Iranian Journal of Radiology
Volume 18 · Issue 3 · e109181

OPEN PEER REVIEW

Investigation of the Relationship Between the Degree of Peritumoral Brain Edema and Pathological Features of Glioma Before Surgery

Zhenhua Wang, Xinlan Xiao

SUBMITTED	REVISED	ACCEPTED	DOI
10 Sep 2020	6 Jul 2021	7 Jul 2021	10.5812/iranjradiol.109181

About this report

This open peer review (OPR) report shows the public comments made on this article during peer review, by the reviewers, the associate editor and the editor-in-chief, for every revision round, together with the authors' replies. Comments appear only with the consent of the people who wrote them. Reviewers who chose to sign their report are named; the others are shown as "Referee". Comments are edited for language only, and confidential remarks to the editors are not included.

More about open peer review: brieflands.com/knowledgebase/opr

Contents

1 **Original submission** Referee 1, Mahyar Mohammadifard, Referee 2, Referee 3, Associate Editor, Editor-... 2

2 **Revision 1** Referee 1, Editor-in-Chief 6

Authors' reply to reviewers 7

Reviewer and editor comments 12

3 **Revision 2** Editor-in-Chief 13

Authors' reply to reviewers 14

Reviewer and editor comments 16

1 Original submission

6 comments · 1 Nov 2020 – 13 Feb 2021

Referee 1 Reviewer

MINOR REVISION 1 Nov 2020

This study was relatively well designed and conducted appropriately, but the manuscript draft needs some revision, as follows:
1. The study design is cross-sectional, and this must be stated in the abstract and the methods section of the full text.
2. In the results section, each group's value must be reported in parentheses rather than the critical value of the test.
3. Method: This part of the method, "Thus, 82 eligible cases with an age range of 12–84 years (average age: 50.8 ± 14.4 years) were obtained after rigorous screening, of which 48 were male and 34 were female. Of the 82 patients, 29 were LGGs and 53 were high-grade gliomas (HGGs), whereas 26 were IDH1 mutant type and 56 were wild type.", relates to the results and must be moved to the results section.
4. Table titles must be self-explanatory.
5. Tables 2 and 3 must be merged.
6. In table 5, all rows except those for correlation coefficients and p-values must be deleted.
7. In this study, only univariate tests, such as t, Mann-Whitney, Spearman correlation coefficients, etc., were used. However, regression modeling must be used to adjust for possible confounders.

Mahyar Mohammadifard Reviewer

ACCEPT 30 Nov 2020

Proper article TITLE, structured ABSTRACT, accurate RESULTS, and relevant DISCUSSION ... I think it is Approved.

Referee 2 Reviewer

MAJOR REVISION 11 Dec 2020

1-What is the meaning of “secondary glioblastoma”?
2-The authors mentioned that “images in which the tumor and edema area boundaries were difficult to distinguish were excluded from the study”. I have two questions in this regard:
I-How many patients were excluded based on this criterion? [Because in many cases, the boundary is unclear.] [If the number of patients excluded for this reason is considerable, we can identify a selection bias, and in fact, we can generalize the data to patients with clear delineation between the core and edema, not to all gliomas. Please explain in this regard.]
II-What were the criteria for determining that the tumor and edema area boundaries were difficult to distinguish? How did they determine the tumoral core and edema?
3-Why did the authors exclude patients with preoperative biopsy from the study? If a patient underwent imaging before biopsy, it is OK to include the patient in the study.
4-Please define LGG and HGG.
5-What is the C parameter in the formula for volume calculation?
6-The authors mentioned: “severe edema around the tumor (grade III) when EI = 3”. This seems to be: EI>3.
7-There are two sets of definitions for EI here. Please correct and clarify.
8-What are the criteria for the tumoral core borders and edema borders? [For distinguishing these two parts from each other.] These are challenging and controversial. Which sequences did they use for this purpose? [T1-

