BMJ Open

^{18}F-FDG-PET hypometabolism as a predictor of favourable outcome in epilepsy surgery: protocol for a systematic review and meta-analysis

Merran R Courtney ,[1,2,3] Ana Antonic-Baker ,[1] Benjamin Sinclair,[1] John-Paul Nicolo ,[1,2,3,4] Andrew Neal,[1,2,3,4] Meng Law,[1,5,6] Patrick Kwan,[1,2,3,4] Terence J O'Brien,[1,2,3,4] Lucy Vivash [1,2,3,4]

To cite: Courtney MR, Antonic-Baker A, Sinclair B, *et al*. ^{18}F-FDG-PET hypometabolism as a predictor of favourable outcome in epilepsy surgery: protocol for a systematic review and meta-analysis. *BMJ Open* 2022;**12**:e065440. doi:10.1136/bmjopen-2022-065440

► Prepublication history and additional supplemental material for this paper are available online. To view these files, please visit the journal online (http://dx.doi.org/10.1136/bmjopen-2022-065440).

Received 06 June 2022
Accepted 22 September 2022

For numbered affiliations see end of article.

Correspondence to
Dr Lucy Vivash;
lucy.vivash@monash.edu

ABSTRACT

Introduction A substantial proportion of patients who undergo surgery for drug resistant focal epilepsy do not become seizure free. While some factors, such as the detection of hippocampal sclerosis or a resectable lesion on MRI and electroencephalogram-MRI concordance, can predict favourable outcomes in epilepsy surgery, the prognostic value of the detection of focal hypometabolism with ^{18}F-fluorodeoxyglucose positive emission tomography (^{18}F-FDG-PET) hypometabolism is uncertain. We propose a protocol for a systematic review and meta-analysis to examine whether localisation with ^{18}F-FDG-PET hypometabolism predicts favourable outcomes in epilepsy surgery.

Methods and analysis A systematic literature search of Medline, Embase and Web of Science will be undertaken. Publications which include evaluation with ^{18}F-FDG-PET prior to surgery for drug resistant focal epilepsy, and which report ≥12 months of postoperative surgical outcome data will be included. Non-human, non-English language publications, publications with fewer than 10 participants and unpublished data will be excluded. Screening and full-text review of publications for inclusion will be undertaken by two independent investigators, with discrepancies resolved by consensus or a third investigator. Data will be extracted and pooled using random effects meta-analysis, with heterogeneity quantified using the I^2 analysis.

Ethics and dissemination Ethics approval is not required. Once complete, the systematic review will be published in a peer-reviewed journal.

PROSPERO registration number CRD42022324823.

STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ This protocol has been devised in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses protocols guidelines.
⇒ Publication of the protocol provides transparency regarding the methodology of the systematic review, reduces the risk of meta-bias and avoids duplication.
⇒ We anticipate that most publications addressing the review question will be non-randomised, which are inherently associated with a high risk of bias. We intend to evaluate each included publication for bias, using the Newcastle-Ottawa Scale for non-randomised studies and the Cochrane Risk of Bias 2 tool for randomised studies.
⇒ Relevant data may be missed by excluding non-English language publications

INTRODUCTION

Surgical resection is an efficacious and safe treatment for selected patients with drug resistant focal epilepsy,[1–3] and is also associated with higher rates of seizure freedom compared with continued best medical therapy.[4] Seizure freedom is a widely used epilepsy surgery outcome measure and is a strong predictor of improvement in health-related quality of life.[5] However, despite rigorous patient selection practices, approximately one third of patients who undergo epilepsy surgery do not become seizure free.[6–8] Identifying predictive factors of favourable outcome in epilepsy surgery may improve the proportion of patients achieving seizure freedom by better informing the patient selection process.

