase in ictal perfusion, an initial visual analysis of periictal images was performed by a nuclear medicine expert, blinded to patient data. Grey scale of the images was modified to achieve optimal localisation of the hyperperfused region. Ictal-interictal subtractions were not performed. For the purposes of the study, SPECT images were independently re-evaluated by two reviewers (BM and AJ) who were blinded to the clinical, EEG, and MRI data. SPECT findings were classified into the following groups: (1) non-localised; (2) well-localised (*i.e.* focal findings confined to a region of one or two contiguous gyri and findings limited to a part of a single lobe); and (3) extensive findings (multilobar or hemispheric). If there was disagreement between the assessments from the two primary reviewers, a third blinded reviewer (PK) analysed the images and a final assessment was based on agreement between the third reviewer and one of the primary reviewers.

Data for injected seizures, EEG and MRI findings

Video/EEG recordings of all injected seizures were re-evaluated from the original files. Seizure types were classified according to the international classification of seizures as simple partial seizures (SPS), complex partial seizures (CPS), and secondary generalised tonic-clonic seizures (SGTCS). Timing of injection and duration of injected seizures was determined as described previously (O'Brien *et al.*, 1998a; O'Brien *et al.*, 1998b; O'Brien *et al.*, 1999a). Seizure onset was considered as the time of the earliest indication of a warning (verbal or by pushing the call button) or the presence of abnormal movements, behaviour, or impaired awareness. The end of a seizure was defined as the time when ictal movements or behaviour ceased. When the start and end of the seizure could not be confidently established based on clinical features, the ictal EEG of the injected seizure was reviewed in order to establish the beginning and end of the rhythmic seizure discharge. The time of the injection was defined as the time when the plunger on the syringe containing the radiotracer was fully depressed. Ictal EEG patterns of injected seizures were classified as regional (appearing exclusively over a single lobe or in two contiguous regions, such as centroparietal patterns), widespread (*i.e.* multilobar or hemispheric), and non-localised.

MRI findings were re-evaluated as described previously (Krsek *et al.*, 2008), and for the purposes of the current study, were classified as lesional (showing a cortical malformation) or non-lesional.

Surgery performed after the SPECT study was identified as temporal, extratemporal in a single lobe, or multilobar (including hemispheric cases).

Neuropathological analysis and classification

Brain tissue analysis was performed as described previously (Krsek *et al.*, 2008). Neuropathological findings were classified according to the scheme of Palmini and Lüders (Palmini *et al.*, 2004), since a subgroup of patients presented with mild malformations of cortical development (mMCD) not recognised by a recent ILAE classification of FCD (Blümcke *et al.*, 2011). Only features definitive of mMCD/FCD were accepted. Subjects with malformations of cortical development other than FCD/mMCD (such as tuberous sclerosis complex or hemimeganencephaly) were excluded.

Correlations with ictal SPECT findings

The above-mentioned types of SPECT findings (*i.e.* non-localised, well-localised, and extensive) were statistically compared with individual variables of injected seizures; *i.e.* type of seizure, EEG ictal onset zone of a particular injected seizure, injection time, and length of injected seizure. We further analysed SPECT findings in order to determine any correlation with the presence of MRI abnormality (MRI findings were classified as lesional or non-lesional), consequent surgical procedure (temporal, extratemporal, and multilobar), and finally, histological types of mMCD/FCD.

Statistical analysis

All statistical calculations were performed using Statistica® software. In the first step, we tested the nominal variables using 2×2 contingency tables for the combinations of the variable "type of SPECT finding" with other nominal variables such as "type of seizure", "ictal scalp EEG finding", "type of MRI finding", "surgical procedure", and "histology". In each table, we compared the frequency of the presence or absence of a particular variable with a particular SPECT finding. We used the Fisher exact test for accepting or rejecting the null hypothesis of independency of the variables.

The relationship between continuous variables ("injection time" and "length of injected seizures") and "type of SPECT finding" was analysed using the non-parametric Kruskal-Wallis variance test. Next, the Wilcoxon test was performed in order to compare particular "types of SPECT finding" with the continuous variables. Moreover, analysis of continuous variables was calculated twice; (1) using all values (all patients in the study) and (2) excluding extreme values using the Dixon's test.

We also transformed the continuous variable "injection time" into a nominal variable. We classified the variable as "early" (less than 30 seconds) or "late" injection time. Independency was then tested in the same way as for the other nominal values.

