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ORIGINAL ARTICLE

Determinants of successful ictal SPECT injection in phase 1 epilepsy presurgical evaluation: Findings from the pediatric epilepsy research consortium surgery database project

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Abstract

Objectives: The main goal of presurgical evaluation in drug-resistant focal epilepsy is to identify a seizure onset zone (SOZ). Of the noninvasive, yet resource-intensive tests available, ictal single-photon emission computed tomography (SPECT) aids SOZ localization by measuring focal increases in blood flow within the SOZ via intravenous peri-ictal radionuclide administration. Recent studies indicate that geographic and center-specific factors impact utilization of these diagnostic procedures. Our study analyzed successful ictal SPECT acquisition (defined as peri-ictal injection during inpatient admission) using surgery-related data from the Pediatric Epilepsy Research Consortium (PERC) surgery database.

Rani Singh and Lily Wong-Kisiel contributed equally to this manuscript.

We hypothesized that a high seizure burden, longer duration of video EEG monitoring (VEEG), and more center-specific hours of SPECT availability would increase the likelihood of successful ictal SPECT.

Methods: We identified study participants (≤18 years of age) who underwent SPECT as part of their phase 1 VEEG from January 2018 to June 2022. We assessed association between ictal SPECT outcomes (success vs. failure) and variables including patient demographics, epilepsy history, and center-specific SPECT practices.

Results: Phase 1 VEEG monitoring with ictal SPECT injection was planned in 297 participants and successful in 255 participants (85.86%). On multivariable analysis, the likelihood of a successful SPECT injection was higher in patients of non-Hispanic ethnicity ($p = 0.040$), shorter duration VEEG ($p = 0.004$), and higher hours of available SPECT services ($p < 0.001$). Higher seizure frequency ($p = 0.033$) was significant only in bivariate analysis. Patients treated at centers with more operational hours were more likely to experience pre-admission protocols prior to VEEG ($p = 0.002$).

Significance: There is inter-center variability in protocols and SPECT acquisition capabilities. Shorter duration of EEG monitoring, non-Hispanic ethnicity (when on private insurance), extended operational hours of nuclear medicine as noted on multivariate analysis and higher seizure frequency in bivariate analysis are strongly associated with successful ictal SPECT injection.

Plain Language Summary: In pediatric patients with drug-resistant epilepsy, single-photon emission computed tomography (SPECT) scans can be helpful in localizing seizure onset zone. However, due to many logistical challenges described below, which include not only the half-life of the technetium isotope used to inject intravenously during a seizure (called the ictal SPECT scan) but also available nuclear scanner time in addition to the unpredictability of seizures, obtaining an ictal SPECT during a planned elective inpatient hospital stay is not guaranteed. Thus, as healthcare costs increase, planning a prolonged hospital stay during which an ictal SPECT scan is not feasible is not optimal. We leveraged our prospective surgery database to look at center-specific factors and patient-specific factors associated with an ictal SPECT injection in the first, pediatric-focussed, large-scale, multicenter, prospective, SPECT feasibility study. We found that longer availability of the scanner is the most important center-specific factor in assuring ictal SPECT injection. Although seizure frequency is an important patient-specific factor on bivariate analysis, this factor lost statistical significance when other factors like patient insurance status and video EEG duration were also considered in our multivariable logistical model.

KEYWORDS

epilepsy surgery, institutional factors, nuclear medicine, operational hours, video EEG duration

1 | INTRODUCTION

Epilepsy affects 1%–2% of children, and of these, one-third experience drug-resistant epilepsy (DRE), with many becoming candidates for epilepsy surgery.[1] One goal of the presurgical evaluation or a phase 1 evaluation in the epilepsy monitoring unit (EMU), henceforth referred to as phase 1 VEEG, is the identification of a seizure onset zone (SOZ) or network. There is an expanding range of neurophysiologic and imaging modalities available for presurgical evaluation that may assist in localization of the SOZ, ideally leading to surgical disruption or disconnection of the seizure network to cure or significantly improve the patient's epilepsy. Choosing the noninvasive imaging modality that is best suited for the evaluation of DRE is tailored to an individual patient according to the presumed underlying etiology, electro-clinical features, and availability of resources at the evaluating institutions.[2] Data continue to support the clinical benefits of multimodal imaging with combined analysis of magnetic resonance imaging (MRI), positron emission tomography (PET), and/or single-photon emission computed tomography (SPECT) to optimize the detection of subtle epileptogenic lesions such as focal cortical dysplasia.[2] In patients with DRE that do not have an MRI-evident lesion, PET, SPECT, and magnetoencephalography (MEG) scans hold special value in localizing interictal and ictal changes that can suggest the location of the SOZ and may guide further invasive electroencephalography (EEG) studies.[3–5]

While PET and MEG scans can be obtained on an outpatient basis, SPECT scans are typically obtained during a phase 1 VEEG. The goal of a phase 1 VEEG with SPECT is not only to record habitual seizures but also to further achieve injection of a technetium –Tc99m radiotracer (hexamethylene propylene amine – HMPAO or ethyl cysteine dimer – ECD) within seconds of seizure onset (meaning a peri-ictal injection, henceforth called ictal SPECT) followed by a computed tomography-based scan to study regional cerebral blood perfusion. Since there is a significant increase in cerebral perfusion during a seizure, the ictal SPECT is compared to that obtained interictally (baseline or interictal SPECT) either visually or through special procedures like subtraction ictal SPECT co-registered to MRI (SISCOM) to identify focal areas of increased cerebral perfusion and further localize the SOZ.[6]

