

# World Journal of *Gastroenterology*

*World J Gastroenterol* 2020 August 28; 26(32): 4729-4888



**MINIREVIEWS**

- 4729 New advances in radiomics of gastrointestinal stromal tumors  
*Cannella R, La Grutta L, Midiri M, Bartolotta TV*
- 4739 Novel virulence factor *dupA* of *Helicobacter pylori* as an important risk determinant for disease manifestation: An overview  
*Alam J, Sarkar A, Karmakar BC, Ganguly M, Paul S, Mukhopadhyay AK*
- 4753 Etiology and management of liver injury in patients with COVID-19  
*Yang RX, Zheng RD, Fan JG*

**ORIGINAL ARTICLE****Basic Study**

- 4763 Immune and microRNA responses to *Helicobacter muridarum* infection and indole-3-carbinol during colitis  
*Alkarkoushi RR, Hui Y, Tavakoli AS, Singh U, Nagarkatti P, Nagarkatti M, Chatzistamou I, Bam M, Testerman TL*
- 4786 Dual targeting of Polo-like kinase 1 and baculoviral inhibitor of apoptosis repeat-containing 5 in TP53-mutated hepatocellular carcinoma  
*Li Y, Zhao ZG, Luo Y, Cui H, Wang HY, Jia YF, Gao YT*
- 4802 Promising xenograft animal model recapitulating the features of human pancreatic cancer  
*Miao JX, Wang JY, Li HZ, Guo HR, Dunmall LSC, Zhang ZX, Cheng ZG, Gao DL, Dong JZ, Wang ZD, Wang YH*

**Case Control Study**

- 4817 Association between human leukocyte antigen gene polymorphisms and multiple EPIYA-C repeats in gastrointestinal disorders  
*Saribas S, Demiryas S, Yilmaz E, Uysal O, Kepil N, Demirci M, Caliskan R, Dinc HO, Akkus S, Gareayaghi N, Kirmusaoglu S, Ozbey D, Tokman HB, Koksal SS, Tasci I, Kocazeybek B*

**Retrospective Study**

- 4833 Features of extrahepatic metastasis after radiofrequency ablation for hepatocellular carcinoma  
*Yoon JH, Goo YJ, Lim CJ, Choi SK, Cho SB, Shin SS, Jun CH*
- 4846 Current status of *Helicobacter pylori* eradication and risk factors for eradication failure  
*Yan TL, Gao JG, Wang JH, Chen D, Lu C, Xu CF*
- 4857 Development of a novel score for the diagnosis of bacterial infection in patients with acute-on-chronic liver failure  
*Lin S, Yan YY, Wu YL, Wang MF, Zhu YY, Wang XZ*

**Observational Study**

**4866** Inactive matrix Gla protein is elevated in patients with inflammatory bowel disease

*Brnic D, Martinovic D, Zivkovic PM, Tokic D, Vilovic M, Rusic D, Tadin Hadjina I, Libers C, Glumac S, Supe-Domic D, Tonkic A, Bozic J*

**Prospective Study**

**4878** Emergency department targeted screening for hepatitis C does not improve linkage to care

*Houri I, Horowitz N, Katchman H, Weksler Y, Miller O, Deutsch L, Shibolet O*

**ABOUT COVER**

Editorial Board of *World Journal of Gastroenterology*, Dr. Conrado M Fernandez-Rodriguez is Chief of the Gastroenterology Unit at Alcorcon Foundation University Hospital and Associate Professor of Medicine at University Rey Juan Carlos. His main research interest is chronic liver diseases, for which he has authored more than 140 peer-reviewed publications, including in top gastroenterology and hepatology journals. He serves as Director of the Scientific Committee of the Spanish Society of Digestive Diseases, Associate Editor of Hepatology for *Spanish Journal of Gastroenterology*. He is also a member of the Spanish Steering Committee of Alcohol-Related Liver Disease National Registry (ReHalc) and Scientific Advisor of the Spanish Committee for Hepatitis C virus Elimination, and direct participant in several multicenter international clinical trials (Respond-2, REGENERATE, STELLAR-4) and national trials and registries (TRIC-1, HEPAMet, Hepa-C, ColHai). (L-Editor: Filipodia)

**AIMS AND SCOPE**

The primary aim of *World Journal of Gastroenterology* (*WJG, World J Gastroenterol*) is to provide scholars and readers from various fields of gastroenterology and hepatology with a platform to publish high-quality basic and clinical research articles and communicate their research findings online. *WJG* mainly publishes articles reporting research results and findings obtained in the field of gastroenterology and hepatology and covering a wide range of topics including gastroenterology, hepatology, gastrointestinal endoscopy, gastrointestinal surgery, gastrointestinal oncology, and pediatric gastroenterology.

**INDEXING/ABSTRACTING**

The *WJG* is now indexed in Current Contents®/Clinical Medicine, Science Citation Index Expanded (also known as SciSearch®), Journal Citation Reports®, Index Medicus, MEDLINE, PubMed, PubMed Central, and Scopus. The 2020 edition of Journal Citation Report® cites the 2019 impact factor (IF) for *WJG* as 3.665; IF without journal self cites: 3.534; 5-year IF: 4.048; Ranking: 35 among 88 journals in gastroenterology and hepatology; and Quartile category: Q2.

**RESPONSIBLE EDITORS FOR THIS ISSUE**

Production Editor: Yan-Liang Zhang; Production Department Director: Yun-Xiaojuan Wu; Editorial Office Director: Ze-Mao Gong.

**NAME OF JOURNAL**

*World Journal of Gastroenterology*

**ISSN**

ISSN 1007-9327 (print) ISSN 2219-2840 (online)

**LAUNCH DATE**

October 1, 1995

**FREQUENCY**

Weekly

**EDITORS-IN-CHIEF**

Andrzej S Tarnawski, Subrata Ghosh

**EDITORIAL BOARD MEMBERS**

<http://www.wjgnet.com/1007-9327/editorialboard.htm>

**PUBLICATION DATE**

August 28, 2020

**COPYRIGHT**

© 2020 Baishideng Publishing Group Inc

**INSTRUCTIONS TO AUTHORS**

<https://www.wjgnet.com/bpg/gerinfo/204>

**GUIDELINES FOR ETHICS DOCUMENTS**

<https://www.wjgnet.com/bpg/GerInfo/287>

**GUIDELINES FOR NON-NATIVE SPEAKERS OF ENGLISH**

<https://www.wjgnet.com/bpg/gerinfo/240>

**PUBLICATION ETHICS**

<https://www.wjgnet.com/bpg/GerInfo/288>

**PUBLICATION MISCONDUCT**

<https://www.wjgnet.com/bpg/gerinfo/208>

**ARTICLE PROCESSING CHARGE**

<https://www.wjgnet.com/bpg/gerinfo/242>

**STEPS FOR SUBMITTING MANUSCRIPTS**

<https://www.wjgnet.com/bpg/GerInfo/239>

**ONLINE SUBMISSION**

<https://www.f6publishing.com>

## New advances in radiomics of gastrointestinal stromal tumors

Roberto Cannella, Ludovico La Grutta, Massimo Midiri, Tommaso Vincenzo Bartolotta

**ORCID number:** Roberto Cannella 0000-0002-3808-0785; Ludovico La Grutta 0000-0002-3557-0084; Massimo Midiri 0000-0003-1824-7549; Tommaso Vincenzo Bartolotta 0000-0002-8808-379X.

**Author contributions:** Cannella R and Bartolotta TV wrote and revised the manuscript for important intellectual content; La Grutta L and Midiri M made critical revisions related to important intellectual content of the manuscript; all the Authors approved the final version of the article.