CE or T2WI.] Please clarify.
9-How did the two radiologists combine their delineations of the tumoral core and edema borders?
10-Did the authors calculate the interrater and intrarater reliability of measurements on images?
11-The authors should describe the method for determining Ki67 and socitrate dehydrogenase (IDH) mutations. The pathological description [in brief; appropriate for a radiology journal] should be included in the paper.
12-When did the authors determine Ki67 and IDH? After surgery? Did all patients undergo surgery?
13-It is probable that the degree of Ki67 and IDH differs in different parts of the tumor. Which part of the tumor was considered for the assessment of Ki67 and IDH?
14-Did the authors determine Ki67 using a quantitative or qualitative measurement method?
15- Did the authors determine IDH using a quantitative or qualitative measurement method?
16-There are two different types of edema around gliomas: reactive edema [without tumoral involvement] and infiltrative edema [with tumoral involvement]. What is the meaning of edema in this study? Did the authors consider both of them as edema, or did they consider only infiltrative edema? Please explain.
17-If the authors can differentiate reactive and infiltrative edema, performing the analyses for the whole edema and infiltrative edema [only] separately would be interesting [if the data are available].
18-Gender and grade are dichotomous parameters, and their correlations with continuous parameters are not based on Spearman's and Pearson's coefficients.
19-The authors can assess the grade variable as a variable with 4 classes. [Grades I-IV.] Why did they consider only HGG and LGG?
20-What is grade 0 for EI in table 2? Please define EI grades 0, I, II and III in the text or in a table footnote.
21-P-values of 0.000 should be written as <0.001.
22- Can the authors determine Ki67 and IDH based on EI in regression models? [They can use multivariate regression models using EI, tumor grade and age.] Please present the data in the paper if the models are precise and considerable.
23-Please add the mean±SD for EI in the different subgroups in table 4 [for example, in men and women, in HGG and LGG, …]. The mean rank and sum of ranks are not tangible.
24-Did the authors not have any cases of cystic glioma? In such cases, what were the borders of the tumoral core and edema?
25-Can the authors implement a ROC analysis on EI for differentiating HGG from LGG [based on EI]? If yes, please add the data to the paper. It could be interesting if we could present a cutoff point for EI for differentiating HGG from LGG.

Referee 3 Reviewer

REJECT 31 Jan 2021

The study is quite interesting; however, there are some points that need to be reconsidered before it is suitable for publication.

The major concern in this study is that, instead of designing a retrospective study using old conventional T1+Gad and T2 sequences for measuring tumor volume and edema, it would have been much more thoughtful and knowledgeable if the authors had designed a prospective study and considered volumetric imaging with 3D sequences. For instance, since they used a 3T GE machine, they could have used CUBE sequences for both T2 and T1 postcontrast images. Also, they could have used postcontrast 3D FSPGR (LAVA), which is a 3D gradient echo sequence alternative to CUBE, which is a spin echo sequence.
Other than this, there are some other points that I would like the authors to take into consideration:

Abstract:
Methods:

What do the authors mean by saying that the edema of all patients was then graded and correlated with the difference in each pathological parameter? The term pathological parameter creates a bit of confusion here. For instance, the grade of edema was correlated with the patient's age and gender. Are age and gender pathological parameters?
Results:
The authors stated that the degree of EI (edema index) was higher in IDH1 wild type and mutant groups. This conflicts with their Spearman correlation. I assumed from the study that EI had a negative correlation with the IDH1 mutant group.

Main Manuscript
Background:
In sentences 37 and 38, the authors stated that although ki-67 and IDH1 mutation status are estimated prognostic markers of glioma characteristics, they require an invasive method to obtain.
This sentence suffers from very poor English writing and is not clear to the reader.
Objectives:
The authors stated that this study aimed to use T2-weighted and contrast-enhanced T1 imaging sequences to investigate whether the grade of malignancy, IDH1 mutation status, and ki-67 expression level of glioma were correlated with the degree of PTBE.
This sentence should be rephrased as "This study aimed to use T2-weighted and contrast enhanced T1- imaging sequence to investigate whether the grade of malignancy,IDH1 mutation status and ki-67 expression level of glioma were correlated with grade of PTBE."
Methods:
Calculation of Peritumoral Edema Area:
In sentence 69, the authors stated that T1CE and T2W images were selected for measuring the edema area. Did the authors use both sequences to measure tumor size and tumor+edema?
If so, how did they overcome the difficulty when they obtained different measurements in CE T1 versus T2 images?
Also, the authors stated that images were delineated (it would have been better to use interpreted instead of delineated) by two senior neuroimaging diagnosticians. Did they then consider intraobserver and interobserver reliability? I did not find such a thing in the study.

In sentence 73, it is not obvious which measurement was considered the maximum height on the coronal or sagittal planes. I think the authors should add c before maximum height. Also, it is better to use planes instead of position.