The unpredictability of seizure occurrence and the limited availability of injection windows due to radiotracer decay (typically radiotracer is usable for only 6 h) make it challenging to execute successfully an ictal SPECT scan during the EMU admission.[7] Variables that affect ictal SPECT injection include those related to access to a SPECT scanner, such as availability of radiotracer doses through each day and/or duration of admission, availability of scanner time in the nuclear medicine department, availability of personnel trained to handle and inject the radiotracer at the bedside, and availability of unmanned injectors.[7]

In pediatric DRE, a good quality scan often also necessitates the need for anesthesia support in young children and those with developmental delay. Although no standardized protocols exist, in real-world practice, patient and EMU variables affecting ictal SPECT injection include EEG monitoring practices (protocols that triage patients with more frequent seizures to be admitted for SPECT), as well as patients' seizure cycles, including nighttime versus daytime seizures and frequency of seizures. Obtaining an ictal SPECT scan is therefore highly resource intensive. It involves not only commitment on part of the patient to allow seizure capture during a limited time frame but also extensive preplanning for the admission while balancing safety considerations (e.g., weaning antiseizure medications [ASMs], changing sleep cycles in the EMU, implementing activation procedures). While the clinical effectiveness and cost-effectiveness of MRI and VEEG are established,[8] there are limited data on the cost-effectiveness of advanced neuroimaging techniques including SPECT.[9] A phase 1 VEEG that does not achieve the goal of ictal SPECT

Key points

- Ictal SPECT as a presurgical imaging modality is resource intensive.
- Factors associated with a successful ictal SPECT injection in children have not been studied systematically.
- Among patient-specific factors, daily seizure frequency, non-Hispanic ethnicity, and short video EEG stay were associated with SPECT success.
- Among center-specific variables, longer hours of SPECT availability had the strongest association with increased likelihood of SPECT success.
- Pre-admission medication wean or pre-admission assessment was not associated with SPECT success.
- Centers with longer SPECT availability were more likely to include phone calls as part of their pre-admission assessment process.

injection adds to the cost of presurgical monitoring and may delay eventual epilepsy surgery if ictal SPECT is deemed to be a critical component of the presurgical evaluation.

Considering that ictal SPECT requires significant resources and there is a notable shortage of detailed data on patient or seizure characteristics that predict successful ictal SPECT injection, we leveraged the Pediatric Epilepsy Research Consortium (PERC) surgery database to investigate and identify factors linked with successful SPECT injections and to analyze how these factors differ across a national network of pediatric epilepsy centers in the United States (US).

This is the first feasibility study in pediatric DRE on such a large-scale detailing factors associated with completing an ictal SPECT during a phase 1 VEEG admission.

Since 2018, the PERC Special Interest Group on Pediatric Epilepsy Surgery has maintained a multicenter, prospective, observational institutional review board (IRB)-approved registry including data from collaborating US pediatric epilepsy centers. Although we planned to analyze all available data, we hypothesized that higher frequency of pre-admission seizures, longer duration of phase 1 VEEG and longer hours of availability of SPECT scanner time would be strongly correlated with obtaining a successful ictal SPECT injection during phase 1 VEEG.

2 | METHODS

The Pediatric Epilepsy Surgery Database, a project of PERC (www.pediatricerc.com), is a collaboration of US pediatric epilepsy centers that prospectively enroll children (0–18 years of age) referred for evaluation of surgical therapy for epilepsy. Sites identify patients for enrollment if they are (i) admitted for presurgical epilepsy evaluation; (ii) discussed in a multidisciplinary epilepsy surgery conference; or (iii) undergo epilepsy surgery during the enrollment period. Patients may be enrolled regardless of whether they ultimately progress to surgical therapy. Database enrollment began in January 2018 and continues with rolling inclusion and data contribution. Detailed methods of the database project and data collection have been described previously.[10]

This study included patients enrolled between January 2018 and June 2022 from 20 centers for which SPECT scan was a planned portion of the evaluation (Appendix A). Phase 1 VEEG data for presurgical evaluation were included. Factors abstracted included patient demographic factors (center, sex, race, ethnicity, distance from hospital, insurance type); clinical and epilepsy history (cognitive state, neurological exam, age at seizure onset, age at referral for presurgical evaluation, number of current ASMs, seizure frequency, seizure types including focal versus generalized, aware versus impaired awareness, motor versus non-motor, and duration of phase 1 VEEG monitoring). SPECT successes were defined as cases in which ictal SPECT was obtained, and failures were all other outcomes, regardless of the SPECT localization results.

2.1 | Secondary analyses

Details regarding center-specific SPECT practices were solicited from site principal investigators, and their associations with the likelihood of SPECT success were analyzed. The principal investigator at each participating institution was surveyed regarding center-specific practices through an email questionnaire (Appendix B). Access to SPECT varied greatly among centers, not only in the number of hours of SPECT available per day but also number of days available per week with most centers limited to selected weekdays. Due to this variability, the number of hours per week when SPECT was available was used as the unit measure of SPECT availability. In addition, case volume for each center was determined. Quartile rankings were assigned to each center for the total number of cases contributed during the study period and for the hours per week of SPECT availability. Practice data also included pre-admission medication wean practices and pre-admission assessments (phone calls).