**Conflict-of-interest statement:** All authors have no any conflict of interests.

**Open-Access:** This article is an open-access article that was selected by an in-house editor and fully peer-reviewed by external reviewers. It is distributed in accordance with the Creative Commons Attribution NonCommercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: <http://creativecommons.org/licenses/by-nc/4.0/>

**Manuscript source:** Invited Manuscript

**Roberto Cannella, Ludovico La Grutta, Massimo Midiri, Tommaso Vincenzo Bartolotta**, Section of Radiology - BiND, University Hospital "Paolo Giaccone", Palermo 90127, Italy

**Tommaso Vincenzo Bartolotta**, Department of Radiology, Fondazione Istituto Giuseppe Giglio, Ct.da Pietrapollastra, Cefalù (Palermo) 90015, Italy

**Corresponding author:** Tommaso Vincenzo Bartolotta, MD, PhD, Assistant Professor, Section of Radiology - BiND, University Hospital "Paolo Giaccone", Via del Vespro 129, Palermo 90127, Italy. [tv\\_bartolotta@yahoo.com](mailto:tv_bartolotta@yahoo.com)

### Abstract

Gastrointestinal stromal tumors (GISTs) are uncommon neoplasms of the gastrointestinal tract with peculiar clinical, genetic, and imaging characteristics. Preoperative knowledge of risk stratification and mutational status is crucial to guide the appropriate patients' treatment. Predicting the clinical behavior and biological aggressiveness of GISTs based on conventional computed tomography (CT) and magnetic resonance imaging (MRI) evaluation is challenging, unless the lesions have already metastasized at the time of diagnosis. Radiomics is emerging as a promising tool for the quantification of lesion heterogeneity on radiological images, extracting additional data that cannot be assessed by visual analysis. Radiomics applications have been explored for the differential diagnosis of GISTs from other gastrointestinal neoplasms, risk stratification and prediction of prognosis after surgical resection, and evaluation of mutational status in GISTs. The published researches on GISTs radiomics have obtained excellent performance of derived radiomics models on CT and MRI. However, lack of standardization and differences in study methodology challenge the application of radiomics in clinical practice. The purpose of this review is to describe the new advances of radiomics applied to CT and MRI for the evaluation of gastrointestinal stromal tumors, discuss the potential clinical applications that may impact patients' management, report limitations of current radiomics studies, and future directions.

**Key words:** Gastrointestinal stromal tumors; Radiomics; Texture analysis; Computed tomography; Magnetic resonance imaging; Clinical applications

©The Author(s) 2020. Published by Baishideng Publishing Group Inc. All rights reserved.

**Core tip:** Radiomics researches have demonstrated promising results for the differential

**Received:** May 28, 2020**Peer-review started:** May 28, 2020**First decision:** June 4, 2020**Revised:** June 16, 2020**Accepted:** August 1, 2020**Article in press:** August 1, 2020**Published online:** August 28, 2020**P-Reviewer:** Akai H**S-Editor:** Ma YJ**L-Editor:** A**P-Editor:** Ma YJ

diagnosis of gastrointestinal stromal tumors (GISTs) with other gastrointestinal neoplasms in the stomach and duodenum. Excellent performances have been reported for the evaluation of risk status, the preoperative identification of high-risk tumors, and the prediction of prognosis after target therapies. Radiogenomics studies are still lacking, with only initial evidences describing the potential of radiomics for the diagnosis of GISTs without KIT mutations. In this work we review the new advances in radiomics applied to the computed tomography and magnetic resonance imaging of GISTs.

**Citation:** Cannella R, La Grutta L, Midiri M, Bartolotta TV. New advances in radiomics of gastrointestinal stromal tumors. *World J Gastroenterol* 2020; 26(32): 4729-4738

**URL:** <https://www.wjgnet.com/1007-9327/full/v26/i32/4729.htm>

**DOI:** <https://dx.doi.org/10.3748/wjg.v26.i32.4729>

## INTRODUCTION

Gastrointestinal stromal tumors (GISTs) are uncommon mesenchymal neoplasms of the gastrointestinal tract, originating from the interstitial cells of Cajal<sup>[1]</sup>. GISTs may arise anywhere along all the gastrointestinal tract, being more commonly encountered in the stomach (50%-60% of cases) or small intestine (30%-40%), while they are rarely observed in the esophagus and colorectum<sup>[1,2]</sup>. All GISTs have malignant potential with varying degree of biological aggressiveness. Liver and peritoneum are the most common sites of metastatic disease or recurrence after curative resection, which occurs in about 40% of patients<sup>[3-5]</sup>. GISTs are also characterized by peculiar genetic alterations, with 85% of tumors presenting with activating mutations in the KIT proto-oncogene, while a minority of lesions show mutations of platelet-derived growth factor  $\alpha$  (PDGFR $\alpha$ ), or occasionally may lack of known mutations (wild type GISTs)<sup>[6]</sup>. The advent of imatinib mesylate, a selective tyrosine kinase inhibitor of the KIT and PDGFR $\alpha$  receptors, has revolutionized the treatment of GISTs, significantly improving the patients' survival even in advanced stages.

Contrast-enhanced computed tomography (CT) is the imaging modality of choice for preoperative diagnosis, staging, as well as postoperative follow-up and assessment of treatment response in patients with GISTs<sup>[7,8]</sup>. On contrast-enhanced CT, GISTs usually present with peculiar imaging features, most often with large (> 5 cm) abdominal mass, heterogeneous enhancement, and variable amount of necrosis<sup>[9-12]</sup>. Other imaging findings include presence of calcifications, ulceration or cystic degeneration<sup>[11,12]</sup>. Magnetic resonance imaging (MRI) may provide additional information for the evaluation of primary tumors in peculiar location (*i.e.*, rectum) and may be preferred for the differential diagnosis of liver metastasis from other benign hepatic lesions<sup>[13,14]</sup>. In clinical practice, predicting the behavior of GISTs is challenging, unless the lesions have already metastasized at the time of diagnosis. Although some imaging predictors of malignant potential have been identified (size, location, margins, enhancement pattern) and variably correlated with prognosis and survival of GISTs, small tumors lacking of concerning imaging features may still metastasize, making difficult to predict aggressive tumors.

Radiomics is emerging as a promising tool that allows to quantify lesion heterogeneity, extracting additional quantitative data from radiological imaging that cannot be evaluated by human eyes<sup>[15,16]</sup>. In recent years, multiple researches have explored the performance of radiomics models in abdominal oncologic applications, with significant results for lesions characterization, evaluation of therapeutic response and prediction of patients' survival after surgical or systemic treatments<sup>[17-22]</sup>. The application of radiomics in GISTs could be used to further improve the patients' management and provide new advances in quantitative lesion evaluation due to the unique clinical, genetic, and imaging characteristics of these tumors.

With this review, we aim to describe the new advances of radiomics applied to CT and MR imaging for the evaluation of gastrointestinal stromal tumors, discuss the potential clinical applications that may impact patients' management, report limitations of current radiomics studies, and future directions.

## WORKFLOW OF RADIOMICS ANALYSIS

Radiomics is based on the mathematical quantification of images heterogeneity, through the analysis of distribution and relationships of pixel intensities within a region of interest (ROI)<sup>[15,16]</sup>. Radiomics analysis requires a multistep process, starting from imaging acquisition, and including lesion segmentation, features extraction, features selection and reduction, predictive model building, and finally validation and clinical interpretation of the results<sup>[19,20,23]</sup>.