Successful epilepsy surgery relies on the accurate identification and resection of the epileptogenic zone. Brain ^{18}F-fluorodeoxyglucose positive emission tomography (^{18}FFDG-PET) measures regional cerebral glucose uptake and is a marker of neuronal cellular activity. Hypometabolism is an important abnormal finding in interictal ^{18}FFDG-PET and reflects dysfunctional brain tissue. It is commonly used in combination with other invasive and non-invasive methods of identifying the epileptogenic zone, such as MRI, ictal scalp electroencephalogram (EEG) and stereotactic EEG, to formulate hypotheses regarding epileptogenic zone localisation, which in turn informs surgical planning. Several factors, for example, the

detection of hippocampal sclerosis[8 9] or a resectable lesion on MRI,[7–10] and concordant MRI and ictal EEG abnormalities,[8 9 11 12] have been shown to be consistently predictive of favourable outcomes for patients following epilepsy surgery.[13] Previous meta-analyses addressing the role of localisation with ^{18}FFDG-PET as a predictor of epilepsy surgery outcome have focused on temporal[14 15] or frontal[10] lobe epilepsy surgery with inconsistent results. However, these meta-analyses were underpowered, and only one provided a detailed analysis of the role of ^{18}F-FDG-PET. Furthermore, currently ^{18}F-FDG-PET hypometabolism extending beyond a single brain lobe may be considered 'not useful' in the decision-making process regarding epilepsy surgery,[16] however, the presence of focal (involving a single lobe), compared with regional (involving two adjacent lobes) or diffuse (extending beyond two adjacent lobes) hypometabolism may be of prognostic importance. We propose a protocol for a systematic review and meta-analysis designed to examine the primary question: does localisation with ^{18}F-FDG-PET hypometabolism predict favourable outcomes in surgery for drug resistant focal epilepsy? Secondary questions that will also be addressed include:

1. Is the extent of ^{18}F-FDG-PET hypometabolism, for example focal, regional or diffuse, associated with differences in outcome following surgery for drug resistant focal epilepsy?
2. Does a certain proportion of the ^{18}F-FDG-PET hypometabolism region need to be resected to achieve seizure freedom, and does this differ between brain lobes?
3. Do differences in the underlying pathology on histological examination of the resected tissue impact localisation with ^{18}F-FDG-PET hypometabolism, and is this associated with differences in outcome following surgery for drug resistant focal epilepsy?

METHODS AND ANALYSIS

Protocol and registration

This protocol was written in accordance with thePreferred Reporting Items for Systematic Reviews and Meta-Analyses protocols guidelines[17] (online supplemental table 1). The protocol is registered in PROSPERO (CRD42022324823).

Population

The population are patients of all ages who have undergone resective surgery (lesionectomy or lobectomy) for drug resistant focal epilepsy.

Intervention assessed

The intervention to be assessed is localising ^{18}F-FDG-PET hypometabolism, as defined by concordance with other diagnostic methods (MRI, ictal scalp EEG, stereotactic EEG and/ or final decision regarding surgical site alone) and ipsilateral to the surgical site.

Control population

The control population will be individuals who undergo resective surgery for drug resistant focal epilepsy who have non-localising or no ^{18}F-FDG-PET hypometabolism.

Outcome

We will include Engel or International League Against Epilepsy (ILAE) outcome classification systems, which are widely used measures of epilepsy surgery outcomes. Favourable outcome will be defined as Engel class I 'free of disabling seizures,' ILAE class 1 'completely seizure free; no auras' or ILAE class 2 'only auras; no other seizures'.[18]

Eligibility criteria

The systematic review will include publications with ≥10 participants who were preoperatively evaluated with ^{18}F-FDG-PET prior to resective surgery for drug resistant focal epilepsy. In addition, only studies with ≥12 months of postsurgical follow-up and reporting seizure outcome data will be included.

Review articles, letters, unpublished data, non-human studies and publications in languages other than English will be excluded from the systematic review. Patients who have undergone non-resective surgeries, or procedures primarily performed with palliative intent, including hemispherectomy, will be excluded. Studies in which the surgical outcome is unable to be correlated with the ^{18}F-FDG-PET finding(s) will also be excluded.

