Peer Review File

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Reviewer #A

Comment 1: Line 26: is it really morphological quantitative? Or should it be morphological qualitative?

Response 1: Thank you for your comment, we changed the text from “quantitative” to “qualitative” (Page 2, Line 27).

Comment 2: Line 79: patients who don’t respond, instead of response

Response 2: Thank you for your comment, we changed the text from “response” to “respond” (Page 4, Line 79).

Comment 3: Line 119: provides a higher signal, instead of an higher

Response 3: Thank you for your comment, we changed the text from “an” to “a” (Page 6, Line 119).

Comment 4: Line 157: appropriate, instead of appropiate

Response 4: Thank you for your comment, we changed the text from “appropiate” to “appropriate” (Page 8, Line 156).

Comment 5: Line 169: In addition to the 3D sequences we suggest axial and coronal 2D T2 spin echo sequences…with what slice thickness?

Response 5: Thank you for your comment, we added in the text “with 2 mm slice thickness” (Page 8, Line 168-169).

Comment 6: Line 183: what is the value of perfusion (including ASL) in epilepsy? What is it used for?

Response 6: Thank you for your comment, we added in the text “which provides useful information about vascularisation and vascular proliferation, which is directly applicable to the assessment of

brain tumours" (Page 9, Line 183-185), explaining the value of perfusion studies in evaluating epileptogenic neoplasms.

Comment 7: Line 199: Is there any alternative to DESTIR? What sequence(s) could be used if you don't have it?

Response 7: Thank you for your comment, we added in the text "(however conventional 2D T2-weighted sequences can be used if DESTIR is not available)" (Page 10, Line 200-201), explaining how, if you don't have DESTIR sequences, conventional 2D T2-w can be used.

Comment 8: Line 200: do you use FLAIR in infants and neonates? but you said at lines 166-67 that FLAIR images are less sensitive to epileptogenic pathology in infants (0-2 years)

Response 8: Apology for the mistake, we agree with you that the sentence appears incoherent with the previous statements. We changed the text and deleted the whole period (see Page 10, Line 201).

Comment 9: Line 213: it would be interesting if you could mention the earliest age in which hippocampal sclerosis can be seen

Response 9: Thank you for your comment, we added "MTS can be seen as early as 14 months (29) and has been recognized by Dunleavy et al. in some neonatal murine models (30)."(Page 11, Line 214-215)

Comment 10: Line 214: hippocampal, instead of hippocamapl

Response 10: Thank you for your comment, we changed the text from "hippocampl" to "hippocampal" (Page 11, Line 217).

Comment 11: Line 216: neuronal, instead of neuonal

Response 11: Thank you for your comment, we changed the text from "neuonal" to "neuronal" (Page 11, Line 218).

Comment 12: Line 220: Usually the hippocampal formation is not uniformly affected, with the dentate gyrus, and the CA1, CA4 and to a lesser degree CA3 sections of the hippocampus being primarily involved. Is it easy, and is it important, to figure out which parts of the hippocampus are affected on imaging studies.

Response 12: Thank you for your comment, we added "Although the dentate gyrus, the CA1, CA4 and to a lesser degree CA3 sections of the hippocampus are primarily involved, regional involvement may be difficult to characterize on clinical MRI exams and does not impact the clinical management of the patients." (Page 11, Line 223-225)

Comment 13: Line 243: juxtacortical, instead of iuxta-cortical

Response 13: Thank you for your comment, we changed the text from "iuxta-cortical" to "juxtacortical" (Page 13, Line 257).

Comment 14: Line 249: forty percent of children…have, instead of has

Response 14: Thank you for your comment, we changed the text from "has" to "have" (Page 13, Line 264).

Comment 15: Line 252: Cortical dysplasia can be focal…,instead of FCD can be focal; although (?), instead of atlight

Response 15: Thank you for your comment, we changed the text from "FCD" to "Cortical dysplasia" (Page 13, Line 267) and "atlight" to "although" (Page 13, 268).

Comment 16: Line 259: Don't you think that blurring of white matter-grey matter junction with abnormal architecture of subcortical layer (taken from radiopedia) is a better construction than architectural subvert of the subcortical layers of grey-white matter interface?