Radiomics can be potentially applied to any type of radiological images, including ultrasound, CT, MRI and positron emission tomography/CT, but most of studies are nowadays based on CT or MRI examinations<sup>[19]</sup>. Image acquisition is one of the most critical steps for radiomics, since scanning and technical parameters may influence the reproducibility of radiomics features. Particularly, reconstruction algorithm and slice thickness had demonstrated to largely impact on the reproducibility of radiomics features on CT<sup>[24-26]</sup>. The heterogeneous imaging acquisition may be problematic for evaluation of retrospective data acquired with different CT or MRI scanners, while prospective study should ensure that all patients will be imaged using standardized parameters<sup>[27]</sup>. It is also important to select the optimal phase/sequence for image analysis. Pre-contrast images are not affected by the contrast administration, but lesion segmentation is more difficult, especially for smaller tumors that are difficult to distinguish on non-contrast CT. Contrast-enhanced images may provide better assessment of lesion heterogeneity, but type and non-standardized timing of contrast agent administration may represent additional confounding factors, especially for images acquired on arterial phase.

Lesion segmentation is the most critical step of radiomics process. Segmentation may be performed manually by expert radiologists, using semi-automatic, or automatic software<sup>[27]</sup>. Although manual segmentation is time consuming and it is subject to intra- and inter-reader variability, it is still considered as the gold standard for most of radiomics studies<sup>[18,19,23]</sup>. The segmentation is usually realized by drawing a ROI within the tumor margins (Figure 1), avoiding the inclusion of any extra-tumoral tissues such as bowel mucosa, intestinal content, or peritumoral vessels. The ROI can be placed on a single slice (2D ROI) on the largest tumor cross section or include the whole lesion (3D ROI). Although the latter may capture more tissue heterogeneity, its clinical advantage remains debated.

Several in-house build or commercially available radiomics research software are nowadays used for extract a large number of radiomics features. These features may be divided into semantic (qualitative features usually reported by radiologists such as size, margins, enhancement pattern) or agnostic (which are mathematical and quantitative descriptors of heterogeneity) features. Agnostic features are further classified in first, second and third order features<sup>[19]</sup>. The first order features are obtained from the analysis of the gray level histogram within a defined ROI, without considering spatial relations among pixels. Most common histogram-based features include mean (average of the pixels within the ROI), standard deviation (dispersion from the mean), skewness (asymmetric of the histogram), kurtosis (peakedness/flatness of the histogram), and entropy (image irregularity or complexity)<sup>[20]</sup>. The second order texture features consider the spatial relationship among pixels, and most commonly include grey level co-occurrence matrix (GLCM), that quantifies the arrangements of pairs of pixels with the same values in specific directions, and grey-level run length matrix (GLRLM), that quantifies consecutive pixels with the same intensity along specific directions. Third or higher order features evaluate spatial relationship among three or more pixels through statistical methods after applying filters or mathematical transforms. These features include fractal analysis, wavelet transform, and Laplacian transforms of Gaussian-filtered image. Due to the large number of extracted parameters, features reduction should be performed in order to excluded features that are not reproducible or with high similarity (*i.e.*, redundant features). This is a significant step to avoid overfitting problems, especially in small cohorts<sup>[18-20,24]</sup>.

Only uncorrelated features with significant diagnostic performance are selected for final radiomics models. The choice of statistical methods and models may depend on multiple factors such as evaluation of primary outcome, number of features, and number of analyzed lesions<sup>[23]</sup>. These models can be also combined with other patient clinical characteristics in order to increase their predictive power<sup>[15]</sup>. Finally, radiomics models should be tested and validated using independent internal validation cohort or external population<sup>[18]</sup>. To assess the quality of radiomics studies, scores have been proposed, such as the Radiomics Quality Score developed by Lambin *et al.*<sup>[28]</sup>, which evaluates 16 key components of radiomics workflow<sup>[28,29]</sup>.



Figure 1 Examples of lesion segmentation using a texture analysis software (LIFEx, [www.lifexsoft.org](http://www.lifexsoft.org)) on axial (A), coronal (B) and sagittal (C) contrast-enhanced computed tomography images on venous phase in an 82-year-old man with 4.5 cm gastric gastrointestinal stromal tumor.

## RADIOMICS METHODOLOGY IN GISTS

Existing articles of radiomics in GISTs (Table 1) have been performed with heterogeneous methodology regarding the imaging studies, type of radiomics features and analysis<sup>[30-44]</sup>. Up to May 2020, all the radiomics research studies on GISTs were performed in retrospective population, and only four studies were multicentric<sup>[31,32,35,44]</sup>. The number of included GISTs widely ranged from 15 to 440 lesions. All except one of radiomics GIST studies used CT imaging for features extraction, while only one study<sup>[36]</sup> evaluated the MRI. On CT studies, radiomics analysis was most commonly carried out on venous phase (48%), followed by arterial phase (38%), and pre-contrast images (14%) (Figure 2). No study included the delayed phase in radiomics evaluation. First, second, and third order features were extracted in 80%, 67%, and 20% of studies, respectively. Volumetric analysis (3D ROI) was performed in 60% of cases, while 2D ROIs were placed in 47% cases. Only one study<sup>[41]</sup> compared the accuracy of 2D vs 3D ROIs in GISTs, reporting an excellent agreement between the two segmentation methods.

Few studies have investigated the intra- and inter-reader variability of radiomics features in GISTs, with promising results for reproducibility of tumor segmentation and features extraction. A recent study<sup>[41]</sup> described an almost perfect intra- and inter-reader reproducibility of radiomics features (reported ICC > 0.98) using both single-ROI and whole lesions-ROI manual segmentations. Other studies assessed the inter-reader variability for manual segmentation, all reporting an excellent inter-observer agreement for whole tumor radiomics parameters extracted by two abdominal radiologists (ICC ranging from 0.85 to 0.99)<sup>[35,37-39]</sup>.

Validation of radiomics models in independent cohorts was performed in 47% of studies. However only three of them<sup>[31,32,44]</sup> included external validation cohorts.

## RADIOMICS APPLICATIONS IN GISTS

### **Differential diagnosis between GIST and other tumors**

Stomach is the most common organ affected by GISTs. The differential diagnosis should be carried with other gastric benign mesenchymal neoplasms (*i.e.*, schwannomas and leiomyomas) or malignant tumors (*i.e.*, gastric adenocarcinomas and lymphomas), and it may be difficult due to the overlap in imaging appearance<sup>[45-47]</sup>. Using a texture analysis approach, Ba-Ssalamah *et al*<sup>[30]</sup> differentiated GISTs from gastric adenocarcinomas and lymphomas with a high successful rate on arterial and venous phase CT images.