In sentences 78 &79, the authors stated that A1,B1,C1 represent the maximum diameters of the measured tumor volume in the axial, sagittal, and coronal aspects of the measured tumor and peritumoral edema tissue, respectively.
This should be rephrased as "Measurements A1,B1,C1 & A2,B2,C2 represent the maximum diameters in axial,sagittal,and coronal planes of tumor itself and tumor+peritumoral edema respectively."

Discussion:
The authors stated that measurement of edema was not accurate enough. They are right, since they did not use 3D volumetric sequences for their measurements, as I stated at the beginning of my comments. They could easily have overcome this issue by designing a prospective study.

Figures
Figure1 (d) seems to be coronal FLAIR, not T2. The authors stated that they used T2 and CE T1 for measurements. Here, I'm seeing measurements in a FLAIR sequence!

Associate Editor

MAJOR REVISION 13 Feb 2021

dear editor in chief
This article needs major revision.

Editor-in-Chief

MAJOR REVISION 13 Feb 2021

Dear authors,
Your article needs Major Revision.
Regards

2

Revision 1

AUTHORS' RESPONSE TO REVIEWERS

Authors' reply to reviewers

The next pages contain the authors' point-by-point reply to the comments of this revision round, as submitted with the revised manuscript. It is published as the authors wrote it.

The revision for the comments

Dear Editors:

Thank you for your precious comments and suggestions , we have revised the manuscript according to your comments,here is the our revised results:

Commen of reviewer 1:	Our answer and revision:
1.what is the meaning of"secondary glioblastoma"?	Primary glioblastoma develops de novo without clinical or histological evidence of a low-grade precursor lesion, while secondary glioblastoma develops from a low-grade glioma.
2.*the authors mentioned "images in which the tumor and edema area boundaries were difficult to distinguish were excluded from the study". I have two questions in this regards:* *ı-how many patients were excluded based on this criteria? [because in many cases, the boundary is unclear] [if the number of excluded patients for this reason is considerable, we can judge a selection bias and in fact we can generalize the data to patients with clear delineation between core and edema; not to all gliomas. Please explain in this regard]* *ıı-what was the criteria for difficult distinguish between tumor and edema area? How did they determine the tumoral core and edema?*	ı:According to your comments,a flow-process diagram has been displayed in the article to show the number of exclusion;and the excluded patients is relatively less comparing with the included patients. ıı:"Images in which the tumor and edema area boundaries were difficult to distinguish were excluded from the study",which I mentioned in the paper is not rigorous enough,so the sentence has been omitted and we supplied the method about how to delineate the region of tumor core and peritumoral edema.(These sentence was highlighted with yellow background)
3.why did the authors exclude the patients with preoperative biopsy from the study? if the patient underwent imaging before biopsy, it is OK to be included in study.	We considered that preoperative biopsy may injury some brain tissue and augment the area of edema,so it was excluded.
4.please define LGG and HGG.	It has been revised in line 18:"according to World Health Organization(WHO) 2016 classification of central nervous system tumors,of which 29 were pathologically confirmed as low-grade gliomas (LGGs) and the remaining 53 were pathologically confirmed as high-grade gliomas (HGGs)."
5.what is C parameter in formula for volume calculation	"C"represent the maximum diameter of the measured tumor volume in coronal aspects. Additionally,it was also illustrated in the annotation of Fig 1.
6.the authors mentioned: "severe edema around the tumor (grade III) when EI = 3" this seems to be: EI>3	It has been revised.
7.here is two set of definition for EI. Please correct and clarify.	One of the definition has been omitted.
8.what is the criteria for tumoral core borders and edema borders? [for distinguishing these two parts from each others] These are challenging and controversial. Which sequences did use for this purpose? [T1-CE or T2WI]. Please clarify.	The method for distinguish the tumoral core borders and edema borders has been displayed under the subtitle:"Calculation of peritumoral edema area and edema index",which highlighted with yellow background.
9.how did the two radiologists combib=ned their delineation on the tumoral core and edema borders?	According to the comment,the original expression is changed to "The image was delineated by two senior neuroimaging diagnosticians with more than ten years of work experience using double-blind method , they delineated each image respectively,In case of any disagreement on the position of the borders, a consensus was reached by discussion, especially if the positional variations resulted in a discrepancy"