2.2 | Statistical analyses

The demographic and clinical characteristics of the patient population and the practices of contributing centers were detailed using frequencies and percentages for categorical variables and means with standard deviation (SD) or medians with interquartile ranges (IQR) for continuous variables, as applicable. Subsequently, mixed-effects logistic regression was employed to investigate the influence of patient (demographic and clinical) characteristics, as well as contributing center practices, on the primary outcome of SPECT success. This approach incorporated a random intercept for each patient while also adjusting for potential clustering effects of patients within institutions. Centers treating three or fewer patients were aggregated to better specify the clustering effect. The analysis proceeded to a multivariable model, including only those variables identified as significant in bivariate analyses. The model also examined the pronounced effect of ethnicity and whether dependent on insurance status. Given the high success rates of SPECT, limitations in statistical power precluded a thorough examination of additional

interaction effects in the final composite model. Statistical analyses were performed using SAS software (version 9.4, SAS Institute Inc., Carey, NC) and IBM SPSS Statistics for Windows (version 29.0, Armonk, NY: IBM Corp).

3 | RESULTS

3.1 | Patient characteristics

Phase 1 VEEG for ictal SPECT was planned in 297 patients from 17 participating centers (see details of demographic and clinical characteristics in Table 1). The average age of patients at the onset of seizures was 5.8 years (SD = 4.5), and age at the time of referral was 11.5 years (SD = 4.7). The majority of patients identified as White (80.3%) and non-Hispanic (83.4%). The gender distribution was nearly equal, with 49.5% male and 50.5% female patients. About 40% were covered by public health insurance. In terms of proximity to the contributing center, 43.7% lived within 50 miles, 21.0% between 51 and 100 miles, 28.5% between 101 and 500 miles, and 6.8% lived more than 500 miles away, including two international cases. The average duration of video EEG was 100.7 h (SD = 62.8). Clinically, 45.9% showed abnormalities on neurological exam and 66.1% had abnormal MRI scans, with 78.2% MRI congruence with EEG localization. Regarding seizure frequency, 32.7% of patients experienced daily seizures, 31.7% weekly, 22.6% monthly, and 13.1% less frequently than monthly. Focal seizures were observed in 88.9% and presented with impaired awareness in 74.0% of patients. Pre-admission assessments were conducted for 30.6% of the patients, and pre-admission ASM weaning occurred in 55.6%. The evaluation of weekly available SPECT hours across the 17 participating centers revealed the following quartiles: Q1 <=30 h/week, Q2 31–32 h/week, Q3 33–40 h/week, and Q4 > 40 h/week. The percentage of patients treated at centers corresponding to these quartiles were 29.3%, 21.5%, 26.3%, and 22.9%, respectively. The number of phase 1 VEEG cases attempted for ictal SPECT per center ranged between 1 and 54 cases. The distribution of SPECT total volume at the contributing centers described by quartiles: Q1 with ≤3 patients, Q2 with 4–11 patients, Q3 with 12–26 patients, and Q4 with more than 26 patients. Correspondingly, the percentages of patients treated at centers within these quartiles were 2.7%, 11.8%, 26.3%, and 59.3%, respectively. At the center level, 9 of 17 centers routinely performed pre-admission (phone call) clinical assessments between a member of the epilepsy team and the patient's family in the weeks prior to admission to obtain details about seizure frequency, last seizure (decision to admit versus postpone admission), distance to be traveled to the hospital, and history of status epilepticus (to determine if pre-admission medication wean was appropriate). Eleven centers routinely instituted ASM weaning during the several days preceding admission for SPECT injection.

3.2 | Impact of patient and seizure characteristics on SPECT success

SPECT was successfully performed in 255 patients, achieving an 85.86% success rate, as detailed in Table 2. This high success rate was largely consistent across various demographic and clinical characteristics, with notable exceptions being the duration of video EEG and patient ethnicity, where differences were statistically significant ($p < .05$). Specifically, the average duration of video EEG in the SPECT success group was 96.9 h (SD = 57.5), in contrast to 123.6 h (SD = 85.5) in the group where SPECT failed. This translated to a 1% reduction in the odds of successful SPECT per additional hour of EEG (OR = 0.99, 95% Confidence Interval [CI] = 0.988–0.998, $p = .004$). Additionally, the odds of success were 56% lower in Hispanic patients compared to non-Hispanic patients (OR = 0.44, 95% CI = 0.20–0.96, $p = .040$). SPECT success was associated with higher frequency of seizures (daily 91.8%, weekly, 86.2%, and monthly or less frequent 80.2%, $p = 0.033$), Table 3. However, seizure onset characteristics, such as focal onset, impaired awareness, and focal to bilateral tonic–clonic transitions, did not significantly influence the likelihood of SPECT success ($p > .05$).

3.3 | Impact of center-specific practices on SPECT success

SPECT success did not demonstrate an association with center case volume, $p = .393$, Table 4. SPECT success was more likely with longer hours of available SPECT per week (median hours of available SPECT per week: SPECT success 40 h, IQR: 40.0 vs. SPECT failure 30 h, IQR: 30–35, $p < 0.001$). Notably, patients treated at centers with more SPECT operational hours (>32 vs. <=32 h/week) were more likely to have pre-admission (phone) protocols (39.0% vs. 22.5%, $X^2_{[df=1]}$, $p = 0.002$). Pre-admission ASM weaning and assessments did not appear to contribute independently to successful SPECT acquisition ($p > .05$).