Search strategy

Three electronic databases will be searched for eligible publications: Medline (Ovid), Embase (Ovid) and Web of Science (all databases), with the initial database searches occurring on 3 May 2022. The search terms include expanded forms and variations on "epilepsy", "seizure", "neurosurgery", "positron emission tomography" and "functional neuroimaging". The initial search will not be filtered for English language or publication type. The full search strategy for each database is available in online supplemental file.

The reference list of all included studies will be screened for other eligible publications that have not already been screened.

Selection process

Retrieved studies from database searches will be managed using Covidence Software (Veritas Health Innovation, Melbourne, Australia). All retrieved studies will be screened using title and abstract by two independent investigators. Any publication considered to be potentially eligible for inclusion by one or both investigators will be included for full-text review. The full-text reviews will be undertaken independently by two investigators, and any disagreements regarding eligibility for inclusion will be resolved by a third investigator.

Data collection

The data to be extracted includes publication details (publication year, first author, author affiliations, title, journal), patient demographics, epilepsy characteristics (seizure type, seizure frequency, age of epilepsy onset), ^{18}F-FDG-PET characteristics, method of ^{18}F-FDG-PET interpretation, presurgical investigations other than ^{18}F-FDG-PET, histopathology, proportion of hypometabolism zone resected, surgical outcome and length of post-operative follow-up.

Data will be extracted by two independent investigators into a predefined data extraction spreadsheet. We intend to contact the authors for further information if the relevant data is not reported in the original publication. The data extraction results will be compared after the first 10 publications, and if congruent, the remainder of the data collection will be performed by a single investigator. Discrepancies will be resolved by discussion and/ or by a third investigator.

Risk of bias assessment

All included studies in our systematic review and meta-analysis will be assessed for bias independently by two reviewers, and discrepancies will be resolved by consensus. Non-randomised studies, including case–control and cohort studies, will be assessed for bias using the Newcastle-Ottawa Scale (NOS).[19] The NOS assesses eight items across three domains: selection, comparability and outcome. Each item is assessed, and stars are awarded for high quality according to the NOS guidelines. The maximum score is four stars for selection, two stars for comparability and three stars for outcome. These scores can then be converted into an assessment of overall study quality as 'good,' which requires 3–4 stars in selection, 1–2 stars in comparability and 2–3 stars in outcome; 'fair,' which requires 2 stars in selection, 1–2 stars in comparability and 2–3 stars in outcome and 'poor', which includes studies with 0–1 stars in selection, or 0 stars in comparability or 0–1 stars in outcome.

If there are any randomised studies eligible for inclusion, these will be assessed for bias using the Cochrane Risk of Bias (RoB) 2 tool.[20] The Cochrane RoB 2 tool assesses randomised studies across five domains, which are the randomisation process, deviations from the intended effect, missing outcome data, measurement of outcome and reported results. The risk of bias in each domain is assessed as low, high or some concerns, according to the RoB 2 guidelines. The overall study risk of bias can then be judged as 'low risk,' if the study is assessed as low risk in all domains, 'some concerns,' if the study is assessed as some concerns in at least one domain, but not high risk in any domain, or 'high risk,' if the study is assessed as high risk in at least one domain, or some concerns in multiple domains.

Data analysis

We intend to calculate an effect size (ES) for each study, which is the proportion of patients who achieve a favourable outcome who have localising ^{18}F-FDG-PET hypometabolism compared with those without localising ^{18}F-FDG-PET hypometabolism, as defined above in the intervention. We will then use Der Simonian and Laird random effects meta-analysis to calculate the summary estimate of ES, pooled favourable outcome rate, and 95% CIs. Pooled ES will be presented as the percentage of patients achieving seizure freedom. Statistical heterogeneity of included studies will be measured with I^2.