10.did the authors calculate the interrater and intrarater reliability of measurements on images?	Although this comment is conducive to improve the reliability of paper,many studies do not display this question,so we think this step is not essential.
11.the authors should describe the method for determining Ki67 and socitrate dehydrogenase (IDH) mutations. The pathological description [in brief; appropriate for a radiology journal] should be mentioned in paper.	It has been revised in line 64-66 highlighted with yellow background.
12.when did the authors determine Ki67 and IDH? After surgery? Did all patients undergo surgery?	All the enrolled patients was diagnosed by postoperative pathological examination,it was mentioned in the “method” paragraph.
13.it is probable the degree of Ki67 and IDH is different in different parts of tumor. Which part of tumor was considered for assessment of Ki67 and IDH?	Hitherto, this question is still a problem that need to be solved,cause it is a retrospective research, we can only develop it by the existed data.
14.did the authors determine Ki67 in a quantitative or qualitative measurement method? *15.did the authors determine IDH in a quantitative or qualitative measurement method?*	These information we obtained in the institutional data base,and according to the pathological examination results.
16.there is two different edema around the gliomas: reactive edema [without tumoral involvement] and infiltrative edema [with tumoral involvement]. What is the meaning of edema in this study? did the authors considered both of the as edema or did they consider only infiltrative edema? Please explain. *17.if the author can differentiate reactive and infiltrative edema, performing the analyses for whole edema and infiltrative edema [only] separately would be interesting [if the data are available].*	So far,from my knowledge,it is difficult to distinguish reactive edema and infiltrative edema by MRI images in the world,so this problem need us research in further study. This question is also an limitation of the article.
18.gender and grade are dichotomous parameter and its correlation with continuous parameters is not based on spearman and pearsons coefficients.	It has been revised.
19-the authors can assess the grade variable in a 4 class variable. [grades I-IV] why did they consider only HGG and LGG?	We didn’t do that because the grade I glioma is too little,in reality,the grade I glioma is too little ether in other institution.
20-what is the degree of 0 for EI in table 2? Please define in text of footnote in table the EI grades of 0, I, II and III.	It has been revised.
21-p values of 0.000 should be written as <0.001	It has been revised.
22- can the authors determine the Ki67 and IDH based on EI in regression models? [they can use multivariate regression models using EI, tumor grade and age]. Please represent the data in paper if the models are precise and considerable.	According to your comment,multivariate regression models were established and corresponding results was display in the section of result with yellow background highlighted
23.please add the mean±SD for EI in different subgroups of table 4 [for example in men and women, in HGG and LGG, ...] the mean rank and sum of rank are not tangible.	It has been revised.
24.did not have the authors cystic glioma? In this case, what were the borders of tumoral core and edema?	In fact,cystic glioma has been excluded because it is difficult to discriminate the border between tumor core and peritumoral edema.we have mentioned it in the method paragraph and with yellow background highlighted
25-can the authors implement a ROC analysis on EI for differentiating HGG from LGG [based on EI]? If yes, please add the data to paper. it could be interesting if we can represent a cut off point of EI for differentiating HGG from LGG.	The ROC curve was plotted to show the prediction performance of EI for differentiating the LGG from HGG.(See Figure 2).

Reviewer 2:	Our answer and revision:
Abstract: *1.Methods:* *What do authors mean by the edema of all patients was then graded and correlated with the difference in each pathological parameter? The term pathological parameter creates a bit of confusion here.For instance grade of edema was correlated with patient's age and gender.Are age and gender pathological parameters?* *2.Results:* *Authors stated that the degree of EI (edema index) was higher in IDH1 wild type and mutant groups.This has conflict with their spearman correlation .I assumed from the study that EI had negative correlation with IDH1 mutant group.*	1.Thank you for your comment and the title was not very rigorous,we will revise it. 2.In fact, spearman correlation analysis was not available for evaluate the correlation between IDH1 and EI,because IDH1 in the study was a binary variables, according to the comment of reviewer 1,a multivariate regression analysis was used for evaluating the relationship and the original results has been revised.
Main Manuscript *1.Background:* *In sentences 37 and 38 authors stated that although ki-67 and IDH1 mutation status is an estimated prognestic marker of the glioma characteristics of the glioma ,its need invasion method to obtain.* *This sentence suffers from very poor English writing and it does not make clear understanding to the reader.* *2.Objectives:* *Authors stated that this study aimed to use T2-weighted and contrast enhanced T1- imaging sequence to investigate whether the degree of malignant and IDH1 mutation status and ki-67 expression level of glioma which were compared and correlated with the different degree of PTBE.* *This sentence should be rephrased as 'This study aimed to use T2-weighted and contrast enhanced T1- imaging sequence to investigate whether the grade of malignancy,IDH1 mutation status and ki-67 expression level of glioma were correlated with grade of PTBE.* *3.Methods:* *3.1 Calculation of Peritumoral Edema Area:* *In sentence 69 authors stated that T1CE and T2W images were selected for measuring the edema area.Did authors use both sequences to measure tumor size and tumor+edema?* *If so did how did they overcome the hassle when they got different measurements in CE T1 versus T2 images?* *Also authors stated that images were delineated (it was better to use interpreted instead of delineated) by two senior neuroimaging diagnosticians.Then did they consider intraobserver and interobserver reliability? I did not find such a thing in the study.* *3.2 In sentence 73, it is not obvious which was considered as maximum height on coronal or sagittal planes.I think authors should add c before maximum height .Also it's better to use planes instead of position .*	1. Sentences 37 and 38 have been revise. 2. According to the reviewer's advisement,the sentence has been revised. 3.1 In the "Calculation of Peritumoral Edema Area" section,some words has been displayed to illustrate how to delineate the tumor and peritumoral edema region by T2WI and T1-CE sequences. 3.2 It has been revised. 3.3 I am very thanks for your precious revised advisement,and the sentences has been revised according to your comment.