3.4 | Composite of factors contributing to SPECT success

The final model incorporates adjustments for factors identified as significant in the bivariate analyses with

TABLE 1 Characteristics of patient population and center-specific practices.

	Overall $N = 297$
Patient demographic and clinical characteristics	
Female, *n* (%)	150 (50.5%)
Age at seizure onset (years), mean (SD)	5.8 (4.5)
Age at referral (years), mean (SD)	11.5 (4.7)
# ASMs at phase 1 evaluation, mean (SD)	2.3 (0.9)
Duration of video EEG (hours), mean (SD)	100.7 (62.8)
Race-White, *n* (%)	237 (80.3%)
Ethnicity-Hispanic, *n* (%)	49 (16.6%)
Insurance type-public[a] *n* (%):	118 (40.0%)
Distance from home to contributing center, (mi), *n* (%)	
<=50 miles	129 (43.7%)
51–100	62 (21.0%)
101–500	84 (28.5%)
>500	20 (6.8%)
Abnormal neurological exam, *n* (%)	133 (45.9%)
No prior phase 1 evaluation, *n* (%)	199 (67.7%)
Abnormal MRI brain, *n* (%)	195 (66.1%)
Abnormal MRI congruent with EEG localization, *n* (%)	151 (78.2%)
Seizure characteristics	
Seizure frequency, *n* (%):	
Daily	97 (32.7%)
Weekly	94 (31.7%)
Monthly	67 (22.6%)
>Monthly	39 (13.1%)
Seizure onset descriptors	
Focal seizure onset, *n* (%)	264 (88.9%)
By impaired awareness, *n* (%)	194 (74.0%)
Focal to bilateral tonic–clonic, *n* (%)	36 (13.6%)
Center-specific practices	
Hours of available SPECT per week, median [IQR]	32.0 [30.0,40.0]
Institutional-level quartiles of SPECT hours available, *n* (%)	
Q1 (≤30 h/week)	87 (29.3%)
Q2 (31–32)	64 (21.5%)
Q3 (33–40)	78 (26.3%)
Q4 (>40)	68 (22.9%)
Institutional-level quartiles of SPECT total volume, *n* (%)	
Q1 (≤3 patients)	8 (2.7%)
Q2 (4–11)	35 (11.8%)
Q3 (12–26)	78 (26.3%)
Q4 (>26)	176 (59.3%)
ASM wean, *n* (%)	165 (55.6%)
Pre-admission assessment, *n* (%)	91 (30.6%)

Note: Table reports mean (SD), median [IQR], or *n* (valid %) among those with known values: $N = 297$ for sex, age at seizure onset, age at referral, MRI brain, site variables. $N = 296$ number of ASMs at phase 1. $N = 295$ for duration of video EEG, race, ethnicity, distance, and insurance type. $N = 294$ for prior phase 1 evaluation. $N = 290$ for neurological exam. $N = 193$ for MRI concordant with EEG localization. $N = 297$ for seizure frequency, mode of seizure onset. $N = 262$ for seizure type "By awareness." $N = 264$ for seizure type "Focal to bilateral tonic–clonic."

Abbreviations: SD, standard deviation, SPECT, single-photon emission computed tomography.

[a]Public insurance includes two self-pay patients.

TABLE 2 Patient characteristics evaluated in relation to SPECT success.

	SPECT success % or mean (SD)	SPECT failure % or mean (SD)	Odds ratio SPECT successful OR (95% CI)[a]	*p*-Val[a] ^p
Overall, *n*=297	85.8%	14.2%	—	
Sex				
Female, *n* = 150	88.0%	12.0%	1.39 (0.71, 2.73)	0.332
Male, *n* = 147	83.7%	16.3%	Reference	
Age at seizure onset, years.	5.9 (4.5)	5.2 (4.5)	1.03 (0.95, 1.11)	0.508
Age at referral, years	11.4 (4.7)	12.0 (4.9)	0.97 (0.90, 1.05)	0.458
# ASMs at phase 1 eval.	2.3 (0.9)	2.2 (0.9)	1.17 (0.80, 1.72)	0.426
Duration video EEG, hours.	96.9 (57.5)	123.6 (85.5)	0.993 (0.988, 0.998)	**0.004**
Race				
White, *n* = 237	86.1%	13.9%	1.32 (0.58, 3.01)	0.514
Non-White, *n* = 58	84.5%	15.5%	Reference	
Ethnicity				
Hispanic, *n* = 49	73.5%	26.5%	0.44 (0.20, 0.96)	**0.040**
Non-Hispanic, *n* = 246	88.2%	11.8%	Reference	
Insurance				
Private, *n* = 177	87.0%	13.0%	1.20 (0.60, 2.39)	0.613
Public, *n* = 118	83.9%	16.1%	Reference	
Distance, home to center				0.506
50 miles or less, *n* = 129	84.5%	15.5%	3.14 (0.38, 26.22)	0.290
51–100 miles, *n* = 62	83.9%	16.1%	1.27 (0.54, 3.00)	0.579
101–500 miles, *n* = 84	86.9%	13.1%	0.74 (0.31, 1.76)	0.488
Over 500 miles, *n* = 20	95.0%	5.0%	Reference	
Neurological exam				
Normal, *n* = 157	84.7%	15.3%	Reference	
Abnormal, *n* = 133	86.5%	13.5%	1.17 (0.59, 2.31)	0.658
Prior phase 1 evaluation				
No, *n* = 199	84.9%	15.1%	Reference	
Yes, *n* = 95	87.4%	12.6%	1.33 (0.63, 2.80)	0.446
MRI brain scan				
Normal, *n* = 100	85.0%	15.0%	Reference	
Abnormal, *n* = 195	86.2%	13.8%	1.06 (0.53, 2.13)	0.873
MRI congruent with EEG localization				
No, *n* = 42	85.7%	14.3%	Reference	
Yes, *n* = 151	86.1%	13.9%	1.11 (0.41, 3.02)	0.839

Note: Institutions where three or fewer patients treated were combined in the random effect term.