In our secondary analysis, we will stratify studies based on age group (adult, paediatric or both), resected lobe (frontal, insular, temporal, parietal or occipital) and histopathology (hippocampal sclerosis, focal cortical dysplasia types 1 and 2, tumour, vascular malformation or other), and perform random effects meta-analyses on stratified groups. We also intend to perform subgroup analyses, expressed as a risk ratio, of the following variables on favourable outcome: extent of ^{18}F-FDG-PET hypometabolism (focal vs regional or diffuse), location of hypometabolism (temporal vs extratemporal) and proportion of hypometabolism zone resected (<50% vs ≥50%).

If sufficient data are available, from a minimum of five publications, we will perform stratified meta-analysis, using the same methodology used for the primary meta-analysis described above, and meta-regression to investigate and characterise sources of heterogeneity based on the following variables: age group (adult vs paediatric vs mixed), seizure freedom classification (Engel vs ILAE vs other), location (temporal vs extra-temporal), and duration of post-operative follow-up reported (12–23 months, 24–59 months or ≥60 months). The risk of publication bias will be assessed using a funnel plot and Egger's test.

PATIENT AND PUBLIC INVOLVEMENT

Patients or the public were not involved in the design, or conduct, or reporting, or dissemination plans of our research.

ETHICS AND DISSEMINATION

The proposed systematic review does not require ethics approval, as the data to be collected cannot be connected to individual patients. We intend to publish the results of the systematic review in a high quality, peer-reviewed journal.

DISCUSSION

Our proposed systematic review and meta-analysis will evaluate and review published data on the role of localisation with ^{18}F-FDG-PET in predicting favourable outcomes in patients undergoing epilepsy surgery. If localisation with ^{18}F-FDG-PET does predict favourable outcomes in epilepsy surgery, then this systematic review will provide evidence for the inclusion of ^{18}F-FDG-PET localisation in future multimodal outcome prediction algorithms for epilepsy surgery. We anticipate that our systematic review will also help to guide future research into the role of

^{18}F-FDG-PET in epilepsy surgery by further characterising knowledge gaps relating to this topic.

To our knowledge, this will be the first systematic review and meta-analysis addressing the role of localisation with ^{18}F-FDG-PET for patients with all types of drug resistant focal epilepsy who have undergone resective epilepsy surgery. The proposed systematic review and meta-analysis will update and build on previous meta-analyses, which focused on temporal or frontal epilepsies.[10 14 15] Wang *et al* published their meta-analysis in 2016, however, the most recent publication that was included in their meta-analysis of localisation with ^{18}F-FDG-PET to predict outcomes in epilepsy surgery was from 2012.[15] Therefore, we believe that undertaking this systematic review and meta-analysis is important and justified, as we expect there will be a considerable number of eligible studies published over the last 10 years.

There are several potential limitations to our proposed study. First, we have adopted a broad definition of ^{18}F-FDG-PET localisation in this study, which considers both the final decision regarding surgical site and concordance with one or more other presurgical diagnostic investigations. While this reflects routine decision-making regarding ^{18}F-FDG-PET, this may be a source of heterogeneity. Second, we have elected to include publications with both randomised and non-randomised study designs, which may lead to the inclusion of low-quality studies. Furthermore, we expect that the majority, if not all, of the included studies will have a non-randomised design, due to the nature of the study question, which are inherently at higher risk of bias than randomised studies. We hope to mitigate this potential risk with a robust assessment of bias as described in our methodology. A third potential limitation is that we are only choosing to include English-language publications, and this may mean that relevant data is missed. Finally, while we hope to have a large enough sample size for our primary meta-analysis, it is possible that our proposed subgroup analyses will be limited by small sample sizes.

Author affiliations
[1]Department of Neuroscience, Monash University Central Clinical School, Melbourne, Victoria, Australia
[2]Department of Neurology, The Royal Melbourne Hospital, Melbourne, Victoria, Australia
[3]Department of Neurology, Alfred Hospital, Melbourne, Victoria, Australia
[4]Department of Medicine, University of Melbourne, Melbourne, Victoria, Australia
[5]Department of Radiology, Alfred Hospital, Melbourne, Victoria, Australia
[6]Department of Electrical and Computer Systems Engineering, Monash University, Melbourne, Victoria, Australia

Contributors MRC wrote the first draft and designed the search strategy. All authors designed and conceptualised the protocol. AA-B, BS, J-PN, AN, ML, PK, TJO' and LV critically revised the manuscript for intellectual content. All authors approved the final version.