Response 16: Thank you for your comment, we changed the text from "architectural subvert of the subcortical layers of grey-white matter interface" to "blurring of white matter-grey matter junction with abnormal architecture of subcortical layer" (Page 14, Line 275-277).

Comment 17: Line 264: classification, instead of calssification

Response 17: Thank you for your comment, we changed the text from "calssification" to "classification" (Page 14, Line 281).

Comment 18: Line 272: oligodendrogliosis or oligodendrocytosis, instead of oligodedroglyosis. Could you elaborate a bit on this subject? What is oligodendrogliosis/oligodendrocytosis?

Response 18: Thank you for your comment, we changed the text from "oligodendroglyosis" to "oligodendrogliosis" (Page 13, Line 273). We also added a brief statement explaining the definition of oligodendrogliosis ("which represents a

spectrum of different oligodendroglial abnormalities, including oligodendroglial hyperplasia, clusters of oligodendroglia, oligodendroglial hamartoma and oligodendroglial-like cells without associated evidence of cortical dyslamination") (Page 14, Line 289-292).

Comment 19: Line 335: through, instead of though

Response 19: Thank you for your comment, we changed the text from “though” to “through” (Page 19, Line 335).

Comment 20: Line 387: edema, instead of edem

Response 20: Thank you for your comment, we changed the text from “edem” to “edema” (Page 21, Line 387).

Comment 21: Line 388: reflecting, instead of refelcting

Response 21: Thank you for your comment, we changed the text from “refelcting” to “reflecting” (Page 21, Line 388).

Comment 22: Line 398: ganglioglioma, instead of ganglioma

Response 22: Thank you for your comment, we changed the text from “ganglioma” to “ganglioglioma” (Page 21, Line 398).

Comment 23: Line 417: leptomeninges, instead of leptomeinges

Response 23: Thank you for your comment, we changed the text from “leptomeinges” to “leptomeninges” (Page 22, Line 417).

Comment 24: Line 426: characterized, instead of charcaterized

Response 24: Thank you for your comment, we changed the text from “charcacterized” to “characterized” (Page 24, Line 436).

Comment 25: Line 428: I don’t understand this phrase: It is critical to recognize the relationship in axial between the lesion and the fornix and mamillo-thalamic tracts.

Response 25: Apology for the mistake, we agree with you that the sentence appears syntactitally incorrect. We changed the text and deleted the whole sentence (see Page 24, Line 438).

Comment 26: Line 486: tipically, instead of tipially

Response 26: Thank you for your comment, we changed the text from “tipially” to “tipically” (Page 28, Line 501).

Comment 27: Line: if no relevant lesions are found or if no relevant lesion is found, instead of if no relevant lesion are found

Response 27: Thank you for your comment, we changed the text from “if no relevant lesion are found” to “if no relevant lesions are found” (Page 29, Line 529).

Comment 28: Line 521: electrical source imaging is the same thing as SEEG? And what about MEG?

Response 28: They are not the same sEEG is invasive while ESI is not invasive and less used.

We added a brief pharapgraph about MEG (page 34, line 625-639).

Comment 30: Line 552: epileptic, instead of eplieptic

Response 30: Thank you for your comment, we changed the text from “eplietic” to “epileptic” (Page 32, Line 574).

Comment 31: Line 595: known, instead of knwon

Response 31: Thank you for your comment, we changed the text from “knwon” to “known” (Page 35, Line 644).

Comment 32: There are some entities that I think that should be mentioned in this paper, even if it is to say that they do not have a well-defined role in the etiology of epilepsy: hippocampal malrotation, multinodular and vacuolating neuronal tumor and venous angioma (in vascular malformations)

Response 32: Thank you for your comment, we added a brief pharagraph about hippocampal malrotation (page 11, line 234-242), MVNT (page 23, line 421-429) and venous angioma (page 24, line 464-468).

Comment 33: Are there clinical characteristics of seizures, such as age at onset, severity and frequency of crises, and difficulty in drug control, which can give the radiologist an idea of the type of lesion to be sought?

Response 33: Normally depending of the EEG (focal, localized lateralized, generalized) there are indications for the radiologist (for instance MTS, Rasmussen etc) but in practice the main information needed is precise EEG localisation of the seizure (if present).

Comment 34: What to expect from imaging studies, especially MRI, in the detection of possible epileptogenic foci? What is the percentage of false negative and false positive studies in specialized epilepsy services and in general hospitals?

