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## AI-Driven insights in pancreatic cancer imaging: from pre-diagnostic detection to prognostication

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### Abstract

Pancreatic ductal adenocarcinoma (PDAC) is the third leading cause of cancer-related deaths in the United States, largely due to its poor five-year survival rate and frequent late-stage diagnosis. A significant barrier to early detection even in high-risk cohorts is that the pancreas often appears morphologically normal during the pre-diagnostic phase. Yet, the disease can progress rapidly from subclinical stages to widespread metastasis, undermining the effectiveness of screening. Recently, artificial intelligence (AI) applied to cross-sectional imaging has shown significant potential in identifying subtle, early-stage changes in pancreatic tissue that are often imperceptible to the human eye. Moreover, AI-driven imaging also aids in the discovery of prognostic and predictive biomarkers, essential for personalized treatment planning. This article uniquely integrates a critical discussion on AI's role in detecting visually occult PDAC on pre-diagnostic imaging, addresses challenges of model generalizability, and emphasizes solutions like standardized datasets and clinical workflows. By focusing on both technical advancements and practical implementation, this article provides a forward-thinking conceptual framework that bridges current gaps in AI-driven PDAC research.

### Keywords

Pancreas; Artificial intelligence; Biomarkers; Detection; Pancreatic ductal adenocarcinoma; Segmentation; Prognostication; Computed tomography

### Introduction

Pancreatic ductal adenocarcinoma (PDAC) is among the most lethal cancers, ranking as the third leading cause of cancer-related deaths in the United States in 2024, with 66,440 new

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**Declarations**

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cases and 51,750 deaths annually [1]. The five-year survival rate remains at a dismal 12% [2], despite recent therapeutic advances. Diagnosis at a late-stage is a key contributor to this poor prognosis, with only 20% of cases detected early enough for curative treatment [3]. Median survival is around 26 months for stage I PDAC but drops to 4.8 months for stage IV, emphasizing the urgent need for earlier detection and intervention. Moreover, PDAC is known for its heterogeneous biology, which presents significant challenges in predicting response to therapy and oncologic outcomes [4].

Artificial intelligence (AI) applied to cross-sectional imaging offers a potentially transformative solution to these challenges [5–10]. AI-based techniques have demonstrated the ability to extract subtle imaging features that traditional methods fail to detect. For instance, AI-augmented standard-of-care imaging can identify sporadic PDAC on portal venous phase pre-diagnostic CTs as early as 398 days before clinical diagnosis, significantly outperforming radiologist evaluations [5]. A critical component of this process is the precise volumetric segmentation of the normal-appearing pancreas on imaging, which AI has made more efficient and reliable. Beyond early detection, AI plays a crucial role in *prognostication* and *treatment response assessment* for PDAC [8, 9, 11–16]. Furthermore, AI-driven quantitative imaging can continuously monitor treatment response, offering dynamic insights into how PDAC tumors evolve during therapy. By analyzing changes in tumor size, shape, and internal heterogeneity, AI tools provide dynamic assessments that can guide treatment adjustments [17–19]. This capability is particularly vital in PDAC, where conventional imaging often lags in detecting therapeutic impact, leading to delays in optimizing treatment strategies.

We explore the latest advancements in AI for early detection, segmentation, prognostication, and treatment response assessment of PDAC in this review. Most AI research in pancreatic imaging has focused on CT due to its widespread use and the availability of detailed, standardized datasets. CT is favored for its high-resolution volumetric data and rapid acquisition, making it an effective platform for AI model development. We chose to focus on CT-based approaches to align with established research and current clinical practices. Additionally, we discuss the challenges and opportunities in integrating AI-driven methods into routine clinical practice, addressing issues such as data variability, standardization, and model generalizability. These insights aim to bridge the gap between innovative AI solutions and their potential application in clinical care.

### AI for pancreas segmentation and early detection of PDAC

Pancreatic cancer is the tenth most common cancer in the United States, with an incidence rate of 3.3%. The lifetime risk by age 85 is 1.7% [20], which does not support population-based screening for PDAC. This is an unfortunate situation as overwhelming majority (85–90%) of all PDAC diagnoses occur in the sporadic setting, i.e., in the general population without clear familial or genetic links, as opposed to those found in individuals with specific risk factors, such as a family history of PDAC or known genetic mutations. Therefore, improving overall oncologic outcomes in PDAC hinges on the early detection of *sporadic* cases. Effective, cost-efficient screening strategies must focus on identifying subtle risk indicators in the general population.