3.3 In sentences 78 &79 authors stated that A1,B1,C1 represents the maximum diameter of the measured tumor volume in the axial,sagittal,and coronal aspects of the measured tumor and peritumoral edema tissue respectively. *This should be rephrased as "Measurements A1,B1,C1 & A2,B2,C2 represent the maximum diameters in axial,sagittal,and coronal planes of tumor itself and tumor+peritumoral edema respectively.*	
Discussion: *Authors stated that measurement of edema was not accurate enough.They are right since they did not use 3D volumetric sequences for their measurements as i stated in the beginning of my comments.They could easily overcome this issue by designing a prospective study.*	Thanks for this comment,and the new measurement method will be considered in the future study.
Figures *Figure1 (d) seems to be coronal FLAIR not T2.Authors stated they used T2 and CE T1 for measurements.Here i'm seeing measurements in FLAIR sequence!*	Thanks for pointing out the fault,the corresponding sentences has been revised,in fact,T2WI or T2-flaire were used for measure the diameter of tumor,the two results have non difference.
Reviewer 4:	
It seems that there is a written mistake in the part "result" : "the degree of EI was higher in IDH1 wild type and mutant groups (Z = −4.116, P < 0.05)". While based on the whole study and as it is mentioned in the "Conclusion", the degree of PTBE is positively correlated with the patient's age, grade of glioma, and Ki-67 level, and negatively correlated with the IDH1 mutation status, so we expect lower degree of EI in IDH mutant group.	It has been revised.
Reviewer 5:	
1. Study design is cross-sectional, and it must be added in the abstract and full-text method section. *2. In results section: Rather than critical value of test, it must be reported each group value in the parenthesis.* *3. Method: This part of method "Thus, 82 eligible cases with an age range of 12–84 years (average age: 50.8 ± 14.4 years) were obtained after rigorous screening, of which 48 were male and 34 were female. Of the 82 patients, 29 were LGGs and 53 were high-grade gliomas (HGGs), whereas 26 were IDH1 mutant type and 56 were wild type." is related to results and it must be transferred to the later section.* *4. Title of tables must be self-explanatory.* *5. Tables of 2 and 3 must be merged.* *6. In table 5, rather than correlation coefficients and p-value rows, other rows must be deleted.* *7. In this study, only univariate tests such as t, Mann-Whitney, Spearman correlation coefficients, and etc. were used. But, for adjusting possible confounders must be used of modeling by regression.*	1.It has been revised in the paper. 2.It has been revised 3.It has been transferred. 4.It has been done 5.They have been merged. 6.It has been revised. 7.Regression model has been established.

Note : Due to work reason,I'm so sorry to reply the revision letter late.

for some reason,May I change the corresponding author to the second author of the manuscript? If it could be,the new corresponding author is as follow:

2 Revision 1

2 comments · 10 Mar 2021 – 5 Jul 2021

Referee 1 Reviewer

ACCEPT 10 Mar 2021

Thanks to the dear authors for addressing the comments in the manuscript. At present, it is acceptable from a methodological point of view.

Editor-in-Chief

MINOR REVISION 5 Jul 2021

Dear authors,
Your article needs Minor Revision.
Regards

3

Revision 2

AUTHORS' RESPONSE TO REVIEWERS

Authors' reply to reviewers

The next pages contain the authors' point-by-point reply to the comments of this revision round, as submitted with the revised manuscript. It is published as the authors wrote it.