Another challenging location for the differential diagnosis of GISTs from other gastrointestinal neoplasms is the duodenum<sup>[48]</sup>. GISTs occur rarely in the duodenum (less than 5% of cases) and the differentiation from more common duodenal adenocarcinomas (DACs), pancreatic ductal adenocarcinomas (PDACs), or pancreatic neuroendocrine tumors is significantly relevant for preoperative management and patient prognosis<sup>[48,49]</sup>. To improve the preoperative characterization of these lesions, a

**Table 1 Summary of radiomics studies including gastrointestinal stromal tumors**

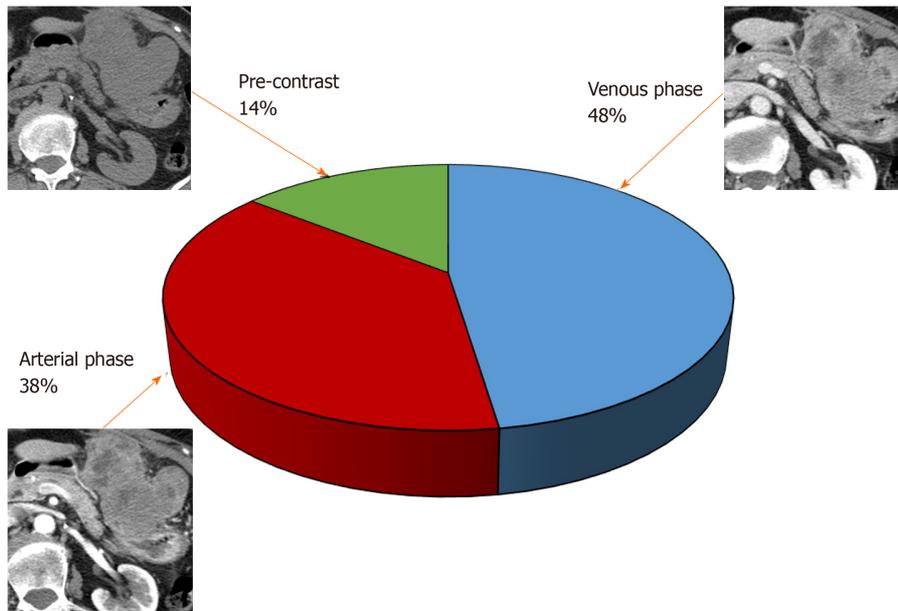
Ref.	Number of lesions	Imaging	Radiomics analysis	Key radiomics results
Ba-Ssalamah <i>et al</i> <sup>[30]</sup>	15 GISTs, 27 gastric adenocarcinomas, 5 lymphomas	CT	Histogram-based, GLCM, GLRLM, absolute gradient, autoregressive model, Wavelet transform.	On AP texture features perfectly differentiated between GIST <i>vs</i> lymphoma. On PVP texture features differentiated GIST <i>vs</i> adenocarcinoma in 90% of cases and GIST <i>vs</i> lymphoma in 92% of cases.
Chen <i>et al</i> <sup>[31]</sup>	222 GISTs	CT	GLCM, GLRLM, GLSZM, NGTDM. Support Vector Machine for model building.	AUROC 0.84-0.86 of radiomics models for GIST risk stratification.
Chen <i>et al</i> <sup>[32]</sup>	147 GISTs	CT	Residual Neural Network for model building.	AUROC of 0.887-0.947 for ResNet nomogram and model for prediction of disease-free survival after surgical resection.
Choi <i>et al</i> <sup>[33]</sup>	145 GISTs	CT	Histogram-based.	AUROC of 0.782-0.779 of mpp and kurtosis for differentiation of high-risk GISTs.
Ekert <i>et al</i> <sup>[34]</sup>	25 GISTs	CT	Histogram-based, GLCM, GLDM, GLRLM, GLSZM, NGLDM.	Ten GLCM, GLRLM, NGLDM features significantly correlated with disease progression and progression free survival.
Feng <i>et al</i> <sup>[35]</sup>	90 GISTs	CT	Histogram-based.	AUROC of 0.823-0.830 of entropy for the differentiation of low from high-risk GISTs.
Fu <i>et al</i> <sup>[36]</sup>	51 GISTs	MRI	Fractal features, GLCM, GLRLM.	Texture features on DWI and ADC map correlated with overall survival in metastatic GISTs.
Liu <i>et al</i> <sup>[37]</sup>	78 GISTs	CT	Histogram-based.	AUROC of 0.637-0.811 for the identification of very low and low-risk GISTs.
Lu <i>et al</i> <sup>[38]</sup>	28 GISTs, 26 DACs, 20 PDACs	CT	Histogram-based.	AUROC of 0.809-0.936 of 90 <sup>th</sup> percentile for differentiation of GISTs from DACs and PDACs.
Ren <i>et al</i> <sup>[39]</sup>	440 GISTs	CT	Histogram-based, GLCM.	AUROC of 0.933-0.935 for the differentiation of low from high-risk GISTs.
Wang <i>et al</i> <sup>[40]</sup>	333 GISTs	CT	Histogram-based, GLCM, GLRLM.	AUROC of 0.882-0.920 for the differentiation of low from high-risk GISTs. AUROC of 0.769-0.820 for the differentiation of low from high mitotic count.
Xu <i>et al</i> <sup>[41]</sup>	86 GISTs	CT	Histogram-based, GLCM, GLRLM.	AUROC of 0.904-0.962 of standard deviation for diagnosis of GIST without KIT exon 11 mutations.
Yan <i>et al</i> <sup>[42]</sup>	213 GISTs	CT	Histogram-based, GLCM, GLRLM, absolute gradient, autoregressive model, Wavelet transform.	AUROC of 0.933 of texture analysis model for preoperative risk stratification.
Zhang <i>et al</i> <sup>[43]</sup>	140 GISTs	CT	Histogram-based, shape-based, GLCM, GLRLM, GLSZM.	AUROC of 0.809-0.935 for discrimination of advanced GISTs and four risk categories of GISTs
Zhang <i>et al</i> <sup>[44]</sup>	339 GISTs	CT	GLCM, GLRLM, GLSZM, GLDM.	AUROC of 0.754-0.787 of radiomics features for prediction of high Ki67 expression.

AUROC: Area under the receiver operating characteristics curve; CT: Computed tomography; DACs: Duodenal adenocarcinomas; GIST: Gastrointestinal stromal tumors; GLCM: Grey level co-occurrence matrix; GLDM: Grey-level dependence matrix; GLRLM: Grey-level run length matrix; GLSZM, Gray-level size zone matrix; GLZLM: Grey-level zone length matrix; MRI: Magnetic resonance imaging; NGLDM: Neighborhood grey-level different matrix; NGTDM: Neighbourhood gray-tone difference matrix; PDACs: Pancreatic ductal adenocarcinomas.

study by Lu *et al*<sup>[38]</sup> investigated the whole lesion histogram analysis on contrast-enhanced CT, reporting an excellent discrimination of GISTs from DACs and PDACs in the periampullary region.

### **Risk stratification and prediction of prognosis of GISTs**

Accurate evaluation of malignant risk and outcome in GISTs is mainly based on tumor size, location (gastric *vs* non-gastric tumors), and mitotic count obtained with resection specimens. These factors are combined in the National Institutes of Health 2008 criteria<sup>[50]</sup>, which classified GISTs four risk classes: very low, low, intermediate and high-risk tumors. However, in clinical practice risk stratification may be limited by the evaluation of mitotic count in patients treated with neoadjuvant therapies, or by the assessment of biopsy specimens that could not be representative of the whole tumor. Therefore, several studies have tried to predict risk stratification based on preoperative CT imaging<sup>[51-53]</sup>. CT features like size, growth pattern, or enlarged feeding vessels have



**Figure 2** Chart shows the frequency of computed tomography imaging phases included in radiomics gastrointestinal stromal tumors studies. Corresponding computed tomography images shows an 8.6 cm gastric gastrointestinal stromal tumor in a 64-year-old woman.

been associated with high-risk tumors<sup>[51-53]</sup>. Nevertheless, risk stratification using qualitative imaging evaluation is affected by the readers' experience, heterogeneous definition of imaging features, and subjective assessment with suboptimal reproducibility of qualitative features<sup>[54]</sup>.