Fortunately, glycemically defined new-onset diabetes (NOD) has been recently established as the only high-risk factor for sporadic PDAC, conferring a 6–8-fold increase in risk relative to the general population [21]. The Enriching New-Onset Diabetes for Pancreatic Cancer (END-PAC) model further refines risk stratification within this group. The END-PAC score is calculated based on age, glycemic control, and weight loss, with each factor contributing to an overall risk assessment. Individuals with a score  $\geq 3$ , indicating significant abnormalities in these parameters, have a 4.4-fold higher likelihood of PDAC compared to those with NOD alone [22]. This refined cohort presents an optimal group for targeted surveillance and screening. In fact, a CT scan performed at the onset of NOD in such high-risk groups could triple the rate of detecting resectable PDAC compared to current rates [23]. Risk-based CT screening in these cohorts has demonstrated economic value across various analyses [24].

Early imaging findings of PDAC are often subtle and easily overlooked on CT scans [23, 25]. Many healthy individuals may also show these indirect signs, as they are not specific to PDAC. Evaluating such findings can be subjective, with low inter-reader agreement. Frequently, the pancreas appears morphologically normal during the pre-diagnostic phase, resulting in missed diagnoses when the disease is still in its early, treatable stages [23, 25]. This highlights the critical necessity of imaging-based biomarkers to improve early detection of sporadic PDAC in high-risk groups. While the pancreas may seem normal to the human eye in these early stages, AI models, such as ML algorithms analyzing radiomic features (e.g., shape, intensity, texture) [26] and DL models like convolutional neural networks (CNNs) [27], excel at processing complex imaging data. These tools can identify subtle patterns that often escape traditional visual assessments.

### **Volumetric pancreas segmentation**

Robust and reproducible pancreas segmentation tools are essential to fully leverage imaging biomarkers from normal-appearing pancreas for the early detection of sporadic PDAC [28]. However, accurate volumetric segmentation of the pancreas is immensely challenging due to the organ's complex shape, variable anatomy, and diverse attenuation patterns. Manual segmentation is labor-intensive, time-consuming, and subject to inter- and intra-reader variability [29]. Conversely, AI has the potential to provide a more efficient solution, reducing segmentation inconsistencies and streamlining workflow [29]. In fact, models trained on diverse and comprehensive datasets have greatly improved the accuracy and generalizability of pancreatic segmentation [28, 30, 31]. The performance of these models is commonly measured by the Dice Similarity Coefficient (DSC). This metric, which ranges from 0 (no overlap) to 1 (perfect overlap), quantifies the similarity between reference or ground-truth and AI-predicted segmentations. Recent studies have shown DL-based segmentation methods can achieve mean DSCs ranging from 0.65 to 0.94 on CT, demonstrating strong accuracy [28, 30–32]. For example, one study highlighted superior performance using portal venous phase CTs, achieving a DSC of 0.94 on an internal test set (Fig. 1). This model, trained on the largest dataset to date—3,031 CTs—achieved high accuracy and generalizability, with a DSC of 0.96 on a multi-institutional international dataset. Additionally, it maintained dose-invariant performance on The Cancer Imaging Archive (TCIA) dataset, showing consistent DSCs of 0.97 with both full and 25%

reduced radiation doses. These results emphasize the robustness of AI-based segmentation, showcasing its ability to adapt across varied imaging conditions and radiation dose levels.

### Detection of PDAC at the pre-diagnostic stage

AI-powered tools for pancreas segmentation enable extraction of critical biomarkers for early PDAC detection at the asymptomatic stage on pre-diagnostic CTs. The latter are defined as incidental CTs conducted for unrelated clinical indications between 3 and 36 months before a clinical PDAC diagnosis. They are typically interpreted as negative for PDAC during routine clinical evaluations and confirmed as such during data curation [5]. It is crucial to distinguish pre-diagnostic CTs from diagnostic CTs where a mass is present but missed during routine interpretation. The latter are referred to as diagnostic CTs with missed cancer.