Revision letter

Dear associate editor ,

Above all,we would like to thank the reviewers and the editors for the positive and constructive comments and suggestions,we have carefully revised the manuscripts according to these invaluable comments.Detailed point-by-point responses to each question are listed below, and all alterations to the manuscript are highlighted in text in red.Except for our heartfelt thanks,we sincerely hope you could comprehend our interpretation and forgive our incomprehensive knowledge and inexpert English.

Associate Editor's Comments:

Associate Editor 1:
dear editor in chief
this manuscript is accepted
Associate Editor 2:
1-line 6, “preoperative grade” is better to be written as “preoperative grading”
Answer:According to your suggestion,it has been revised at line 5.

2-lines 6 and 7, “degree of malignancy judgement” is better to change to: “predicting the degree of malignancy”

Answer:According to your precious suggestion,it has been revised at line 6.

3-in line 24, please add this part in parenthesis: “cut-off :1.722, sensitivity:95.8%, specificity:70.0%,95% confidence interval(CI):0.718 - 0.899.”
Answer: The parenthesis has been added at line 23.

4-in line 31, please change “high grade” to “high grade form”
Answer: It has been revised at line 31.

5-in line 31, please change “determining the preoperative” to “preoperative determining of the”
Answer: The phrase has been revised at line 31.

6-what is GBM? Please add full term of the abbreviations in the first time usage.
Answer:Thank you for pointing out the mistake,according to your advice, it has been revised at line 35-36.

7-this part is unclear: “its need invasive method to obtain” please correct and recheck all paper regarding English writing style.
Answer:The sentence has been replaced by “pathological tissue must be obtained by biopsy or surgery, which limit their use in clinical practice.” at line 41

8-line 46, “T2-weighted(T2WI)” is “T2-weighted imaging (T2WI)”
Answer:Thank you for your reminding and it has been revised at line 46

9-in line 48, the word grade is not appropriate. It could be confused with grade of tumor. Please change t to another word such as “amount” or “extent”
Answer: According to your precious and helpful suggestion,the “grade” was replaced by “extent” at line 48.

10-please add numbers for titles and subtitles according to journal format.

Answer: the titles and subtitles have been amended according to the journal article.

11-the authors have not used full stop “.” For separation of sentences and many sentences have been separated by “,”. Please correct this format.
Answer: Two misuses have been corrected at line 79 and 80.

12-please correct the manufacturer data of SPSS based on the data in: https://www.ibm.com/support/pages/how-cite-ibm-spss-statistics-or-earlier-versions-spss
Answer:the version information has been added in the text at line 90-91.

13-first sentence of result section does not have verb.
Answer:Thank you again for correcting our mistake,the sentence has been displaced by ”The average age of participants was 50.8 ± 14.4 years, and the age range was 12–84 years”.

14-line 109, risk factor is better to be written as associated factor.
Answer:It has been revised at line 110.

15-line 110, please correct: E1 and IDH1 can differentiate LGG from HGG
Answer:It has been corrected at line 111.

16-sentence in line 111 is unclear. please correct.
Answer:The obscure sentence has been replaced by “We used EI as the independent variable and the grade of glioma as the dependent variable, a logistic regression was conducted and a ROC curve was plotted(Figure 3),”

17-please correct studie
Answer:It has been done at line 122.

18-table 2 legend is not appropriate. Please correct.
Answer: It has been revised at line 227.

19-please add full term off abbreviations in the table footnote.
Answer:Abbreviations have been added in the table footnote at line 224,236,248 respectively.

20-it seems in the table 4 and 5 legends, it is better the authors delete the word “risk”
Answer:According to your suggestion,the “risk” has been deleted.

21-References should be cited in order in the text. First reference 10 then 11 in the method.
Answer: It has been revised at line 74 and 85.

22-Reference number 29 is not cited in the manuscript. Please cite it.
Answer: It has been revised at line 156.

23-Figure 2.d. is coronal FLAIR, not T2W. please correct.
Answer: It has been corrected as T2-FLAIR at line 208.

24-Table 5 has not been cited in the manuscript. Please cite it.
Answer:It has been cited at line 111,”(each P <0.05,see Table 5)”.

3 Revision 2

1 comment · 7 Jul 2021

Editor-in-Chief

ACCEPT 7 Jul 2021

Dear authors,
Your article is acceptable for publication in IJR.
Regards