

Dear Editors and Reviewers:

Thank you for your comments concerning our manuscript entitled “Quantitative parameters in novel spectral CT: Assessment of Ki-67 expression in patients with gastric adenocarcinoma” (Manuscript NO.: 79214). Those comments are all valuable and very helpful for revising and improving our paper, as well as the important guiding significance to our researches. We have studied comments carefully and have made correction which we hope meet with approval. We have revised the manuscript step by step according to the relevant requirements. The main corrections in the manuscript and the responds to are as following:

Responds to the reviewer 1#:

The reviewer 1 has no more suggestions for revision.

Responds to the reviewer 2#:

Respond to comment: (I will suggest adding in description of immunohistochemical detection of Ki-67 the origin and dilution of primary antibodies used.)

Response:

In the part of **MATERIALS AND METHODS(2.4 Histopathology Evaluation)**, we have added details about the origin and dilution of primary antibodies used during the detection of Ki-67. The specific content is as following:

The Ki-67 polyclonal antibody used (Roche #, Ventana) was produced by ShangHai Rebiosci Biotech Co., Ltd.

Response to the step 4 (LANGUAGE POLISHING REQUIREMENTS FOR REVISED MANUSCRIPTS SUBMITTED BY AUTHORS WHO ARE NON-NATIVE SPEAKERS OF ENGLISH).

The manuscript has been polished before submit to the journal. As only a few sentences were added to the revised manuscript, so no further language

polishing was needed.

Response to the step 6 (EDITORIAL OFFICE'S COMMENTS)

We have revised the manuscript according to the Editorial Office's comments and suggestions. The figures have been organized into single PowerPoint file. Moreover, we have modified part of content about the highlights of the latest cutting-edge research results in the part of introduction (paragraph 3).

The “Article Highlights” section is added at the end of the manuscript. The specific content are as follows:

Article Highlights:

Research background

The level of Ki-67 expression is a valuable prognostic factor in gastric cancer. However, the quantitative parameters based on the novel dual-layer spectral detector CT(DLSDCT) in discriminating the expression of Ki-67 status are unclear.

Research motivation

The relationship between the Ki-67 expression in gastric carcinoma and part spectral parameters(including the effective atomic number(Z^{eff}) and the monoenergetic CT attenuation) is unclear.

Research objectives

This study aimed to investigate the diagnostic ability of DLSDCT-derived parameters for Ki-67 expression status of gastric carcinoma(GC).

Research methods

Dual-phase enhanced abdominal CT was performed preoperatively for 108 patients with GC. The monoenergetic CT attenuation value at 40–100 keV(kilo

electron volt), the slope of the spectral curve (λ_{HU}), iodine concentration (IC), normalized iodine concentration (nIC), Z^{eff} and normalized Z^{eff} (nZ^{eff}) in the arterial (AP) and venous phase (VP) were retrospectively compared between the group of low and high Ki-67 status. The relationship between the spectral parameters and Ki-67 expression status were analyzed, and the diagnostic efficacy of the statistically significant parameters between two groups were evaluated.

Research results

The low and high Ki-67 expression group is 37 and 71 patients respectively. $CT_{40\text{keV-VP}}$, $CT_{70\text{keV-VP}}$, $CT_{100\text{keV-VP}}$, and Z^{eff} -related parameters were significantly higher, but IC-related parameters were lower in the low Ki-67 group than the high Ki-67 group. $CT_{40\text{keV-VP}}$, $CT_{70\text{keV-VP}}$, $CT_{100\text{keV-VP}}$, Z^{eff} , and nZ^{eff} exhibited negative correlations with Ki-67 status, whereas IC and nIC positively correlated with it. The results of ROC analysis showed that the multi-variable model of spectral parameters performed excellent ability for identifying the Ki-67 status (AUC 0.967; sensitivity 95.77%; specificity 91.89%). Nevertheless, the differentiating capabilities of single-variable model were moderate (AUC value from 0.630 to 0.835).

Research conclusions

Z^{eff} and IC may be a useful noninvasive method for evaluating the Ki-67 expression in GC.

Research perspectives

The spectral CT images are prospective to provide the pathological information of Ki-67 expression of GC in the future.

As regards the references:

The entry type of reference 20 and 26 is book, without doi and PMID.

Reference 27 and 31 is lack of doi online.