The Radiomics Early Detection Model (RED-MOD) [5] exemplifies an ML-based approach designed to identify early oncogenic signatures from volumetrically segmented pancreas on standard-of-care pre-diagnostic CTs (Fig. 2). In a study of 155 pre-diagnostic CTs and 265 age-matched controls, RED-MOD achieved a mean AUC of 0.98 (95% CI: 0.94–0.98) in classifying CT scans as pre-diagnostic (3 to 36 months before clinical diagnosis) versus normal. The model significantly outperformed radiologists, whose mean AUC was 0.66 (95% CI: 0.46–0.86) for detecting PDAC from pre-diagnostic CTs, compared to RED-MOD's mean AUC of 0.98 (95% CI: 0.94–0.98;  $p < 0.001$ ). Additionally, RED-MOD demonstrated robustness across a range of clinically relevant variations, underscoring its potential for clinical application in the early detection of PDAC [33].

The significant differences in radiomic signatures between scans with healthy pancreas and pre-diagnostic cases, acquired 6 months to 3 years before PDAC diagnosis with no visible tumors, were highlighted in a recent study [34]. This analysis, conducted on an internal dataset of 66 patients (22 healthy controls, 22 pre-diagnostic, and 22 diagnostic CTs), identified specific radiomic features that clearly distinguished healthy from pre-diagnostic groups. A method using a step-by-step feature selection process and a simple classification model was developed, achieving a mean accuracy of 86% when categorizing scans as either healthy or pre-diagnostic, validated on an external dataset of 28 scans (14 in each group). Furthermore, the study also demonstrated incremental trends in these features as pre-diagnostic cases progressed toward diagnostic scans.

In a subsequent study [35], the same research team subdivided the pancreas into three regions, the head, body, and tail. The subregion showing the greatest tumor burden on diagnostic scans was then used to classify corresponding areas on pre-diagnostic scans into high- and low-risk groups, while all regions in healthy controls were categorized as low-risk. Pairwise comparisons of radiomic features between high- and low-risk regions revealed that 3.5% of features significantly differed, which were then applied in a similar model for PDAC risk prediction. This model demonstrated 89.3% accuracy on the external dataset.

Another study demonstrated the robustness of a radiomics-based model using features extracted from automated, volumetrically segmented pancreatic scans for the pre-diagnostic detection of PDAC, analyzed in scans acquired 3 to 36 months before diagnosis. A ML

model was developed and trained on 50% of the total dataset (277 pre-diagnostic CTs and 554 matched control CTs), achieving an accuracy of 94–95% on the test set [36].

In addition to detection of subtle, pre-diagnostic imaging signatures within the pancreas, AI can also monitor systemic changes linked to early PDAC, a disease with well-known sequelae in many organ systems. These changes include variations in body composition and metabolic function that contribute to conditions like cancer-induced cachexia, which leads to muscle loss, with or without fat depletion [37]. Cachexia can begin even in the preclinical stages of the disease, when precursor lesions are present [38]. A recent study evaluated longitudinal changes in body composition, specifically, subcutaneous adipose tissue (SAT), visceral adipose tissue (VAT), skeletal muscle area (SMA), and vertebral bone area and density, to assess the potential of extra-pancreatic imaging markers for pre-diagnostic PDAC detection. Analyzing CT scans taken within 36 months of PDAC diagnosis in 516 patients, the study found significant decreases in VAT and SAT per six-month interval approaching diagnosis [39].

These studies underscore the emerging role of AI-driven surveillance tools in early PDAC detection in high-risk cohorts.

### AI for PDAC detection at diagnostic stage

As previously described, detecting visually occult early-stage PDAC on pre-diagnostic CTs presents significant challenges. Another pressing issue is the missed detection of incidental PDAC, including more advanced tumors, on routine imaging. These cases often go undetected due to subtle imaging features that may not raise immediate concern, inadequate scrutiny of the pancreas during general abdominal CT interpretations, or technical limitations such as suboptimal image quality or timing of contrast enhancement [40, 41]. As a result, these CTs, where a lesion is present but overlooked, represent instances of “missed PDAC.” Such diagnostic oversights highlight the need for improved imaging protocols and advanced AI-driven tools capable of enhancing pancreas-focused assessment and increasing the detection rates of subtle PDAC features that are frequently missed during routine evaluations.

