

Dr. Ma,  
Science Editor,  
World Journal of Clinical Cases

February 26, 2021

RE: Manuscript NO.: 62174, entitle “Textural Differences Based on Apparent Diffusion Coefficient Maps for Discriminating the pT3 Subclassification of Rectal Adenocarcinoma”

Dear Dr. Ma,

We are very grateful for your positive assessment of our Manuscript NO.: 62174 titled “Textural Differences Based on Apparent Diffusion Coefficient Maps for Discriminating the pT3 Subclassification of Rectal Adenocarcinoma”. We also thank the reviewers for the sound comments, which have helped us improve our work.

We have provided a point by point response to all remarks, questions and suggestions, as found below. We hope that the revised version will fulfil all your editorial requirements.

In anticipation of a positive outcome, we thank you for allowing us to contribute to your renowned journal.

Thanks also for your consideration and support in this work.

With kind regards,

Dr. Lu

## **Response to the comments of Reviewer #1**

### **Specific Comments to Authors:**

The manuscript is well written and presents an interesting study; however, it needs amendments to address in its different sections in its current form.

**Response:** Thank you for taking the time to review our manuscript and provide us with helpful comments that have enabled us to improve the quality of our paper.

**Comment:** Introduction. Please mention the previous studies that, in recent years, have performed assessments of texture analysis in MRI of rectal cancer, and what challenges remain in the imaging diagnosis.

**Response:** Thanks for this important point. We have supplemented the requested information in the revised Introduction.

**Comment:** Methods and Results. The study is focused on the diagnostic performance of selected TA biomarkers. However, the results tables are incomplete for the assessment of the significant biomarkers. Please include a complete table of each selected TA biomarkers' diagnostic performance, besides its Area Under the Curve (AUROC) evaluation. Authors should include sensitivity, specificity, predictive values and likelihood ratios of the selected TA biomarkers, not only global accuracy and areas under the curve.

**Response:** Thanks for this great comment. Table 4 has been revised per your suggestion.

**Comment:** Authors can use as a reference of the diagnostic performance a previous study of DTI biomarkers in glioblastoma (include the reference in the methods): (2013) Diagnostic performance of regional DTI-derived tensor metrics in glioblastoma multiforme: simultaneous evaluation of p, q, L, Cl, Cp, Cs, RA, RD, AD, mean diffusivity and fractional anisotropy. *Eur Radiol* 23:1112–1121. doi: 10.1007/s00330-012-2688-7

**Response:** Thanks for this suggestion. The reference has been included.

**Comment:** If the authors performed a logistic regression analysis. The TA variables' hazard functions included in the analysis (the equivalent of relative risk). An example of how to present the results of imaging biomarkers using logistic regression in tumours can be found in the next reference (include in the methods): (2016) Choline-to-N-acetyl aspartate and lipids-lactate-to-creatine ratios together with age assemble a significant Cox's proportional-hazards regression model for prediction of survival in high-grade gliomas. *Br J Radiol* 89:20150502. doi: 10.1259/bjr.20150502 The recommended analysis will increase the information in tables, but authors can use a supplementary online-only file if necessary.

**Response:** Thanks for this comment. In this study, a COX PH regression model was applied to assess the risk of imaging biomarkers. Since time-to-event variable was not available in our data, we are unable to use the suggested reference. Our future studies will address this point.

**Comment:** Discussion The study's limitation mentions why the authors did not include MRI post gadolinium to evaluate rectal cancer?

**Response:** Thanks for this comment. Actually, we used gadolinium as the contrast agent for MRI; however, its effect was not examined. This has been included as a study limitation.

**Comment:** What is the hospital's policy and the country about using MRI assessment compared with the international literature?

**Response:** Thanks for this question. To the best of our knowledge, MRI assessment in our hospital is consistent with the international literature.