[a]OR (95% CI) and associated *p*-value comparing factors level to reference group or per one unit increase in continuous variables based on results from mixed-effects model that adjusts for clustering effect of patients within institution.

Bold values indicate statistically significant value < 0.05.

inclusion of a notable interaction between ethnicity and insurance (shown in Table 5). This interaction revealed that the impact of ethnicity on odds of SPECT success was significant among patients with private insurance, where odds of success was 87% lower in Hispanic compared to non-Hispanic patients (OR = 0.13, 95% CI 0.03, 0.49, $p = .003$). No significant differences were observed in the odds of SPECT success due to ethnicity among those covered by public health insurance (OR = 0.84, 95% CI 0.28, 2.55, $p = .759$). More hours available to perform SPECT and shorter duration of VEEG continued to relate to increased odds of SPECT success in the adjusted model,

TABLE 3 Seizure characteristics evaluated in relation to SPECT Success.

	SPECT success % or mean (SD)	SPECT failure % or mean (SD)	Odds ratio SPECT successful OR (95% CI)[a]	*p*-Val[a]
Overall, $n=297$	85.8%	14.2%	—	
Seizure frequency				0.096
Daily, $n=97$	91.8%	8.2%	Reference	
Weekly, $n=94$	86.2%	13.8%	0.59 (0.23, 1.53)	0.259
>=Monthly, $n=106$	80.2%	19.8%	0.38 (0.16, 0.93)	**0.033**
Seizure onset descriptors				
Focal seizure onset				
No, $n=33$	87.9%	12.1%	Reference	0.966
Yes, $n=264$	85.6%	14.4%	0.98 (0.31, 3.08)	
By impaired awareness				
No, $n=68$	88.2%	11.8%	Reference	
Yes, $n=194$	84.5%	15.5%	0.93 (0.39, 2.22)	0.861
Focal to bilateral tonic–clonic				
No, $n=228$	86.8%	13.2%	Reference	
Yes, $n=36$	77.8%	22.2%	0.72 (0.28, 1.82)	0.482

Note: Institutions where three or fewer patients treated were combined in the random effect term.

[a]OR (95% CI) and associated *p*-value comparing factors level to reference group based on results from mixed-effects model that adjusts for clustering effect of patients within institution.

Bold values indicate statistically significant value < 0.05.

$p<.05$. However, the influence of seizure frequency (daily, weekly, >= monthly) became non-significant after adjustment for other significant factors ($p=.207$).

4 | DISCUSSION

This is the first study in pediatric DRE detailing factors associated with completing an ictal SPECT during a phase 1 VEEG admission. This study identified shorter duration of EEG monitoring, higher seizure frequency, non-Hispanic ethnicity in those with private health insurance, and increased hours of SPECT availability per week as factors associated with increased likelihood of success in obtaining an ictal SPECT during presurgical evaluation for pediatric DRE. Our work also highlights the variability in institutional practices around a SPECT admission with more than half the participating centers completing a pre-admission phone assessment and adjusting ASM doses prior to admission. Centers with longer SPECT hours were more likely to have pre-admission protocols in place, suggesting more attention to process implementation at these centers. Yet these characteristics did not lead to higher likelihoods of obtaining a successful SPECT as noted in our study. All patients entered the PERC database have been referred for presurgical assessment. For purposes of this study, we did not further assess the localization of seizures as temporal or extratemporal on VEEG but instead focussed on seizure semiology (focal versus generalized; maintained awareness versus impaired awareness since we felt that semiology was more likely to impact decision to inject during a particular seizure).

Pediatric patients referred for epilepsy surgery are more likely to have complex epilepsies with greater cases of extratemporal, non-lesional, or MRI-negative presentation, warranting more extensive presurgical noninvasive testing.[11] This is further evidenced in the literature from the data published by the National Association of Epilepsy Centers (NAEC) showing that the annual rate of extratemporal surgeries continued to increase.[12,13] Presurgical testing, however, is very resource intensive and is highly dependent on individual epilepsy center policies and geography within the US. These factors may lead to differences in outcomes and contribute to disparities in access to surgical treatment.[14] In the same NAEC paper described above, SPECT was reported to be used by 2%–30% of level 4 epilepsy centers during phase 1 VEEG.[14]

In addition to institution-specific and patient-specific protocols, successful SPECT may also rely on constant vigilance of the epileptologist, bedside nurse and VEEG technician.[15,16]

Despite extensive literature on the value of concordant SPECT findings in epilepsy surgery, there are no published data looking at the logistics of obtaining a pediatric ictal SPECT in multicenter studies in terms of

TABLE 4 Institutional practices at 17 contributing centers evaluated in relation to SPECT success.