A critical step in development of these AI-driven tools is PDAC localization on cross-sectional imaging, typically accomplished using pancreatic masks that include the tumor. These masks are usually generated as the initial step of the PDAC detection model using a CNN-based pancreas segmentation tools [6, 42, 43]. In a study utilizing this approach, a model was trained and validated on 696 portal-phase diagnostic CTs with PDAC and 1,080 control images, achieving an accuracy of 92% on an internal test set of 1,238 cases (409 PDAC scans and 829 control CTs) and 86% on public dataset (194 PDAC scans and 80 control CTs). The model demonstrated strong performance on a simulated high-risk population dataset, achieving 95% accuracy when the case-control distribution was adjusted to reflect the three-year risk of sporadic PDAC in a cohort with NOD and END-PAC scores  $\geq 3$ . This was achieved by creating multiple simulated test groups using a method called bootstrapping, with the PDAC-to-control CT ratio ranging from 1:100 to 5:100. The process was repeated over 1,000 times to ensure reliable results. Accuracy remained consistently high across T-stages 1 through 4 in both internal and external datasets, with

a range between 76% and 100%. Notably, although trained exclusively on larger tumors, the model accurately detected pre-diagnostic CT scans taken 3 to 36 months before PDAC diagnosis, achieving an accuracy of 84%. Furthermore, the model's interpretability was illustrated using heat maps which indicate the regions of the input CT images that received the most attention by the model during outcome prediction. In the diagnostic PDAC cases from both the internal and public datasets, the areas of highest activation coincided with tumor locations in 97% and 92.8% of cases respectively that was further verified by radiologists. Moreover, in instances of misclassified control CTs, radiologists found no systematic abnormalities in the regions of activation or the surrounding pancreatic tissue that could explain the model's focus, despite the absence of tumors. It is worth noting that while the model did show significant activation around the pancreas in relation to certain potentially confounding findings—such as cystic lesions and non-PDAC metastatic lesions—it successfully distinguished these cases as non-PDAC control CTs [6].

Another DL model, PANDA (Pancreatic Cancer Detection with Artificial Intelligence), utilizes pancreas segmentation masks that include lesions as the initial step in a three-stage algorithm. The second stage focuses on lesion detection, identifying both PDAC and non-PDAC lesions, and is followed by differential diagnosis if a lesion is detected. The model was trained on a dataset of 3,208 non-contrast CT scans, where pancreas and lesion annotations were mapped from paired contrast-enhanced CT scans through image registration. PANDA achieved an AUC of 0.987 (95% CI 0.975–0.996) for PDAC identification on an internal dataset of 291 patients (108 PDAC scans, 67 non-PDAC lesion scans, and 116 control scans). On an external validation dataset of 5,337 patients (2,737 PDAC scans, 932 non-PDAC lesion scans, and 1,668 control scans), the model demonstrated a sensitivity of 90.1% (95% CI 89.0–91.2%) for PDAC identification. It maintained sensitivity above 90% for detecting stage 1 and stage 2 tumors across both datasets. PANDA also outperformed radiologists in both lesion detection and PDAC identification tasks, including when it was compared to readers who evaluated non-contrast scans and readers who evaluated contrast scans, while the model only had access to the corresponding non-contrast scan. Additionally, in a real-world clinical evaluation where the model was tested on a cohort of 16,420 scans, including 44 PDACs and 135 non-PDAC scans, the model detected a PDAC on a non-contrast chest CT that was missed by the radiologist and was subsequently diagnosed on a follow-up standard-of-care contrast-enhanced abdominal CT [42].