**Comment:** The evaluation of dozens of TA features is challenging in clinical settings and could benefit a statistical method that simultaneously analyses variables together. What can be the benefits of using a discriminant analysis method that has been previously applied in the simultaneous discrimination of 11 MRI biomarkers in brain tumour (include the reference): (2014) Global diffusion tensor imaging derived metrics differentiate glioblastoma multiforme vs. normal brains by using discriminant analysis: introduction of a novel whole-brain approach. *Radiology and Oncology* 48:127–136. doi: 10.2478/raon-2014-0004

**Response:** Thanks for this insightful suggestion. We have performed discrimination analysis, and the results are shown in the table below. The results indicated that entropy and inertia were strongest diagnostic factors predicting the allocation to the pT3a or pT3b-c group. However, inertia had a relatively small coefficient, indicating is weak effect on this discrimination, albeit statistically significant. As these findings do not add much to the data included in the original manuscript, we believe reporting them might only confuse the reader.

Table. Discriminant analysis including several independent variables.

Standardized Canonical Discriminant Function Coefficients		Structure Matrix		Canonical Discriminant Function Coefficients	
Variable	Function 1	Variable	Function 1	Variable	Function 1
Entropy	0.991	Entropy	0.830	Entropy	0.843
Inertia	0.580	Energy <sup>a</sup>	-0.349	Inertia	0.002
		Inertia	0.306	Constant	-9.927
		Correlation <sup>a</sup>	-0.235		
		uniformity <sup>a</sup>	-0.197		
		5th ADC <sup>a</sup>	-0.153		
		10th ADC <sup>a</sup>	-0.184		
		25th ADC <sup>a</sup>	-0.158		
		90th ADC <sup>a</sup>	-0.093		
		Mean	-0.092		

		ADC <sup>a</sup>			
		skewness <sup>a</sup>	0.045		
		kurtosis <sup>a</sup>	0.011		

Coefficients indicate the partial contribution of each variable to the discriminant function, controlling for all other variables in the equation. <sup>a</sup>Variable not used in the analysis.

**Comment:** Mention the study's short-term clinical applicability and the considerations for the study's generalizability according to the STROBE guidelines.

**Response:** Thanks for this suggestion. The related information has been added to the Discussion.

## **Response to the comments of science editor**

### **EDITORIAL OFFICE'S COMMENTS**

#### **(1) Science editor:**

##### **1 Scientific quality:**

The manuscript describes a case control study of the textural differences based on apparent diffusion coefficient maps for discriminating the pt3 subclassification of rectal adenocarcinoma. The topic is within the scope of the WJCC.

##### **(1) Classification:**

Grade C;

##### **(2) Summary of the Peer-Review Report:**

The manuscript is well written and presents an interesting study. However, it needs amendments to address in its different sections in its current form. The questions raised by the reviewer should be answered;

##### **(3) Format:**

There are 4 tables and 3 figures. A total of 33 references are cited, including 11 references published in the last 3 years. There are no self-citations.

##### **2 Language evaluation:**

Classification: Grade A. A language editing certificate issued by MedSci was provided.

**Response:** We appreciate your interest in our study. We are delighted that you believe that publication of this study would be of merit to readers of the journal.

##### **3 Academic norms and rules:**

The authors provided the Biostatistics Review Certificate, the STROBE Statement, and the Institutional Review Board Approval Form. Written informed consent was waived. The authors need to provide the signed Conflict-of-Interest Disclosure Form and Copyright License Agreement. No academic misconduct was found in the Bing search.

**Response:** Thank you for this important query. The signed Conflict-of-Interest Disclosure Form and Copyright License Agreement have now been provided.

##### **4 Supplementary comments:**

This is an unsolicited manuscript. The study was supported by 5 grants. The topic has not previously been published in the WJCC.

##### **5 Issues raised:**

(1) The authors did not provide the approved grant application form(s). Please upload the approved grant application form(s) or funding agency copy of any approval document(s);

(2) The authors did not provide original pictures. Please provide the original figure documents. Please prepare and arrange the figures using PowerPoint to ensure that all graphs or arrows or text portions can be reprocessed by the editor;

(3) The "Article Highlights" section is missing. Please add the "Article Highlights" section at the end of the main text.

**Response:** The according grant application forms have been provided (in Chinese) and

the original images have been provided. A section of “Article Highlights” has also been written according to the instruction and provided at the end of the main text.