	SPECT success % or mean (SD)	SPECT failure % or mean (SD)	Odds ratio SPECT successful OR (95% CI)[a]	*p*-Val[a]
Overall, $n=297$	85.8%	14.2%	—	
Hours of available SPECT per week, median [IQR]	40.0 [30.0, 40.0]	30.0 [30.0, 35.0]	—	**<0.001**[b]
Institutional-level quartiles of SPECT hours available				**0.007**
Q1 (≤30 h/week), $n=87$	74.7%	25.3%	0.25 (0.09, 0.69)	**0.008**
Q2 (31–32), $n=64$	85.9%	14.1%	0.52 (0.17, 1.62)	0.260
Q3 (33–40), $n=78$	92.3%	7.7%	0.96 (0.29, 3.20)	0.949
Q4 (>40), $n=68$	92.6%	7.4%	Reference	
Short (Q1&Q2), $n=151$	79.5%	20.5%	0.33 (0.15, 0.76)	**0.009**
Long (Q3&Q4), $n=146$	92.5%	7.5%	Reference	
Institutional-level quartiles of SPECT total volume				0.393
Q1 (≤3 patients), $n=8$	62.5%	37.5%	0.24 (0.03, 1.65)	0.144
Q2 (4–11), $n=35$	82.9%	17.1%	0.70 (0.20, 2.44)	0.569
Q3 (12–26), $n=78$	89.7%	10.3%	1.27 (0.39, 4.13)	0.687
Q4 (>26), $n=176$	85.8%	14.2%	Reference	
ASM wean				
No, $n=132$	82.6%	17.4%	Reference	
Yes, $n=165$	88.5%	11.5%	1.28 (0.50, 3.33)	0.606
Pre-admission assessment				
No, $n=206$	85.9%	14.1%	Reference	
Yes, $n=91$	85.7%	14.3%	0.66 (0.25, 1.80)	0.420

Note: Institutions where three or fewer patients treated were combined in the random effect term.

Abbreviation: ASM, antiseizure medication.

[a]OR (95% CI) and associated *p*-value comparing factors level to reference group based on results from mixed-effects model that adjusts for clustering effect of patients within institution.

[b]*p*-Value based on simple non-parametric Mann–Whitney U-test of distributional difference in hours between groups; transformations did not normalize the distribution and factor examined in mixed model on categorical scale by quartiles.

Bold values indicate statistically significant value < 0.05.

obtaining injection during phase 1 VEEG. Most literature related to SPECT speaks to the "utility" of SPECT in terms of concordance of SPECT to EEG and eventual seizure outcomes. Few studies have looked solely at "feasibility" of SPECT like ours did. A past pediatric study from Italy in 2019[6] looking at SISCOM in pediatric DRE indicated that out of 71 hospitalizations for the purpose of obtaining an ictal SPECT only 51 were successful (73%), while other authors[17] describe a rate of 71.9% (64 out of 89 admissions). An adult, single-center study out of Australia that looked at feasibility of SPECT[18] describes unsuccessful admission rate of 19.3% and thus numbers of successful admissions of 80%. Authors describe SPECT availability as 21 h (Tuesday to Thursday from 9 AM to 4 PM). Our ictal SPECT success rate of 86% is higher than that previously reported by another study and is likely due to the fact that >50% of the patients in our study were treated at centers that had an overall higher availability of SPECT hours (>30 h/week described in Table 1). Repeat SPECT or hospitalization could be used as a surrogate for unsuccessful SPECT as we have defined above, but these also include "non-localizing/negative SPECT and injection of non-epileptic events" with a quoted range of 13%–27% for repeated admissions.[7,19] A single-center study published in 2023 that included 103 adults from an Australian EMU showed that only 38.8% of all eligible seizures were successfully injected for ictal SPECT.[18] Reasons for injection failures were due to seizures occurring outside of eligible windows (19.3%) or non-injectable seizures (62.3%). This same study also found PET concordance, high seizure frequency, and ability of patient to indicate seizure onset as factors associated with SPECT success. Our database did not specifically look for or describe

TABLE 5 Adjusted odds SPECT successful relative to reference category.

	Odds ratio SPECT successful OR_{adj} (95% CI)[a]	*p*-Val[a]
Duration video EEG, hours	0.993 (0.988, 0.998)	**0.009**
Interaction: Ethnicity * Insurance		**0.031**
In patients w/private insurance		
Hispanic	0.13 (0.03, 0.49)	**0.003**
Non-Hispanic	Reference	
In patients w/public insurance		
Hispanic	0.84 (0.28, 2.55)	0.759
Non-Hispanic	Reference	
Seizure frequency		0.207
Daily	Reference	
Weekly	0.61 (0.22, 1.67)	0.330
>=Monthly	0.42 (0.16, 1.10)	0.078
Institutional-level SPECT hours available		
Short (Q1&Q2<=32 h/week)	Reference	
Long (Q3&Q4, >32 h/week)	3.04 (1.11, 8.29)	**0.030**

Note: Institutions where three or fewer patients treated were combined in the random effect term.

[a]OR (95% CI) and associated *p*-value comparing factors level to reference group or per 1 h increase in duration video EEG in mixed-effects model that adjusts for all factors significant in bivariate analyses, interaction effect between ethnicity and insurance, and clustering effect of patients within institution.

