

Dear Editors and Reviewers:

Thank you for your correspondence and the valuable feedback provided by the reviewers regarding our manuscript titled "**CT Radiogenomics: a potential tool for prediction of molecular subtypes in gastric stromal tumor**" (ID: 88756). We appreciate the insightful comments, as they have greatly contributed to the revision and improvement of our paper, and have provided valuable guidance for our future research endeavors.

In response to the comments and requests, we have made the necessary modifications to the original manuscript. The revised sections have been highlighted in yellow for your convenience, and we have attached the revised manuscript for your review and approval. We sincerely hope that this revised manuscript will meet the necessary criteria for publication in the "**World Journal of Gastrointestinal Oncology**". The key corrections made in the paper and our responses to the reviewers' comments are outlined as follows:

Specific Comments to Authors:

The paper is beyond my expertise as far as statistical approach and radiomics studies. To my understanding you try to predict the mutation based on preoperative CT scan, but I do not understand how this will be reflected in a benefit for patients. With AUC curves of 0.7-0.8 you have a relatively good prediction but I fail to understand the clinical benefit. Your scoring system takes into account CD34 and Kit expression, meaning you have a sample of tumor on which you can generate genetic analysis. I decline my capacity to judge your paper and ask the editor to send it to another reviewer.

Response: Many thanks for reviewer's comments and suggestions. In current manuscript, we extracted some pathological features, such as CD34 and Ki-67 expression, mitotic index, to build the combined model to predict gastric gastrointestinal stromal tumors (GISTs) with KIT exon 11 mutation and KIT exon 11 codons 557-558 deletions. Although it means we have a sample of tumor on which you can generate genetic analysis. However, for patients who are unable to undergo surgical

resection, fine-needle biopsy samples provide adequate material for pathological examination but are insufficient for genetic analysis. Moreover, genetic testing is not routinely conducted in all hospitals due to its high cost. Therefore, there is an urgent need to establish a noninvasive, accurate, and cost-effective preoperative method for identifying the mutation status of GISTs.

We sincerely appreciate the invaluable comments and suggestions provided by the reviewers. In our current manuscript, we have utilized various pathological features, including CD34 and Ki-67 expression, as well as the mitotic index, to develop a combined model for predicting the presence of KIT exon 11 mutation and KIT exon 11 codons 557-558 deletions in GISTs. While this implies that we possess tumor samples from which genetic analysis can be conducted, it is important to note that patients who are unable to undergo surgical resection often only have access to fine-needle biopsy samples, which provide sufficient material for pathological examination but are inadequate for genetic analysis. Furthermore, the high cost associated with genetic testing prevents its routine implementation in all healthcare facilities. Hence, there is an urgent and pressing need to establish a noninvasive, precise, and cost-effective preoperative method for determining the mutation status of GISTs.

In this study, we developed and validated a radiomics model to predict the genotypes of gastric GISTs using contrast-enhanced CT images. Our findings demonstrated that the radiomics model exhibited a satisfactory performance in distinguishing gastric GISTs with KIT exon 11 mutations and GISTs with KIT exon 11 codons 557-558 deletions. Among the different models evaluated, the combined model $CT_{sign} + rad + clinic$ demonstrated the highest predictive accuracy. This model holds promise as an effective and noninvasive approach to guide personalized treatment decisions prior to surgery.

Yours Sincerely

Correspondence Author: Xijiao Liu
E-mail address: bless_jiao@163.com