Radiomics models have demonstrated to improve the preoperative prediction of high-risk GISTs compared to the conventional visual evaluation<sup>[33,42]</sup>. The added value of radiomics and texture analysis on contrast-enhanced CT was firstly investigated by Yan *et al*<sup>[42]</sup> in a retrospective cohort of 213 small bowel GISTs. In that study, texture analysis model achieved a similar diagnostic accuracy compared to that of clinical and subjective imaging features for preoperative risk prediction of GISTs<sup>[42]</sup>. When combining the clinical and texture analysis features, the diagnostic performance (AUROC of 0.943) significantly improved compared to the model incorporating clinical and imaging features only<sup>[42]</sup>. In a more recent study, Choi *et al*<sup>[33]</sup> investigated the diagnostic performance of histogram-based texture parameters and qualitative analysis of CT imaging features for the differentiation of low-risk from high-risk GISTs. Their results confirmed that the radiomics features showed a higher diagnostic performance (AUROC of 0.782-0.779) compared to conventional qualitative evaluation (AUROC of 0.59-0.70) by two radiologists in the differential diagnosis of low-risk from high-risk GISTs<sup>[33]</sup>.

The potential of radiomics for the risk stratification in GISTs have been further evaluated by other evidences with promising results and excellent diagnostic performance<sup>[35,37,39,40,43]</sup>. Liu *et al*<sup>[37]</sup> applied CT-based texture analysis for the identification of very low and low risk GISTs in a cohort of 78 patients, reporting a fair diagnostic performance (AUROC of 0.637-0.811) for the most discriminant features obtained on pre-contrast, arterial and venous phases CT images. Feng *et al*<sup>[35]</sup> extracted histogram-based parameters from arterial and venous phase CT images of 90 small bowel GISTs. Among them, entropy showed the highest diagnostic accuracy on arterial and venous phases (AUROC of 0.823 and 0.830, respectively) for the identification of high-risk GISTs. Zhang *et al*<sup>[43]</sup> analyzed 140 GISTs using arterial phase CT images, reporting an excellent diagnostic performance for preoperative prediction of advanced (*i.e.*, high and intermediate risk) GISTs and four-class risk stratification (AUROC of 0.935 and 0.809, respectively).

In a large population of 440 pathologically proven GISTs, Ren *et al*<sup>[39]</sup> reported an excellent performance of radiomics models for the differentiation of low-risk from high-risk GISTs (AUROC of 0.935 and 0.933 in training and validation cohort, respectively). In that study, the prediction nomogram (incorporating lesion size, cystic degeneration, and texture-based mean) demonstrated a sensitivity of 90.6% and a specificity of 75.7% for the diagnosis of high-risk GISTs<sup>[39]</sup>. Similarly, Wang *et al*<sup>[40]</sup> analyzed the contrast-enhanced CT images of 333 GISTs and reported an excellent

discrimination capacity of radiomics models between low-risk and high-risk GISTs in both training and validation cohorts (AUROC of 0.882 and 0.920, respectively). In addition, radiomics models enable to discriminate GISTs with low and high mitotic count with a good-to-excellent performance (AUROC: 0.769-0.820)<sup>[40]</sup>.

In two subsequent studies<sup>[31,32]</sup>, Chen *et al*<sup>[31,32]</sup> built support vector machine and residual neural network based models to predict malignant potential or 3-year and 5-year recurrence-free survival after complete surgical resection of localized GISTs, respectively. In those researches, the Authors enrolled an internal patients' cohort for training the model, which was subsequently validated in internal and external cohorts, with a good-to almost perfect performance for GIST risk stratification and prediction of recurrence free survival at 3-year and 5-year, respectively<sup>[31,32]</sup>.

Survival analysis for disease progression according to texture features was carried out also by Ekert *et al*<sup>[34]</sup> on contrast-enhanced CT, while only one study<sup>[36]</sup> has performed radiomics analysis on MRI. Fu *et al*<sup>[36]</sup> extracted texture features from T2-weighted, DWI and ADC map images to determine prognosis of metastatic GISTs, reporting that texture features on DWI and ADC map well-correlated with overall survival.

Finally, Ki67 index represents a marker of proliferation of tumor cells, which have also been associated with poor prognosis in GISTs<sup>[55]</sup>. In a study of 339 GISTs<sup>[44]</sup>, radiomics signature from contrast-enhanced CT have demonstrated a significant correlation with Ki67 expression, providing an added value for prognosis assessment.

### Assessment of mutational status

Genetic alterations and mutational status is crucial for GISTs optimal target therapy. About 80%-85% of GISTs have mutation in KIT genes, 10% of GISTs have mutations in PDGFR $\alpha$ , while the remaining 10%-15% GISTs are wild type due to the lack of mutations in either of these genes<sup>[6]</sup>. Particularly, PDGFR $\alpha$  and wild type GISTs have a lower response rate or resistance to the target therapies with tyrosine kinase inhibitors, depending on the specific mutational status<sup>[1,6]</sup>.

Few data exist regarding the association between CT imaging features and mutations in GISTs<sup>[57,58]</sup>. The performance of radiomics features and radiologists visual analysis for the differentiation of GISTs with and without KIT exon 11 mutations have been explored by Xu *et al*<sup>[41]</sup> in a study cohort and validation group of 69 and 17 GISTs, respectively. In that investigation, the standard deviation was strongly correlated with absence of KIT exon 11 mutations, and achieved an AUROC of 0.904-0.962. Contrarily, there was no statistically significant differences in the visual ratings of lesions heterogeneity between GISTs with and without KIT exon 11 mutations. Further researches are needed to correlate the radiomics signature with the genomics patterns of mutational status (known as radiogenomics analysis<sup>[15]</sup>) in order to provide reliable information to guide the most appropriate treatment, especially in advanced GISTs that are not suitable for surgical resection.

---

## LIMITATIONS AND FUTURE DIRECTIONS

---

Although radiomics has an enormous research potential for the improvement of quantitative tumors evaluation, there are some limitations that challenges its application in everyday clinical practice. Standardization of methodology is the primary problem for radiomics analysis. Differences in imaging acquisition, features extraction, and radiomics software challenge the comparisons between studies and the repeatability or application of radiomics models in different populations. All the current published studies on radiomics of GISTs are retrospective and mostly performed in single centers. The lack of standardization in CT and MRI acquisition is another major problem for radiomics assessment of GISTs. This latter is strictly related to the rarity of GISTs compared to other neoplasms, which require collection of imaging studies obtained during a long period of time. Moreover, the peculiar histopathological characteristics of GISTs, such as mitotic count and mutational status, require pathological diagnosis through resections specimens as reference standard for radiomics studies.

The evaluation of treatment response after tyrosine kinase inhibitors therapy needs also to be further investigated. Indeed, the response to target therapy may occur even without reduction of tumor size<sup>[58]</sup>. As consequence, Choi criteria<sup>[59]</sup>, based on the measurements of CT attenuation values, have been adopted for the evaluation of treatment response in patients undergoing target therapies. The added values of radiomics in the imaging evaluation of treatment response is currently underexplored

and may be investigated in futures studies.

Further prospective multicentric studies will be needed to validate the optimal diagnostic performance of radiomics models provided by retrospective analysis. Future works are also warranted for optimization and standardization of radiomics software, imaging acquisition, features extraction and models analysis.

## CONCLUSION

Radiomics is emerging as a promising tool for quantitative evaluation of GISTs, with excellent diagnostic performance for the differential diagnosis with other gastrointestinal neoplasms, prediction of risk stratification, and evaluation of mutational status. Future implementation of radiomics models in clinical practice may provide additional information from radiological images that will be helpful to guide patients management and more tailored treatments.