Bold values indicate statistically significant value < 0.05.

SPECT injectable seizures and also did not determine if some patients had multiple admissions for SPECT scans. Since the majority of our patients (69.4%, Table 1) had no prior phase 1 evaluations, we believe our data to be representative of SPECT success at initial presentation.

The average length of stay in our study of 4.19 days is similar to other published studies describing SPECT utility.[6,17,18]

In our study, the only patient factor that was associated with lack of ictal SPECT success was having Hispanic/Latino ethnicity. While we did not look for a center effect, how identifying as Hispanic/Latino was associated with SPECT failure remains unclear. Further analysis of this observation revealed that Hispanic patients with private insurance had lower odds of SPECT success compared to their non-Hispanic counterparts. It is possible that communication barriers could contribute to this result. It is also possible that centers serving a larger Hispanic population on public insurance have more comprehensive translation services or other services not evident through our study. This disparity in presurgical evaluation has not been previously described. An unsuccessful SPECT phase 1 VEEG evaluation would be expected to delay eventual epilepsy surgery. Although a paper describing an unexplored association (which would contradict our findings) between Hispanic ethnicity and quicker time to surgery is published by Baca et al.,[20] other literature shows disparities for Black/African-American and Hispanic populations in eventually obtaining epilepsy surgery; however, authors do not delve into details of whether the disparities are concentrated at the presurgical evaluation state.[21,22]

One might expect seizure frequency to correlate positively with successful ictal SPECT injection. Although daily seizures were more likely associated with ictal SPECT success, we did not find a statistically significant difference between daily and weekly seizures with respect to SPECT success. Further details missing from our database were whether seizures were nocturnal/diurnal; whether they were short or long lasting and could have contributed to this finding (e.g., short, frequent, nocturnal seizures leading to failed injections despite occurring daily). The adult study by Cosentino et al. also found that patients with seizures occurring more than once per week had a higher likelihood of successful ictal SPECT.[18]

Duration of VEEG monitoring showed a negative correlation such that longer phase 1 VEEG did not predict ictal SPECT success. Rather, center-specific hours of available SPECT during the VEEG admission contributed to ictal SPECT success. We hypothesize that a successful SPECT resulted in a shorter EMU admission. In other words, once ictal SPECT was successfully obtained, VEEG was no longer needed for those patients with quicker time to ictal SPECT capture. On the other hand, our finding of a negative correlation between a longer VEEG admission and successful SPECT can be explained as follows: in a real-world scenario, a patient might also have to stay longer in the EMU to characterize spells even if they do not occur during the available SPECT window. Additionally, patients who have been weaned off their ASM to obtain a SPECT scan will frequently be kept an additional day or two even after closure of the SPECT window, so that their ASMs can be restarted while continuous EEG monitoring is maintained for safety purposes.

Recent data from the NAEC suggest that 62% of epilepsy centers will wean ASMs prior to a phase 1 VEEG.[23] However, many practitioners do not wean ASMs prior to a presurgical EMU admission due to the risks of increased seizures prior to admission and increased risk of sudden unexpected death in epilepsy (SUDEP). Even in those who do, we found that pre-admission ASM wean was not significantly associated with SPECT injection success. Each institution's SPECT availability (between 16 h per week

and 105 h per week) contributed to local protocols in pre-admission assessments or ASM wean prior to phase 1 VEEG to increase likelihood of ictal injection. Centers with longer SPECT hour availability were also more likely to have in place a pre-admission protocol. Phase 1 VEEG admissions are elective, and several weeks could pass between an outpatient clinic visit where a phase 1 evaluation is discussed and ordered. We feel that pre-admission education of patients and clinical assessment of ongoing need for the admission is overall good clinical practice for any phase 1 presurgical admission.

4.1 | Limitations

The PERC surgery database was designed to assess a wide range of questions related to pediatric epilepsy surgery in the US, allowing rapid selection of cohorts to address specific questions. Our data are limited by the prospective variables collected. Our database did not offer the opportunity to study percentage of seizures that were "non-injectable." The absence of seizure duration in the database presents a notable limitation in our study. Shorter seizures could pose a challenge for ictal SPECT injection, though we assume that treating teams included SPECT as part of the presurgical evaluation because stereotypical seizures for the patient were of a duration appropriate for SPECT. While the intent is to enroll all DRE patients irrespective of eventual outcome, we recognize that patients going to surgery are more likely to be enrolled, which likely biases the database toward surgical candidates and thus more successful ictal SPECT cases. Details about languages spoken and other racial demographic data were not collected to explain the disparity in success of ictal SPECT injection. Future research would benefit from incorporating these parameters to provide a more comprehensive analysis of the factors affecting SPECT success.

5 | CONCLUSIONS

This is the most extensive multicenter study to date that investigates factors which may affect ictal SPECT success in children with DRE undergoing phase 1 VEEG. Despite the variability across centers, the robust size of our study adds weight to the credibility of the factors found to be linked with successful ictal SPECT. Individual center practices associated with ictal SPECT success allow for improvement in practices at other sites and ultimately patient outcomes. Our data suggest that in considering changes to processes and investment in resources, it might be better to extend hours of SPECT availability than to extend VEEG admission days per patient. Further analysis requires prospective collection of data across centers that all follow similar practices of preparation for SPECT admission with similar scanner availability to further study factors that impact the likelihood of obtaining a successful ictal SPECT.

