Reviewer’s report

**Title:** Noninvasive KRAS mutation estimation in colorectal cancer using a deep learning method based on CT imaging

**Version:** 0  **Date:** 22 Mar 2020

**Reviewer:** Tang Lei

**Reviewer's report:**

The authors have submitted a paper describing a deep learning model that used portal venous phase CT images in 2D to estimate KRAS mutations in the axial, coronal, and sagittal directions. This article also developed a radiomics model to predict KRAS mutations and compared it with the deep learning model. Non-invasive methods to investigate KRAS gene mutation has practical significance. It is very innovative to explore the KRAS status with deep learning model based on CT imaging. The content of this paper is substantial and logical. There are the following problems, which need to be further modified and supplemented by the authors.

1. **Page1,line 42-44:**

   “In the training cohort, the AUC was 0.945 (sensitivity: 0.75; specificity: 0.94), and in the validation cohort, the AUC was 0.818 (sensitivity: 0.70; specificity: 0.85).” Is this the result of radiomics model? This meaning seems incomplete. Please reword.

2. **Page2,line 51-53:**

   This sentence has little to do with the subject. It seems redundant, you may consider dropping it.

3. **Page3,line 22-23:**

   "(c) Contrast-enhanced CT without a reconstruction slice thickness of 1.5 mm." in exclusion criteria is the same meaning as (C) in inclusion criteria. Please remove unnecessary repetition to simplify the presentation.

4. **Page3,line 62 to Page4,line6-7:**

   "The annotation process included delineating the tumor outline and then excluding any air area inside the tumor area." What is the basis and purpose of this annotation?

5. **Page 4,line 27-29:**

   "The ROI patch sizes after resizing were 60 × 60 pixels for the axial direction, 68 × 63 pixels for the sagittal direction and 72 × 67 pixels for the coronal direction." Please give the reason why chose different ROI sizes.

6. **Page 4,line 27-29:**

   Data augmentation: What did you do with the validation data set? Please provide details and reasons.
7. Page 5, line 26-29: This sentence is confusing. Please reword.

8. Page 5, line 33-35: Please correct the punctuation and capitalization.

9. Page 5, line 57-61: This is partly repetitive of the discussion. Is it necessary here?

10. Page 5 Radiomics model: How are patients assigned to the training and validation groups in radiomics model?

11. Page 5, Line 31-34 This sentence should focus on KRAS mutational status in CRC.

12. Page 7, Line 55-57 This sentence is confusing. Why clinical background and tumor stage would cause inconsistency in the radiomics model or the ResNet model?

Are the methods appropriate and well described? If not, please specify what is required in your comments to the authors.

Yes

Does the work include the necessary controls? If not, please specify which controls are required in your comments to the authors.

Yes

Are the conclusions drawn adequately supported by the data shown? If not, please explain in your comments to the authors.

Yes

Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review? If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.

I am able to assess the statistics

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