Funding This research received no specific grant from any funding agency in the public, commercial or not-for-profit sectors. MRC is supported by an Australian Government Research Training Programme (RTP) Scholarship.

Competing interests None declared.

Patient and public involvement Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

Patient consent for publication Not applicable.

Provenance and peer review Not commissioned; externally peer reviewed.

ORCID iDs
Merran R Courtney http://orcid.org/0000-0003-1426-0762
Ana Antonic-Baker http://orcid.org/0000-0003-4275-7557
John-Paul Nicolo http://orcid.org/0000-0002-0473-6475
Lucy Vivash http://orcid.org/0000-0002-1182-0907

REFERENCES

1 Wiebe S, Blume WT, Girvin JP, *et al*. A randomized, controlled trial of surgery for temporal-lobe epilepsy. *N Engl J Med* 2001;345:311–8.
2 Engel J, McDermott MP, Wiebe S, *et al*. Early surgical therapy for drug-resistant temporal lobe epilepsy: a randomized trial. *JAMA* 2012;307:922–30 https://dx.doi.org/10.1001/jama.2012.220
3 Dwivedi R, Ramanujam B, Chandra PS, *et al*. Surgery for drug-resistant epilepsy in children. *N Engl J Med* 2017;377:1639–47.
4 Liu J-T, Liu B, Zhang H. Surgical versus medical treatment of drug-resistant epilepsy: a systematic review and meta-analysis. *Epilepsy Behav* 2018;82:179–88.
5 Spencer S, Huh L. Outcomes of epilepsy surgery in adults and children. *Lancet Neurol* 2008;7:525–37.
6 McIntosh AM, Wilson SJ, Berkovic SF. Seizure outcome after temporal lobectomy: current research practice and findings. *Epilepsia* 2001;42:1288–307.
7 Téllez-Zenteno JF, Hernández Ronquillo L, Moien-Afshari F, *et al*. Surgical outcomes in lesional and non-lesional epilepsy: a systematic review and meta-analysis. *Epilepsy Res* 2010;89:310–8.
8 West S, Nevitt SJ, Cotton J, *et al*. Surgery for epilepsy. *Cochrane Database Syst Rev* 2019;6:CD010541.
9 Tonini C, Beghi E, Berg AT, *et al*. Predictors of epilepsy surgery outcome: a meta-analysis. *Epilepsy Res* 2004;62:75–87.
10 Englot DJ, Wang DD, Rolston JD, *et al*. Rates and predictors of long-term seizure freedom after frontal lobe epilepsy surgery: a systematic review and meta-analysis. *J Neurosurg* 2012;116:1042–8.
11 Fallah A, Guyatt GH, Snead OC, *et al*. Predictors of seizure outcomes in children with tuberous sclerosis complex and intractable epilepsy undergoing resective epilepsy surgery: an individual participant data meta-analysis. *PLoS One* 2013;8:e53565.
12 Ibrahim GM, Morgan BR, Fallah A. A partial least squares analysis of seizure outcomes following resective surgery for tuberous sclerosis complex in children with intractable epilepsy. *Childs Nerv Syst* 2015;31:181–4.
13 Alim-Marvasti A, Vakharia VN, Duncan JS. Multimodal prognostic features of seizure freedom in epilepsy surgery. *J Neurol Neurosurg Psychiatry* 2022;93:499–508.
14 Willmann O, Wennberg R, May T, *et al*. The contribution of 18F-FDG PET in preoperative epilepsy surgery evaluation for patients with temporal lobe epilepsy a meta-analysis. *Seizure* 2007;16:509–20.
15 Wang X, Zhang C, Wang Y, *et al*. Prognostic factors for seizure outcome in patients with MRI-negative temporal lobe epilepsy: a meta-analysis and systematic review. *Seizure* 2016;38:54–62.
16 Steinbrenner M, Duncan JS, Dickson J, *et al*. Utility of 18F-fluorodeoxyglucose positron emission tomography in presurgical evaluation of patients with epilepsy: a multicenter study. *Epilepsia* 2022;63:1238–52.
17 Moher D, Shamseer L, Clarke M, *et al*. Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015