AUTHOR CONTRIBUTIONS

Charuta Joshi: Concept and major drafting; study design, initial draft; data contribution; editing of manuscript and final approval. Lily Wong-Kisiel: Study design; initial draft; data contribution; editing of manuscript and final approval. Rani Singh: Study design; initial draft; data contribution; editing of manuscript and final approval. Gang Liu: Initial draft; statistical analysis; editing of manuscript and final approval. Krista Eschbach: Initial draft; data contribution; editing of manuscript and final approval. Michael Ciliberto; Initial draft; data contribution; editing of manuscript and final approval. Cemal Karakas: Initial draft; data contribution; editing of manuscript and final approval. M. Scott Perry: Study design; initial draft; data contribution; editing of manuscript and final approval. Daniel Shrey: Data contribution; editing of manuscript and final approval. Adam P. Ostendorf: Data contribution; editing of manuscript and final approval. Tricia Morphew: Statistical analysis; editing of manuscript and final approval. Shilpa Reddy: Data contribution; editing of manuscript and final approval. Michael McCormack: Data contribution; editing of manuscript and final approval. Samir Karia: Data contribution; editing of manuscript and final approval. Shrishti Nangia: Data contribution; editing of manuscript and final approval.

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CONFLICT OF INTEREST STATEMENT

We confirm that we have read the Journal's position on issues involved in ethical publication and affirm that this report is consistent with those guidelines.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study can be made available from the corresponding author upon reasonable request.

DISCLOSURES

Charuta Joshi serves on the DSMC for Praxis Inc., has received an investigator-initiated grant from Jazz pharma, is a member of and associate site to the Epilepsy Study Consortium, and is on the editorial board of Epilepsy Currents – however has no relevant disclosures to this work. Rani Singh is on the advisory board for Zogenix; AKPharma, Inc.; Prasco pharma; OWPPharma; Eysz; Epilepsy Reach Foundation; Key Opinion Leader for Marinus; Research support from PERF-Pediatric Epilepsy Research Foundation; Marinus, GW Pharma/Jazz; she serves on Executive Board of Western Region of the Epilepsy Foundation of North Carolina but none of the above is relevant to this manuscript. Gang Liu has no disclosures. Cemal Karakas has no disclosures. Michael Ciliberto has no disclosures. Krista Eschbach has no disclosures. M Scott Perry is on the advisory board to UCB, Jazz Pharmaceuticals, Neurelis, Stoke Therapeutics, Marinus, Biocodex, Azurity, Cadence Neurosciences; has speaking relationship for Pyros; is involved in research paid to Cook Children's from Takeda, Encoded, Stoke Therapeutics, Neurocrine, Biocodex, UCB, but has nothing relevant to disclose for this project. Daniel Shrey has research support from the NIH, Pediatric Epilepsy Research Foundation, CHOC PSF Tithe Fund, CHOC CSO Small Grants Program but has nothing relevant to disclose for this project. Mrs. Morphew has a consultancy arrangement with CHOC Children's Research Institute and has no conflicts of interest to report, Adam Ostendorf has no disclosures. Shilpa Reddy has no disclosures. Michael McCormack has no disclosures. Samir Kaira has no disclosures. Lily Wong-Kisiel has no disclosures. The work contained within this manuscript is original and has not been submitted for publication elsewhere. Data used to complete this manuscript were obtained from the Pediatric Epilepsy Research Consortium (PERC) Surgery database and are available upon request from the authors. This study was not funded by any outside source. Patient data were obtained through the PERC database and were collected with consent or consent waived as previously described for that dataset. All institutions participating in the PERC Surgery Workgroup obtained approval from individual Institutional Review Board (IRB) review committees.

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APPENDIX A

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2. Nationwide Children's, Ohio State University, Columbus, OH, USA
3. Mayo Clinic College of Medicine, Rochester, MN, USA
4. University of Michigan, Ann Arbor, MI, USA
5. Ann and Robert H Lurie Children's Hospital, Chicago, IL, USA.
6. Children's National Hospital, Washington, DC, USA
7. Children's Hospital of Wisconsin, Milwaukee, WI, USA
8. Children's Hospital Colorado, Aurora, CO, USA
9. Children's Hospital Orange County, Orange, CA, USA
10. Atrium Health/Levine Children's Hospital, Charlotte, NC, USA
11. Maria Fareri Children's Hospital, New York Medical College, Valhalla, NY, USA
12. Weill-Cornell Medicine, New York, New York, USA.
13. Norton Children's Hospital, Louisville, KY, USA
14. University of Iowa Hospitals and Clinics, Iowa City, IA, USA
15. San Francisco Weill Institute for Neurosciences, San Francisco, California, USA.
16. Boston Children's Hospital, Boston, MA, USA
17. Doernbecher Children's Hospital, Portland, OR, USA
18. Children's Healthcare of Atlanta, Atlanta, Georgia, USA.
19. Monroe Carell Jr Children's Hospital, Nashville, TN, USA
20. University of Texas Southwestern, Children's Health, Dallas, TX, USA

APPENDIX B

Please answer the following questions about your institution SPECT practice for epilepsy surgery workup.

1. How many hours per day is SPECT available?
2. Which days of the week is SPECT available?
3. Is antiseizure medication (ASM) wean a routine option prior to EMU admission?
4. Is there routine pre-admission assessment to decide on ASM reduction?
   - What was asked in the pre-admission assessment: _____