Results

Characteristics of patients and ictal SPECT studies

In total, 98 SPECT studies were performed for the cohort of 40 males and 27 females, aged seven weeks to 20 years at the time of (first) surgery (mean: 8.5 years). One ictal SPECT study was evaluated for 45 patients, two for 17 patients, three for 2 patients, four for 2 patients, and five for 1 patient. Twenty-eight ictal SPECT studies from 21 patients were performed after the first surgical procedure as part of the diagnostic work-up, at which time further surgery was considered. Four ictal SPECT studies from 2 patients were performed after the second epilepsy surgical procedure.

SPECT findings were divided as described above: 27 SPECT findings were non-localised, 44 well-localised, and 27 extensive. Thirty-five SPECT studies were performed for 21 patients with normal MRI findings. Localisation of surgery was temporal after 14 SPECT studies, extratemporal in a single lobe after 36 SPECT studies, and multilobar or hemispheric after 37 SPECT studies. No surgery was performed after 11 SPECT studies.

Relationship between SPECT findings and type of seizure *(table 1)*

There was no statistically significant difference between the studied groups regarding the type of injected seizure.

Relationship between SPECT findings and scalp EEG pattern *(table 1)*

Whereas widespread scalp EEG ictal onset zones (n=24) were significantly associated with extensive SPECT findings (n=11; p=0.023), they were less frequently associated with non-localised SPECT findings (n=3; p=0.046). There was a non-significant trend in association between localised EEG findings and well-localised SPECT findings (22 of 46 SPECT studies with localised EEG findings exhibited well-localised hyperperfusion).

Relationship between SPECT and MRI findings (*table 1*)

Patients with non-lesional MRI (n=35) demonstrated SPECT findings that were significantly more well-localised (n=20) than extensive (n=5; p=0.022).

Relationship between SPECT findings and type of surgery (*table 1*)

No surgery was performed after 11 SPECT studies. Significantly more subjects with well-localised SPECT findings (n=38) underwent extratemporal surgery of a single lobe (n=23; p=0.001) than multilobar surgery (n=10; p=0.020). In patients with extensive SPECT findings (n=26), multilobar surgery (n=15) was performed more frequently than extratemporal surgery of a single lobe (n=6; p=0.020).

Relationship between SPECT and histopathological findings *(table 1)*

No mMCD was histopathologically proven in subjects with extensive SPECT findings (n=27; p=0.001). Extensive SPECT findings significantly associated with FCD type I (n=16; p=0.048).

Relationship between SPECT findings and injection time *(tables 1 and 2)*

No significant difference in mean injection time was identified when the different types of SPECT findings were analysed using the non-parametric Kruskal-Wallis variance test. A significant difference, however, was observed when the mean injection time, corresponding to well-localised (25.1 seconds) and extensive (37.9 seconds) SPECT findings, was compared using the Wilcoxon test (p=0.034). Similar results were obtained when statistical evaluation was performed without three extreme values of injection times (SPECT studies with 105, 180, and 202 seconds of injection time).
A statistically significant difference was also observed when early and late injections were compared between groups of patients with well-localised and extensive ictal SPECT findings (after transforming the continuous variable "injection time" into a nominal variable). For 33 of 44 SPECT studies with well-localised findings, the radiotracer injection was early (*i.e.* <30 seconds; p=0.016), in comparison to 12 of 27 studies with extensive findings (p=0.023).

Relationship between SPECT findings and length of seizure *(table 2)*

A statistically significant difference in mean seizure duration was observed between the different types of SPECT findings using the Kruskal-Wallis test (p=0.002). A significant difference was also observed when either the mean seizure duration of non-localised (73.1 sec) or well-localised (68.5 seconds) SPECT findings were compared with extensive SPECT findings (144.4 sec) using the Wilcoxon test (p=0.004 and p=0.019, respectively). Similar results were found when statistical evaluation was performed without extreme values (ictal SPECT studies with seizure duration of 340, 660, 660, 700, and 900 seconds).