## REFERENCES

- 1 **Parab TM**, DeRogatis MJ, Boaz AM, Grasso SA, Issack PS, Duarte DA, Urayeaza O, Vahdat S, Qiao JH, Hinika GS. Gastrointestinal stromal tumors: a comprehensive review. *J Gastrointest Oncol* 2019; **10**: 144-154 [PMID: 30788170 DOI: 10.21037/jgo.2018.08.20]
- 2 **Akahoshi K**, Oya M, Koga T, Shiratsuchi Y. Current clinical management of gastrointestinal stromal tumor. *World J Gastroenterol* 2018; **24**: 2806-2817 [PMID: 30018476 DOI: 10.3748/wjg.v24.i26.2806]
- 3 **Plumb AA**, Kochhar R, Leahy M, Taylor MB. Patterns of recurrence of gastrointestinal stromal tumour (GIST) following complete resection: implications for follow-up. *Clin Radiol* 2013; **68**: 770-775 [PMID: 23663875 DOI: 10.1016/j.crad.2013.03.002]
- 4 **D'Ambrosio L**, Palesandro E, Boccone P, Tolomeo F, Miano S, Galizia D, Manca A, Chiara G, Bertotto I, Russo F, Campanella D, Venesio T, Sangiolo D, Pignochino Y, Siatis D, De Simone M, Ferrero A, Pisacane A, Dei Tos AP, Aliberti S, Aglietta M, Grignani G. Impact of a risk-based follow-up in patients affected by gastrointestinal stromal tumour. *Eur J Cancer* 2017; **78**: 122-132 [PMID: 28448856 DOI: 10.1016/j.ejca.2017.03.025]
- 5 **Burkill GJ**, Badran M, Al-Muderis O, Meirion Thomas J, Judson IR, Fisher C, Moskovic EC. Malignant gastrointestinal stromal tumor: distribution, imaging features, and pattern of metastatic spread. *Radiology* 2003; **226**: 527-532 [PMID: 12563150 DOI: 10.1148/radiol.2262011880]
- 6 **Oppelt PJ**, Hirbe AC, Van Tine BA. Gastrointestinal stromal tumors (GISTs): point mutations matter in management, a review. *J Gastrointest Oncol* 2017; **8**: 466-473 [PMID: 28736634 DOI: 10.21037/jgo.2016.09.15]
- 7 **Vernuccio F**, Taibbi A, Picone D, LA Grutta L, Midiri M, Lagalla R, Lo Re G, Bartolotta TV. Imaging of Gastrointestinal Stromal Tumors: From Diagnosis to Evaluation of Therapeutic Response. *Anticancer Res* 2016; **36**: 2639-2648 [PMID: 27272772]
- 8 **Inoue A**, Ota S, Sato S, Nitta N, Shimizu T, Sonoda H, Tani M, Ban H, Inatomi O, Ando A, Kushima R, Murata K. Comparison of characteristic computed tomographic findings of gastrointestinal and non-gastrointestinal stromal tumors in the small intestine. *Abdom Radiol (NY)* 2019; **44**: 1237-1245 [PMID: 30600381 DOI: 10.1007/s00261-018-1865-9]
- 9 **Bartolotta TV**, Taibbi A, Galia M, Cannella I, Lo Re G, Sparacia G, Midiri M, Lagalla R. Gastrointestinal stromal tumour: 40-row multislice computed tomography findings. *Radiol Med* 2006; **111**: 651-660 [PMID: 16791466 DOI: 10.1007/s11547-006-0063-y]
- 10 **Xing GS**, Wang S, Sun YM, Yuan Z, Zhao XM, Zhou CW. Small Bowel Stromal Tumors: Different Clinicopathologic and Computed Tomography Features in Various Anatomic Sites. *PLoS One* 2015; **10**: e0144277 [PMID: 26646242 DOI: 10.1371/journal.pone.0144277]
- 11 **Baheti AD**, Shinagare AB, O'Neill AC, Krajewski KM, Hornick JL, George S, Ramaiya NH, Tirumani SH. MDCT and clinicopathological features of small bowel gastrointestinal stromal tumours in 102 patients: a single institute experience. *Br J Radiol* 2015; **88**: 20150085 [PMID: 26111069 DOI: 10.1259/bjr.20150085]
- 12 **Scola D**, Bahoura L, Copelan A, Shirkhoda A, Sokhandon F. Getting the GIST: a pictorial review of the various patterns of presentation of gastrointestinal stromal tumors on imaging. *Abdom Radiol (NY)* 2017; **42**: 1350-1364 [PMID: 28070658 DOI: 10.1007/s00261-016-1025-z]
- 13 **Yu MH**, Lee JM, Baek JH, Han JK, Choi BI. MRI features of gastrointestinal stromal tumors. *AJR Am J Roentgenol* 2014; **203**: 980-991 [PMID: 25341135 DOI: 10.2214/AJR.13.11667]
- 14 **Kang TW**, Kim SH, Jang KM, Choi D, Ha SY, Kim KM, Kang WK, Kim MJ. Gastrointestinal stromal tumours: correlation of modified NIH risk stratification with diffusion-weighted MR imaging as an imaging biomarker. *Eur J Radiol* 2015; **84**: 33-40 [PMID: 25466773 DOI: 10.1016/j.ejrad.2014.10.020]
- 15 **Gillies RJ**, Kinahan PE, Hricak H. Radiomics: Images Are More than Pictures, They Are Data. *Radiology* 2016; **278**: 563-577 [PMID: 26579733 DOI: 10.1148/radiol.2015151169]
- 16 **Vernuccio F**, Cannella R, Comelli A, Salvaggio G, Lagalla R, Midiri M. [Radiomics and artificial intelligence: new frontiers in medicine.]. *Recenti Prog Med* 2020; **111**: 130-135 [PMID: 32157259 DOI: 10.1701/3315.32853]
- 17 **Lubner MG**, Smith AD, Sandrasegaran K, Sahani DV, Pickhardt PJ. CT Texture Analysis: Definitions, Applications, Biologic Correlates, and Challenges. *Radiographics* 2017; **37**: 1483-1503 [PMID: 28898189 DOI: 10.1148/rg.2017170056]
- 18 **Wakabayashi T**, Ouhmich F, Gonzalez-Cabrera C, Felli E, Saviano A, Agnus V, Savadjiev P, Baumert TF,