statement. *Syst Rev* 2015. ;;4:1. Jan 1 http://dx.doi.org/10.1186/2046-4053-4-1
18 Wieser HG, Blume WT, Fish D, *et al*. ILAE Commission report. proposal for a new classification of outcome with respect to epileptic seizures following epilepsy surgery. *Epilepsia* 2001;42:282–6.
19 Wells G, Shea B, O'Connell D. The Newcastle-Ottawa Scale (NOS) for assessing the quality of nonrandomised studies in meta-analyses. Ottawa, Ontario, Canada Department of Epidemiology and Community Medicine, University of Ottawa; 2022. http://www.ohri.ca/programs/clinical_epidemiology/oxford.asp
20 Sterne JAC, Savović J, Page MJ, *et al*. RoB 2: a revised tool for assessing risk of bias in randomised trials. *BMJ* 2019;366:l4898.

Supplementary Table 1: PRISMA-P (Preferred Reporting Items for Systematic review and Meta-Analysis Protocols) 2015 checklist: recommended items to address in a systematic review protocol*

Section and topic	Item No	Checklist item	(Page No.#)
ADMINISTRATIVE INFORMATION			
Title:			
Identification	1a	Identify the report as a protocol of a systematic review	1
Update	1b	If the protocol is for an update of a previous systematic review, identify as such	
Registration	2	If registered, provide the name of the registry (such as PROSPERO) and registration number	2
Authors:			
Contact	3a	Provide name, institutional affiliation, e-mail address of all protocol authors; provide physical mailing address of corresponding author	1
Contributions	3b	Describe contributions of protocol authors and identify the guarantor of the review	
Amendments	4	If the protocol represents an amendment of a previously completed or published protocol, identify as such and list changes; otherwise, state plan for documenting important protocol amendments	N/A
Support:			
Sources	5a	Indicate sources of financial or other support for the review	
Sponsor	5b	Provide name for the review funder and/or sponsor	14
Role of sponsor or funder	5c	Describe roles of funder(s), sponsor(s), and/or institution(s), if any, in developing the protocol	
INTRODUCTION			
Rationale	6	Describe the rationale for the review in the context of what is already known	3,4
Objectives	7	Provide an explicit statement of the question(s) the review will address with reference to participants, interventions, comparators, and outcomes (PICO)	4,5
METHODS			
Eligibility criteria	8	Specify the study characteristics (such as PICO, study design, setting, time frame) and report characteristics (such as years considered, language, publication status) to be used as criteria for eligibility for the review	5,6
Information sources	9	Describe all intended information sources (such as electronic databases, contact with study authors, trial registers or other grey literature sources) with planned dates of coverage	6
Search strategy	10	Present draft of search strategy to be used for at least one electronic database, including planned limits, such that it could be repeated	6, supplementary