Discussion

The ability to define and fully remove dysplastic cortex is the most powerful variable that influences outcome in surgical patients with mMCD/FCD (Palmini *et al.*, 1995; Paolicchi *et al.*, 2000; Krsek *et al.*, 2009a). It has been demonstrated that a portion of the epileptogenic zone may extend beyond the MRI-detected lesion (Najm *et al.*, 2002; Boonyapisit *et al.*, 2003). Noninvasive functional neuroimaging techniques could thus be crucial in planning epilepsy surgery in these patients. Previous studies suggested that appropriately performed ictal SPECT may indicate the region of seizure onset (O'Brien *et al.*, 1998a; O'Brien *et al.*, 1998b; So, 2000; Gupta *et al.*, 2004; Dupont *et al.*, 2006; Krsek *et al.*,

Table 1. Relationship between SPECT findings and type of seizure, scalp EEG ictal onset zone, MRI findings, early (<30 seconds) and late injection time (>30 seconds), type of surgical procedure, and histopathological findings.

		Ictal SPECT findings Non-localised (*n*=27)	Well-localised (*n*=44)	Extensive (*n*=27)
Seizure type (*n*=98)	**SPS** (*n*=38)	12	16	10
	CPS (*n*=36)	9	18	9
	SGTCS (*n*=24)	6	10	8
Scalp EEG ictal onset zone (*n*=98)	**Non-localised** (*n*=28)	9	12	7
	Localised (*n*=46)	15	22	9
	Widespread (*n*=24)	3 (*p*=0.046)	10	11 (*p*=0.023)
MRI findings (*n*=98)	**Non-lesional** (*n*=35)	10	20	5 (*p*=0.022)
	Lesional (*n*=63)	17	24	22 (*p*=0.022)
Early/late injection time (*n*=98)	**Early**	16	33 (*p*=0.016)	12 (*p*=0.023)
	Late	11	11 (*p*=0.016)	15 (*p*=0.023)
Histopathology (*n*=98)	mMCD (*n*=18)	8	10	0 (*p*=0.001)
	FCD type I (*n*=43)	12	15	16 (*p*=0.048)
	FCD type II (*n*=37)	7	19	11
		Non-localised (*n*=23)	**Well-localised** (*n*=38)	**Extensive** (*n*=26)
Type of surgery (*n*=87)	**Temporal** (*n*=14)	4	5	5
	Extra-temporal (*n*=36)	7	23 (*p*=0.001)	6 (*p*=0.020)
	Multilobar (*n*=37)	12	10 (*p*=0.020)	15

SPS: simplex partial seizures; CPS: complex partial seizures; SGTCS: secondary generalised tonic-clonic seizures; mMCD: mild malformation of cortical development; FCD: focal cortical dysplasia.

2013) and this is especially valuable for MR-negative subjects (O'Brien *et al.,* 2000; O'Brien *et al.,* 2004; Siegel *et al.,* 2001; Cascino *et al.,* 2004). If the hyperperfusion zone is concordant with results of other non-invasive tests, intracranial electrode implantation may be avoided (Buchhalter and So, 2004; Cascino *et al.,* 2004; Dupont *et al.,* 2006; Kudr *et al.,* 2013). Recognition of factors that influence ictal SPECT findings is therefore important for appropriate interpretation of results.

Performing ictal SPECT in paediatric patients may be complicated by certain features specific to children with epilepsy (Gupta *et al.,* 2004): clinical onset of seizures is often difficult to recognise, prevailing extratemporal seizures may be brief and spread rapidly, and it is often necessary to perform SPECT under general anaesthesia. There are only a few studies concerning ictal SPECT in children with FCD (Kaminska *et al.,* 2003; Gupta *et al.,* 2004; Krsek *et al.,* 2013), however, the localising value of ictal SPECT for epileptogenic zone localisation in children appears comparable to that in adult patients.

Our study was based on a large population of paediatric epilepsy surgery patients with histologically-proven mMCD/FCD and thus facilitated a comprehensive analysis of factors influencing ictal SPECT findings. We investigated potential predictors of SPECT findings, including seizure variables

Table 2. (A) Relationship between SPECT findings and mean injection time and seizure duration. (B) Statistical analysis of a comparison of SPECT findings in relation to mean injection time and seizure duration.