- Pessaux P, Marescaux J, Gallix B. Radiomics in hepatocellular carcinoma: a quantitative review. *Hepatol Int* 2019; **13**: 546-559 [PMID: 31473947 DOI: 10.1007/s12072-019-09973-0]
- 19 **Lewis S**, Hectors S, Taouli B. Radiomics of hepatocellular carcinoma. *Abdom Radiol (NY)* 2020 [PMID: 31925492 DOI: 10.1007/s00261-019-02378-5]
- 20 **Miranda Magalhaes Santos JM**, Clemente Oliveira B, Araujo-Filho JAB, Assuncao-Jr AN, de M Machado FA, Carlos Tavares Rocha C, Horvat JV, Menezes MR, Horvat N. State-of-the-art in radiomics of hepatocellular carcinoma: a review of basic principles, applications, and limitations. *Abdom Radiol (NY)* 2020; **45**: 342-353 [PMID: 31707435 DOI: 10.1007/s00261-019-02299-3]
- 21 **Kocak B**, Durmaz ES, Erdim C, Ates E, Kaya OK, Kilickesmez O. Radiomics of Renal Masses: Systematic Review of Reproducibility and Validation Strategies. *AJR Am J Roentgenol* 2020; **214**: 129-136 [PMID: 31613661 DOI: 10.2214/AJR.19.21709]
- 22 **Park HJ**, Park B, Lee SS. Radiomics and Deep Learning: Hepatic Applications. *Korean J Radiol* 2020; **21**: 387-401 [PMID: 32193887 DOI: 10.3348/kjr.2019.0752]
- 23 **Varghese BA**, Cen SY, Hwang DH, Duddalwar VA. Texture Analysis of Imaging: What Radiologists Need to Know. *AJR Am J Roentgenol* 2019; **212**: 520-528 [PMID: 30645163 DOI: 10.2214/AJR.18.20624]
- 24 **Berenguer R**, Pastor-Juan MDR, Canales-Vázquez J, Castro-García M, Villas MV, Mansilla Legorburo F, Sabater S. Radiomics of CT Features May Be Nonreproducible and Redundant: Influence of CT Acquisition Parameters. *Radiology* 2018; **288**: 407-415 [PMID: 29688159 DOI: 10.1148/radiol.2018172361]
- 25 **Ahn SJ**, Kim JH, Lee SM, Park SJ, Han JK. CT reconstruction algorithms affect histogram and texture analysis: evidence for liver parenchyma, focal solid liver lesions, and renal cysts. *Eur Radiol* 2019; **29**: 4008-4015 [PMID: 30456584 DOI: 10.1007/s00330-018-5829-9]
- 26 **Meyer M**, Ronald J, Vernuccio F, Nelson RC, Ramirez-Giraldo JC, Solomon J, Patel BN, Samei E, Marin D. Reproducibility of CT Radiomic Features within the Same Patient: Influence of Radiation Dose and CT Reconstruction Settings. *Radiology* 2019; **293**: 583-591 [PMID: 31573400 DOI: 10.1148/radiol.2019190928]
- 27 **Koçak B**, Durmaz EŞ, Ateş E, Kılıçkesmez Ö. Radiomics with artificial intelligence: a practical guide for beginners. *Diagn Interv Radiol* 2019; **25**: 485-495 [PMID: 31650960 DOI: 10.5152/dir.2019.19321]
- 28 **Lambin P**, Leijenaar RTH, Deist TM, Peerlings J, de Jong EEC, van Timmeren J, Sanduleanu S, Larue RTHM, Even AJG, Jochems A, van Wijk Y, Woodruff H, van Soest J, Lustberg T, Roelofs E, van Elmpot W, Dekker A, Mottaghy FM, Wildberger JE, Walsh S. Radiomics: the bridge between medical imaging and personalized medicine. *Nat Rev Clin Oncol* 2017; **14**: 749-762 [PMID: 28975929 DOI: 10.1038/nrclinonc.2017.141]
- 29 **Park JE**, Kim D, Kim HS, Park SY, Kim JY, Cho SJ, Shin JH, Kim JH. Quality of science and reporting of radiomics in oncologic studies: room for improvement according to radiomics quality score and TRIPOD statement. *Eur Radiol* 2020; **30**: 523-536 [PMID: 31350588 DOI: 10.1007/s00330-019-06360-z]
- 30 **Ba-Ssalamah A**, Muin D, Scherthaner R, Kulinna-Cosentini C, Bastati N, Stift J, Gore R, Mayerhoefer ME. Texture-based classification of different gastric tumors at contrast-enhanced CT. *Eur J Radiol* 2013; **82**: e537-e543 [PMID: 23910996 DOI: 10.1016/j.ejrad.2013.06.024]
- 31 **Chen T**, Ning Z, Xu L, Feng X, Han S, Roth HR, Xiong W, Zhao X, Hu Y, Liu H, Yu J, Zhang Y, Li Y, Xu Y, Mori K, Li G. Radiomics nomogram for predicting the malignant potential of gastrointestinal stromal tumours preoperatively. *Eur Radiol* 2019; **29**: 1074-1082 [PMID: 30116959 DOI: 10.1007/s00330-018-5629-2]
- 32 **Chen T**, Liu S, Li Y, Feng X, Xiong W, Zhao X, Yang Y, Zhang C, Hu Y, Chen H, Lin T, Zhao M, Liu H, Yu J, Xu Y, Zhang Y, Li G. Developed and validated a prognostic nomogram for recurrence-free survival after complete surgical resection of local primary gastrointestinal stromal tumors based on deep learning. *EBioMedicine* 2019; **39**: 272-279 [PMID: 30587460 DOI: 10.1016/j.ebiom.2018.12.028]
- 33 **Choi IY**, Yeom SK, Cha J, Cha SH, Lee SH, Chung HH, Lee CM, Choi J. Feasibility of using computed tomography texture analysis parameters as imaging biomarkers for predicting risk grade of gastrointestinal stromal tumors: comparison with visual inspection. *Abdom Radiol (NY)* 2019; **44**: 2346-2356 [PMID: 30923842 DOI: 10.1007/s00261-019-01995-4]
- 34 **Ekert K**, Hinterleitner C, Horger M. Prognosis assessment in metastatic gastrointestinal stromal tumors treated with tyrosine kinase inhibitors based on CT-texture analysis. *Eur J Radiol* 2019; **116**: 98-105 [PMID: 31153581 DOI: 10.1016/j.ejrad.2019.04.018]
- 35 **Feng C**, Lu F, Shen Y, Li A, Yu H, Tang H, Li Z, Hu D. Tumor heterogeneity in gastrointestinal stromal tumors of the small bowel: volumetric CT texture analysis as a potential biomarker for risk stratification. *Cancer Imaging* 2018; **18**: 46 [PMID: 30518436 DOI: 10.1186/s40644-018-0182-4]
- 36 **Fu J**, Fang MJ, Dong D, Li J, Sun YS, Tian J, Tang L. Heterogeneity of metastatic gastrointestinal stromal tumor on texture analysis: DWI texture as potential biomarker of overall survival. *Eur J Radiol* 2020; **125**: 108825 [PMID: 32035324 DOI: 10.1016/j.ejrad.2020.108825]
- 37 **Liu S**, Pan X, Liu R, Zheng H, Chen L, Guan W, Wang H, Sun Y, Tang L, Guan Y, Ge Y, He J, Zhou Z. Texture analysis of CT images in predicting malignancy risk of gastrointestinal stromal tumours. *Clin Radiol* 2018; **73**: 266-274 [PMID: 28969853 DOI: 10.1016/j.crad.2017.09.003]
- 38 **Lu J**, Hu D, Tang H, Hu X, Shen Y, Li Z, Peng Y, Kamel I. Assessment of tumor heterogeneity: Differentiation of periampullary neoplasms based on CT whole-lesion histogram analysis. *Eur J Radiol* 2019; **115**: 1-9 [PMID: 31084752 DOI: 10.1016/j.ejrad.2019.03.021]
- 39 **Ren C**, Wang S, Zhang S. Development and validation of a nomogram based on CT images and 3D texture analysis for preoperative prediction of the malignant potential in gastrointestinal stromal tumors. *Cancer Imaging* 2020; **20**: 5 [PMID: 31931874 DOI: 10.1186/s40644-019-0284-7]
- 40 **Wang C**, Li H, Jiaerken Y, Huang P, Sun L, Dong F, Huang Y, Dong D, Tian J, Zhang M. Building CT Radiomics-Based Models for Preoperatively Predicting Malignant Potential and Mitotic Count of Gastrointestinal Stromal Tumors. *Transl Oncol* 2019; **12**: 1229-1236 [PMID: 31280094 DOI: 10.1016/j.tranon.2019.06.005]
- 41 **Xu F**, Ma X, Wang Y, Tian Y, Tang W, Wang M, Wei R, Zhao X. CT texture analysis can be a potential tool to differentiate gastrointestinal stromal tumors without KIT exon 11 mutation. *Eur J Radiol* 2018; **107**: 90-97 [PMID: 30292279 DOI: 10.1016/j.ejrad.2018.07.025]