			3,4
Study records:			
Data management	11a	Describe the mechanism(s) that will be used to manage records and data throughout the review	7
Selection process	11b	State the process that will be used for selecting studies (such as two independent reviewers) through each phase of the review (that is, screening, eligibility and inclusion in meta-analysis)	7
Data collection process	11c	Describe planned method of extracting data from reports (such as piloting forms, done independently, in duplicate), any processes for obtaining and confirming data from investigators	7
Data items	12	List and define all variables for which data will be sought (such as PICO items, funding sources), any pre-planned data assumptions and simplifications	7
Outcomes and prioritization	13	List and define all outcomes for which data will be sought, including prioritization of main and additional outcomes, with rationale	6
Risk of bias in individual studies	14	Describe anticipated methods for assessing risk of bias of individual studies, including whether this will be done at the outcome or study level, or both; state how this information will be used in data synthesis	7,8
Data synthesis	15a	Describe criteria under which study data will be quantitatively synthesised	8
	15b	If data are appropriate for quantitative synthesis, describe planned summary measures, methods of handling data and methods of combining data from studies, including any planned exploration of consistency (such as I^2, Kendall's τ)	8
	15c	Describe any proposed additional analyses (such as sensitivity or subgroup analyses, meta-regression)	8,9
	15d	If quantitative synthesis is not appropriate, describe the type of summary planned	N/A
Meta-bias(es)	16	Specify any planned assessment of meta-bias(es) (such as publication bias across studies, selective reporting within studies)	9
Confidence in cumulative evidence	17	Describe how the strength of the body of evidence will be assessed (such as GRADE)	9

*** It is strongly recommended that this checklist be read in conjunction with the PRISMA-P Explanation and Elaboration (cite when available) for important clarification on the items. Amendments to a review protocol should be tracked and dated. The copyright for PRISMA-P (including checklist) is held by the PRISMA-P Group and is distributed under a Creative Commons Attribution Licence 4.0.**

From: Shamseer L, Moher D, Clarke M, Ghersi D, Liberati A, Petticrew M, Shekelle P, Stewart L, PRISMA-P Group. Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015: elaboration and explanation. BMJ. 2015 Jan 2;349(jan02 1):g7647.

SEARCH STRATEGY

MEDLINE (Ovid)

1. Exp epilepsy
2. Exp seizures
3. (epilep* or seizure* or convuls*).mp.
4. Or/1-3
5. neurosurgical procedures/ or anterior temporal lobectomy/ or cerebral decortication/ or hemispherectomy/
6. (resect* or lobectom* or lesionectom* or hemispherectom*).mp.
7. neurosurg*.mp.
8. (neurologic* adj (surg* or operation*)).mp.
9. Or/ 5-8
10. 4 and 9
11. (epilep* adj4 (surg* or operation*)).mp.
12. ((extratemporal or temporal or TLE) adj4 (surg* or operation*)).mp.
13. Or/ 10-12
14. Exp positron emission tomography
15. neuroimaging
16. Exp functional neuroimaging
17. (PET or positron emission tomograph* or neuroimag*).mp.
18. (functional adj2 (neuroimag* or imag*)).mp.
19. Or/ 14-18
20. 13 and 19

EMBASE (Ovid)

1. Exp epilepsy
2. Exp seizure
3. (epilep* or seizure* or convuls*).mp.
4. Or/1-3
5. neurosurgery
6. (hemispherectom* or resect* or lobectom* or lesionectom*).mp.
7. neurosurg*.mp.
8. (neurologic* adj (surg* or operation*)).mp.
9. Or/5-8
10. 4 and 9
11. (epilep* adj4 (surg* or operation*)).mp.
12. ((extratemporal or temporal or TLE) adj4 (surg* or operation*)).mp.
13. Or/10-12
14. Exp positron emission tomography
15. Exp neuroimaging
16. Exp functional neuroimaging
17. (PET or positron emission tomograph* or neuroimag*).mp.
18. (functional adj2 (neuroimag* or imag*)).mp.
19. Or/ 14-18
20. 13 and 19

Web of Science (all databases)

1. TS=(epilep* or seizure* or convuls*)
2. TS=(neurosurg* or hemispherectom* or lobectom* or lesionectom* or resect*)
3. TS=(neurologic NEAR/0 (surg* OR operation*))
4. #2 or #3
5. #1 and #4
6. TS=(epilep* NEAR/4 (surg* OR operation*))
7. TS=((extratemporal or temporal or TLE) NEAR/4 (surg* OR operation*))
8. #5 or #6 or #7
9. TS=(PET or neuroimag* or “positron emission tomograph*”)
10. TS=(functional NEAR/2 (neuroimag* or imag*))
11. #9 or #10
12. #8 and #11