(A)		**Mean injection time (seconds)**		**Mean seizure duration (seconds)**	
		All (*n*=98)	**Without extreme values (*n*=95)**	**All (*n*=98)**	**Without extreme values (*n*=93)**
Ictal SPECT findings	**Non-localised**	33.3 (*n*=27)	26.8 (*n*=26)	73.1 (*n*=27)	49.0 (*n*=26)
	Well-localised	25.1 (*n*=44)	23.3 (*n*=43)	68.5 (*n*=44)	54.7 (*n*=43)
	Extensive	37.9 (*n*=27)	32.5 (*n*=26)	144.4 (*n*=27)	83.3 (*n*=24)
(B)		***p* value**			
		All (*n*=98)	**Without extreme values (*n*=95)**	**All (*n*=98)**	**Without extreme values (*n*=95)**
Kruskal Wallis test	Non-localised/Well-localised /Extensive	0.168	0.177	**0.002***	**0.017***
Wilcoxon test	Non-localised *vs* Well-localised	0.149	0.228	0.581	0.469
	Non-localised *vs* Extensive	0.292	0.424	**0.004***	**0.008***
	Well-localised *vs* Extensive	**0.034***	**0.01***	**0.019***	**0.039***

Significant values are depicted by asterisks and are in bold.

(injection time and duration, type of injected seizure and respective scalp EEG pattern), MRI, and surgical variables, as well as histological findings.

We showed that radiotracer injection time and mean seizure duration significantly influenced the zone of hyperperfusion on ictal SPECT. The mean injection time for well-localised ictal SPECT findings was significantly shorter than for extensive ictal SPECT findings. Well-localised SPECT findings were also significantly associated with early radiotracer injections (<30 sec). We thus confirm the observations of O'Brien *et al.* (1998b), who reported late injections (>45 seconds after seizure onset) significantly more frequently in patients with non-localising or falsely localising SPECT data. The same study demonstrated that late injections reduced the clarity of SISCOM localisation, as shown by the inability of reviewers to agree on localisation or to label the study as non-localising (O'Brien *et al.*, 1998b). Other studies have supported the view that injection times are later in patients with non-localising or falsely localising ictal SPECT results (Weis *et al.*, 1994; Smith *et al.*, 1999).

The explanation for the association between localised SPECT findings and early radiotracer injections is based on the fact that regions of ictal hyperperfusion primarily reflect the site of predominant seizure activity at the time of radioisotope injection (Stefan *et al.*, 2000; Van Paesschen *et al.*, 2007) and thus, for early injections, there is a greater probability that the predominant seizure activity will be centred focally around the epileptogenic zone. In contrast, when the injection is late there is more time for spread of seizure activity (and perfusion changes) in secondary areas. Also, the "postictal switch" phenomenon (*i.e.* the time point when blood flow at the seizure focus rapidly evolves from hyperperfusion to hypoperfusion) might help to account for the association between falsely localised SPECT findings and late radiotracer injections (Rowe *et al.*, 1991; Newton *et al.*, 1992).

Extensive SPECT findings were associated with greater mean seizure duration, compared to well-localised SPECT findings. The first-pass extraction for ^{99m}Tc-HMPAO is about 85% (Van Paesschen, 2004). We hypothesize that more extensive patterns of SPECT

hyperperfusion in longer seizures are caused by the spread of epileptic activity to secondary areas during subsequent radiotracer brain extractions.

Another plausible explanation for differences in the extent of SPECT hyperperfusion is that extensively hyperperfused areas simply reflect a larger (multilobar or hemispheric) area of dysplastic cortex. Our data support this view since extratemporal surgical procedures of a single lobe were significantly more frequent than multilobar surgical procedures following well-localised SPECT findings (in contrast to extensive SPECT studies).

However, there was no difference in the extent of hyperperfusion zone between subjects undergoing either single temporal lobe or extratemporal surgery. Frontal lobe seizures are reported to be more difficult to localise using ictal SPECT because of their shorter duration and faster ictal spread, when compared to temporal lobe seizures (Van Paesschen *et al.,* 2007). Newton *et al*. (1995), nevertheless, reported a comparable yield of ictal SPECT studies in temporal and extratemporal cases (in which correct localisation was identified in 97 and 92% of patients with a known epileptogenic zone, respectively).