- 42 **Yan J**, Zhao X, Han S, Wang T, Miao F. Evaluation of Clinical Plus Imaging Features and Multidetector Computed Tomography Texture Analysis in Preoperative Risk Grade Prediction of Small Bowel Gastrointestinal Stromal Tumors. *J Comput Assist Tomogr* 2018; **42**: 714-720 [PMID: 30015796 DOI: 10.1097/RCT.0000000000000756]
- 43 **Zhang L**, Kang L, Li G, Zhang X, Ren J, Shi Z, Li J, Yu S. Computed tomography-based radiomics model for discriminating the risk stratification of gastrointestinal stromal tumors. *Radiol Med* 2020; **125**: 465-473 [PMID: 32048155 DOI: 10.1007/s11547-020-01138-6]
- 44 **Zhang QW**, Gao YJ, Zhang RY, Zhou XX, Chen SL, Zhang Y, Liu Q, Xu JR, Ge ZZ. Personalized CT-based radiomics nomogram preoperative predicting Ki-67 expression in gastrointestinal stromal tumors: a multicenter development and validation cohort. *Clin Transl Med* 2020; **9**: 12 [PMID: 32006200 DOI: 10.1186/s40169-020-0263-4]
- 45 **Choi JW**, Choi D, Kim KM, Sohn TS, Lee JH, Kim HJ, Lee SJ. Small submucosal tumors of the stomach: differentiation of gastric schwannoma from gastrointestinal stromal tumor with CT. *Korean J Radiol* 2012; **13**: 425-433 [PMID: 22778564 DOI: 10.3348/kjr.2012.13.4.425]
- 46 **Choi YR**, Kim SH, Kim SA, Shin CI, Kim HJ, Kim SH, Han JK, Choi BI. Differentiation of large ( $\geq 5$  cm) gastrointestinal stromal tumors from benign subepithelial tumors in the stomach: radiologists' performance using CT. *Eur J Radiol* 2014; **83**: 250-260 [PMID: 24325848 DOI: 10.1016/j.ejrad.2013.10.028]
- 47 **Huh CW**, Jung DH, Kim JS, Shin YR, Choi SH, Kim BW. CT Versus Endoscopic Ultrasound for Differentiating Small (2-5 cm) Gastrointestinal Stromal Tumors From Leiomyomas. *AJR Am J Roentgenol* 2019; **213**: 586-591 [PMID: 31063418 DOI: 10.2214/AJR.18.20877]
- 48 **Cai PQ**, Lv XF, Tian L, Luo ZP, Mitteer RA Jr, Fan Y, Wu YP. CT Characterization of Duodenal Gastrointestinal Stromal Tumors. *AJR Am J Roentgenol* 2015; **204**: 988-993 [PMID: 25905932 DOI: 10.2214/AJR.14.12870]
- 49 **Ren S**, Chen X, Wang J, Zhao R, Song L, Li H, Wang Z. Differentiation of duodenal gastrointestinal stromal tumors from hypervascular pancreatic neuroendocrine tumors in the pancreatic head using contrast-enhanced computed tomography. *Abdom Radiol (NY)* 2019; **44**: 867-876 [PMID: 30293109 DOI: 10.1007/s00261-018-1803-x]
- 50 **Joensuu H**. Risk stratification of patients diagnosed with gastrointestinal stromal tumor. *Hum Pathol* 2008; **39**: 1411-1419 [PMID: 18774375 DOI: 10.1016/j.humpath.2008.06.025]
- 51 **Zhou C**, Duan X, Zhang X, Hu H, Wang D, Shen J. Predictive features of CT for risk stratifications in patients with primary gastrointestinal stromal tumour. *Eur Radiol* 2016; **26**: 3086-3093 [PMID: 26699371 DOI: 10.1007/s00330-015-4172-7]
- 52 **O'Neill AC**, Shinagare AB, Kurra V, Tirumani SH, Jagannathan JP, Baheti AD, Hornick JL, George S, Ramaiya NH. Assessment of metastatic risk of gastric GIST based on treatment-naïve CT features. *Eur J Surg Oncol* 2016; **42**: 1222-1228 [PMID: 27178777 DOI: 10.1016/j.ejso.2016.03.032]
- 53 **Li H**, Ren G, Cai R, Chen J, Wu X, Zhao J. A correlation research of Ki67 index, CT features, and risk stratification in gastrointestinal stromal tumor. *Cancer Med* 2018; **7**: 4467-4474 [PMID: 30123969 DOI: 10.1002/cam4.1737]
- 54 **Maldonado FJ**, Sheedy SP, Iyer VR, Hansel SL, Bruining DH, McCollough CH, Harmsen WS, Barlow JM, Fletcher JG. Reproducible imaging features of biologically aggressive gastrointestinal stromal tumors of the small bowel. *Abdom Radiol (NY)* 2018; **43**: 1567-1574 [PMID: 29110055 DOI: 10.1007/s00261-017-1370-6]
- 55 **Basilio-de-Oliveira RP**, Pannain VL. Prognostic angiogenic markers (endoglin, VEGF, CD31) and tumor cell proliferation (Ki67) for gastrointestinal stromal tumors. *World J Gastroenterol* 2015; **21**: 6924-6930 [PMID: 26078569 DOI: 10.3748/wjg.v21.i22.6924]
- 56 **Tateishi U**, Miyake M, Maeda T, Arai Y, Seki K, Hasegawa T. CT and MRI findings in KIT-weak or KIT-negative atypical gastrointestinal stromal tumors. *Eur Radiol* 2006; **16**: 1537-1543 [PMID: 16397744 DOI: 10.1007/s00330-005-0091-3]
- 57 **Yin YQ**, Liu CJ, Zhang B, Wen Y, Yin Y. Association between CT imaging features and KIT mutations in small intestinal gastrointestinal stromal tumors. *Sci Rep* 2019; **9**: 7257 [PMID: 31076599 DOI: 10.1038/s41598-019-43659-9]
- 58 **Apfaltrer P**, Meyer M, Meier C, Henzler T, Barraza JM Jr, Dinter DJ, Hohenberger P, Schoepf UJ, Schoenberg SO, Fink C. Contrast-enhanced dual-energy CT of gastrointestinal stromal tumors: is iodine-related attenuation a potential indicator of tumor response? *Invest Radiol* 2012; **47**: 65-70 [PMID: 21934517 DOI: 10.1097/RLI.0b013e31823003d2]
- 59 **Choi H**, Charnsangavej C, Faria SC, Macapinlac HA, Burgess MA, Patel SR, Chen LL, Podoloff DA, Benjamin RS. Correlation of computed tomography and positron emission tomography in patients with metastatic gastrointestinal stromal tumor treated at a single institution with imatinib mesylate: proposal of new computed tomography response criteria. *J Clin Oncol* 2007; **25**: 1753-1759 [PMID: 17470865 DOI: 10.1200/JCO.2006.07.3049]



Published by **Baishideng Publishing Group Inc**  
7041 Koll Center Parkway, Suite 160, Pleasanton, CA 94566, USA

**Telephone:** +1-925-3991568

**E-mail:** [bpgoffice@wjgnet.com](mailto:bpgoffice@wjgnet.com)

**Help Desk:** <https://www.f6publishing.com/helpdesk>

<https://www.wjgnet.com>