Response 34: This is variable depending on the published literature and multidisciplinary approach, it is not possible to give reliable percentage.

Comment 35: Any tips on how to improve the performance of radiologists when evaluating MRI scans of patients with epilepsy? Or, how to improve the detection of epileptogenic lesions on MRI.

Response 35: Knowing EEG Localization, use of 3T and multidisciplinary meetings.

Reviewer #B

Comment 1: It would be useful to have a comment about visibility of FCD in premyelination and postmyelination MRIs (in my experience both scenarios may happen i.e. the lesion may be more visible in the premyelinated brain and vice versa)

Response 1: Thank you for your comment, we added a brief statement about the visibility of FCD (page 13, Line 270-271).

Comment 2: Line 25 neuroradiologists

Response 2: Thank you for your comment, we changed the text from “neuroradiologist” to “neuroradiologists” (Page 2, Line 25).

Comment 3: Line 50 all ages

Response 3: Thank you for your comment, we changed the text from “all age” to “all ages” (Page 3, Line 50).

Comment 4: Line 67 detail

Response 4: Thank you for your comment, we changed the text from “details” to “detail” (Page 4, Line 67).

Comment 5: Line 75 remain

Response 5: Thank you for your comment, we changed the text from “remains” to “remain” (Page 4, Line 75).

Comment 6: Line 92 have some clues change to have some knowledge of

Response 6: Thank you for your comment, we changed the text from “have some clues in” to “have some knowledge of” (Page 4, Line 92).

Comment 7: 227 rises

Response 7: Thank you for your comment, we changed the text from “rise to “rises” (Page 11, Line 231).

Comment 8: 238 pathophysiological

Response 8: Thank you for your comment, we changed the text from “pato-physiological” to “patophysiological” (Page 13, Line 252).

Comment 9: 325 is

Response 9: Thank you for your comment, we changed the text from “are” to “is” (Page 18, Line 325).

Comment 10: 345 remember

Response 10: Thank you for your comment, we changed the text from “remeber” to “remember” (Page 19, Line 345).

Comment 11: 372 remove the word brain?

Response 11: Thank you for your comment, we changed the text deleting the word "brain" (Page 20, Line 372).

Comment 12: 386 juxta

Response 12: Thank you for your comment, we changed the text from "iuxta-" to "juxta-" (Page 21, Line 386).

Comment 13: 394 to recognize

Response 13: Thank you for your comment, we changed the text from "recognizing" to "to recognize" (Page 21, Line 394).

Comment 14: 407 typically

Response 14: Thank you for your comment, we changed the text from "tipically" to "typically" (Page 22, Line 407).

Comment 14: 488 becomes

Response 14: Thank you for your comment, we changed the text from "become" to "becomes" (Page 28, Line 504).

Comment 15: 511 optimize

Response 15: Thank you for your comment, we changed the text from "optimising" to "optimize" (Page 29, Line 526).

Comment 16: 518 epileptogenic zone instead of surgical candidate?

Response 16: Thank you for your comment, we changed the text from "surgical candidate" to "epileptogenic zone" (Page 29, Line 535).

Comment 17: 521 not SEEG but ESI

Response 17: Thank you for your comment, we changed the text from "SEEG" to "ESI" (Page 29, Line 538).

Comment 18: 526-7 assess and becomes

Response 18: Thank you for your comment, we changed the text from "asses" to "assess" and from "become" to "becomes (Page 29, Line 543-544).

Comment 19: 529-534 the whole fMRI paragraph needs re-wording as it is not clear

Response 19: Thank you for your comment, we changed the text and re-phrased the whole paragraph (Page 30, Line 552-557).

Comment 20: I think the PET section needs some expansion e.g. to comment on its contribution in identifying the epileptogenic zone. I would keep the EEG-fMRI section less expanded as this is not a method commonly used.

Response 20: Thank you for your comment, we expanded a bit the PET section (Page 32, Line 586-598).

Comment 21: SEEG- it would be useful to know the contribution and success rate of this method as well as have specific references

Response 21: Thank you for your comment, we changed the text and added a brief paragraph about the topic with references (Page 36, Line 651-661).

Comment 22: 607 MRI for cases

Response 22: Thank you for your comment, we changed the text from "and" to "for" (Page 37, Line 667).