We did not compare the extent of SPECT hyperperfusion with dysplastic cortical regions detected by MRI since MRI does not reliably reflect the extent of the epileptogenic zone in mMCD/FCD patients (Najm *et al*., 2002; Boonyapisit *et al*., 2003) and because of the significant number of MRI-negative cases in our series (36% of SPECT examinations were performed in 31% patients with non-lesional MRI). We, however, compared SPECT findings between subjects with a visible structural lesion and those with no lesion and found significantly more zones of localised hyperperfusion in patients with normal presurgical MRI. This observation is in accord with reports showing a high sensitivity and specificity of ictal SPECT in patients without detectable MRI lesions (O'Brien *et al.,* 2000; O'Brien *et al.,* 2004; Siegel *et al.,* 2001; Cascino *et al.,* 2004). A possible explanation for more restricted hyperperfusion in these subjects is based on the fact that seizures may be caused by subtle cortical lesions associated with a limited volume of the brain tissue involved in the seizure. It is, however, important to remember that MRI-negative FCD type I may still be associated with large epileptogenic zones (Krsek *et al.,* 2009b).

Extensive SPECT findings were more frequently reported for cases of FCD type I than type II. This finding might be related to the observation that FCD type I demonstrates a difficult-to-localise pathology (Krsek *et al.,* 2008) that may extend beyond boundaries of an MRI-visible lesion (Najm *et al.,* 2002, Krsek *et al.,* 2009b). We found no extensive SPECT hyperperfusion findings in patients with mMCD (based on 18 SPECT studies performed for 10 patients, three of whom had confirmed MRI features typical of cortical malformations). This observation is difficult to reconcile as our knowledge of mMCD is limited to one report of a large series of patients (Krsek *et al.,* 2008) and mMCD is not included in the new classification system of FCD (Blümcke *et al*., 2011). We speculate that minor structural pathology, such as mMCD, is associated with more localised epileptogenic zones with a more restricted ictal zone of hyperperfusion.

We did not find an association between SPECT findings and type of seizure, according to the international classification (SPS, CPS, SGTCS). Van Paesschen *et al*. (2000) reported lowest sensitivity of ictal SPECT in simple partial seizures, with no information reported in 40% of cases. The greatest sensitivity in complex partial seizures was reported in a series of temporal lobe epilepsy patients (Shin *et al.,* 2002). We suggest that these different results might be explained by the age of our cohort. Previous reports include mainly adults, whereas in this study, we focused on paediatric cases. It is well known that the international classification of seizures is difficult to apply for children younger than 3 years (Troester and Rekate, 2009).

Regarding the extent of SPECT hyperperfusion and ictal scalp EEG pattern during injected seizures, we observed that widespread EEG findings were more frequently associated with extensive SPECT findings than with non-localised SPECT findings. There was a non-significant trend in association between well-localised SPECT findings and more localised scalp EEG ictal onset zones. These data are in accord with the study of Lee *et al*. (2006) who showed a trend in accurate ictal SPECT localisation in patients with localising ictal scalp EEG. The same study, nevertheless, reported the correct localisation of the seizure onset zone even in patients with non-localising EEG and suggested that imaging of the cerebral hyperperfusion zone might be independent of neuronal activity detected by scalp EEG (Lee *et al*., 2006).

A limitation of our report is the retrospective nature of the study and the fact that ictal-interictal subtractions and the SISCOM technique was not performed. However, in our previous study, we evaluated the predictive value of ictal SPECT for outcome after excisional epilepsy surgery in the same group of patients (Krsek *et al.,* 2013) and the results were comparable to studies using the SISCOM technique.

The radioligand used in our study was 99mTc-HMPAO. The 99mTc-HMPAO radioligand has been replaced in some institutions by 99mTc-ECD due to some technical advantages. After brain uptake, 99mTc-ECD is stable for 6-8 hours and 99mTc-HMPAO for four hours. 99mTc-ECD is cleared from the body more rapidly than 99mTc-HMPAO (Van Paesschen, 2004). The sensitivity and specificity of 99mTc-ECD was greater than that of unstabilised 99mTc-HMPAO in patients with partial

intractable epilepsy (O'Brien *et al*., 1999b). Léveillé *et al*. (1992) described factors that make images using 99mTc-ECD "easier to interpret". However, Lee *et al*. (2002) reported that stabilised 99mTc-HMPAO and 99mTc-ECD demonstrate a similar level of sensitivity in temporal lobe epilepsy, moreover, sensitivity to 99mTc-HMPAO was superior in neocortical epilepsy. Some differences in cerebral distribution of both radioligands have been described (Asenbaum *et al*., 1998). We therefore cannot exclude a minor effect based on the differences between the radioligands on SPECT findings, however, we do not expect this to significantly alter the overall results of our study. □

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