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Letter to the Editor

Radiomics in Pancreatic Cancer: Present and Future

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Dear editor,

Pancreatic cancer (PC) is the fourth most common cause of cancer-related mortality, with a meager 5-year survival rate of under 20%.[1] Patients with PC often exhibit nonspecific symptoms such as abdominal pain and weight loss, leading to delayed diagnosis. However, even when promptly diagnosed after symptom onset, the majority of PC patients are found to have advanced-stage disease. Despite notable progress in surgical methods, chemotherapy, and radiation therapy, the 5-year survival rate remains dishearteningly low at 8.2%.[2]

While the exact causes of PC remain poorly understood, several risk factors have been identified. These include a family history of PC, obesity, chronic pancreatitis (CP), smoking, the presence of preneoplastic lesions, or certain hereditary syndromes associated with a high risk of developing PC.[3]

Cross-sectional imaging is a vital tool in initially assessing symptomatic individuals suspected of having PC. It is also crucial in screening asymptomatic individuals at a heightened risk of developing PC.[4] Computed tomography (CT) is the predominant imaging diagnostic method, often complemented by endoscopic ultrasound with fine needle biopsy or aspiration for pinpointing small lesions and confirming diagnoses definitively.[5] Additionally, magnetic resonance imaging (MRI) and positron emission tomography (PET) play significant roles in systematically staging the disease and determining whether the primary tumor is resectable, borderline resectable, or unresectable.[5] Radiomics, a subset of medical imaging, involves extracting quantitative data from various medical images like CT scans, MRI scans, or PET scans. This data is then meticulously analyzed to glean valuable insights into tumor heterogeneity.[6] Quantitative imaging facilitates integrating radiomics and dynamic imaging features, independently or together, enabling the construction of clinical prediction models. These models, based on radiomics signatures or imaging phenotypes, estimate clinical outcomes associated with tumor biology.[7] Radiomics represents a promising non-invasive tool for various applications in PC, including early diagnosis, evaluating treatment response, predicting prognosis, and precise diagnosis.

One of the significant challenges physicians often face in managing PC is the early detection of high-risk individuals and the timely diagnosis of patients exhibiting suspected symptoms. Our recent exploration into radiomics unveiled a promising avenue for distinguishing early-stage from late-stage PCs.[6] Our findings highlighted the remarkable performance of the radiomics model, with an impressive accuracy of 97.7%, alongside notable sensitivity of 97.6%, specificity of 97.8%, positive predictive value of 98.4%, and negative predictive value of 96.8%. Moreover, our rigorous validation process, employing a 10-fold LGOCV (leave-group-out cross-validation) method, demonstrated the model's robustness and reproducibility. On average, the area under the curve stood at 0.75 across the 10 newly developed models, further enhancing the credibility of our radiomics approach.

In clinical practice, several neoplastic and inflammatory conditions can mimic PC, such as paraduodenal "groove" pancreatitis, autoimmune pancreatitis, focal acute and CP, neuroendocrine tumors, solid pseudopapillary neoplasms, metastases, and lymphoma. Differentiating these conditions from PC can be challenging due to overlapping CT and MRI features.[8] Accurate diagnosis plays a crucial role in guiding therapeutic strategies and potential outcomes in PC, while also preventing unnecessary biopsy or surgical interventions for conditions that mimic it. Previous studies have illustrated the capacity of radiomics to effectively differentiate PC from its mimics, including autoimmune pancreatitis, CP, and neuroendocrine tumors, among others, demonstrating promising performance.[9–11]

Conventional methods encounter challenges in identifying changes following chemotherapy and/or radiotherapy treatments, prompting the investigation of radiomic features for improved detection. Changes in radiomic features over time in longitudinal images, referred to as delta radiomics, have the potential to serve as a biomarker for predicting treatment response.[12] Nasief *et al*. developed a delta-radiomic process based on machine learning (ML). This process involves acquiring and registering longitudinal images, segmenting and populating regions of interest, extracting radiomic features, calculating their changes - delta-radiomic features (DRFs), reducing feature space, identifying candidate DRFs with treatment-induced changes, and finally, creating outcome prediction models using ML. Their results indicated that 13 DRFs successfully passed the tests, showing significant changes after two to four weeks of treatment. The most effective combination for dis-

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tinguishing good responders from bad ones (cross-validated area under the curve = 0.94) comprised normalized entropy to standard deviation difference, kurtosis, and coarseness. These findings suggest that the radiomics approach could be valuable for evaluating treatment response.[13,14] However, certain studies need validation of their findings.[15,16] This necessity arises due to various factors influencing clinical outcomes, such as pre-and post-CRT effects, potentially insufficient sample size, and heterogeneous population characteristics. More substantial evidence is warranted.

Despite the numerous treatment options available, the prognosis for patients with PC remains poor. However, the prediction of tumor phenotype, treatment response, and patient prognosis is becoming increasingly feasible through the use of comprehensive and integrated radiomics models.[2] A recent study demonstrated that prognostic radiomics models, incorporating MRI features and clinical data, are effective in predicting progression-free survival, overall survival, and objective response rate in PC patients with hepatic metastasis undergoing chemoimmunotherapy.[17] These models hold promise for evaluating patient prognosis.

Despite significant advancements, challenges persist in applying radiomics to PC.[18,19] Firstly, the effectiveness of any radiomics model depends on the quality of the training data. The predictive performance of automated tools is hindered by the absence of optimal thresholds needed to balance sensitivity and specificity during data acquisition and curation. Secondly, the heterogeneity of patient data, influenced by factors such as age, sex, race, and demographics, requires future algorithms and ML technologies to accommodate such variations. Validating the robustness of radiomics tools using both prospective and retrospective real-life populations is essential for their successful integration into clinical practice. Thirdly, integrating multi-omics data represents an essential advancement in enhancing the clinical adoption of radiomics.[20] This approach involves a multifaceted workflow, employing various software and expertise. Substantial technological investments are imperative to develop integrated, user-friendly tools for broad implementation in clinical settings. Additionally, segmentation, a pivotal but time-intensive process, is prone to variability among observers.[20] Automating or semi-automating segmentation, especially through deep learning techniques, is crucial to streamline this critical stage.

In conclusion, radiomics, as an emerging quantitative technique, is rapidly gaining momentum in the management of PC, with its methodology continually evolving. The primary obstacles hindering the application of radiomics in cancer diseases include the limited availability of high-quality data and a lack of biological mechanistic explanations. Bridging this gap could be achieved through data sharing and collaborations among institutions, focusing on tasks such as data cleaning and labeling.

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Conflict of interest

The authors have no conflict of interests related to this publication.

Author contributions

Study concept and design (SR), funding acquisition (SR, YT, ZQW), drafting of the manuscript (SR, LNS, MJD), critical revision of the manuscript for important intellectual content (MJD, YT, ZQW), and study supervision (YT, ZQW). All authors have made significant contributions to this study and have approved the final manuscript.

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