One study used a manually segmented 3D volume of pancreas, including both tumor and background pancreatic regions, to train and evaluate the model. Radiomic features extracted from the segmented regions were used to train a ML classifier model. This model, trained on 255 CT scans (130 PDAC and 125 normal controls) and validated on an additional 125 scans (60 PDAC and 65 controls), achieved an accuracy of 99.2% with an AUC of 0.99 [44]. Similarly, another study employing manual segmentations utilized a patch-based model, dividing the pancreas and surrounding tumor regions into smaller “patches.” Radiomic features from each patch were extracted to build a classification system that labeled patches within a region of interest (ROI) as either cancerous or non-cancerous, contributing to a patient-level PDAC prediction. This was tested on a cohort of 436 PDAC cases and 479 healthy controls, this model achieved over 85% accuracy across both Taiwanese and U.S.

datasets. The model also showed a sensitivity of > 90% for detection of stage 1 and 2 tumors in the local test set [45, 46]. However, the primary limitations of manual segmentation are its labor-intensive and time-consuming nature, especially when large datasets are needed for effective model training [47].

Hybrid models that combine DL with radiomics or texture analyses are also being explored [48, 49]. This approach could augment AI's ability to detect PDAC at earlier stages by integrating structural and textural information with radiomic signatures extracted from cross-sectional images. Additionally, larger, diverse datasets, including multi-institutional and multi-modal imaging data, will be critical to refining these models and ensuring their generalizability across different clinical settings.

### AI for PDAC segmentation and prognostication

Effective prognostic markers are crucial for optimizing treatment strategies and personalizing patient care, given PDAC's low survival rates and high recurrence. Traditional survival prediction models for advanced PDAC often rely on limited clinical data, with commonly used markers like CA-19-9 having only limited predictive accuracy [50].

Imaging plays a central role in PDAC assessment. Recent advances in hybrid molecular imaging (i.e., PET/CT and PET/MR) using radiotracers like 18 F-FDG and FAPI-targeted PET have improved therapy response assessment and outcomes prediction by providing superior metabolic and molecular tumor characterization [51–53]. AI-based imaging biomarkers can further refine prognostic strategies. Radiomic features, for example, have successfully categorized patients into high-risk (survival under one year) and low-risk (survival over one year) groups with high accuracy [9]. Additionally, CNN-extracted features from PDAC segmentations have demonstrated potential in predicting survival, further emphasizing AI's role in enhancing prognostic approaches [8].

### Volumetric PDAC segmentation

Accurate tumor segmentation is essential to leverage these imaging markers systematically and effectively. This task is especially challenging in PDAC due to the tumor's variable shape, size, and density. PDAC often exhibits poorly defined boundaries, hypo- or iso-dense tissue on CT scans, and intertwines with non-tumoral pancreatic tissue [54]. While manual segmentation is possible, it is labor-intensive and prone to variability, driving interest in DL-based segmentation methods to overcome these challenges [47, 55, 56].

The performance of DL-based segmentation of PDAC has historically been limited, with DSCs ranging from 0.52 to 0.70—lower than the performance seen for other solid tumors on CT scans [47, 55, 56]. This variability is attributable to the inherent challenges of segmenting PDAC, such as its poorly defined tumor margins and the significant overlap between cancerous and healthy pancreatic tissue. Multi-phase imaging (e.g., arterial and venous phases) has shown promise in improving segmentation [57, 58], as it allows for better spatial alignment and registration between different tissue types. For instance, a recent study [59] introduced a specialized 3D neural network to combine information from different CT scan phases, enabling automated segmentation of PDAC. Compared to single-phase algorithms, multi-phase algorithms achieved superior performance, with

DSCs improving from 0.55 to 0.64. This approach highlights the potential of leveraging multi-phase imaging to refine PDAC segmentation accuracy.

Despite the incremental improvements offered by multi-phase approaches, there remains a need to standardize segmentation methodologies. Institutions often differ in the timing of CT phases, the use of contrast, and imaging protocols, which can result in varied segmentation outcomes. Portal venous phase CT imaging has emerged as the most standardized and widely used imaging phase for PDAC segmentation, as it typically offers the clearest distinction between the tumor and surrounding structures [60].

Recent innovations aim to address the limitations of DL-based segmentation. A notable study [61] developed a semi-automated, bounding-box CNN for PDAC segmentation, designed to focus on peri-tumoral regions rather than the entire pancreas. By limiting the input to this focused area, the CNN was able to significantly improve segmentation performance. This model was trained on the largest dataset reported to date—1,151 portal venous-phase CTs from treatment-naïve patients with biopsy-confirmed PDAC. The bounding-box CNN achieved a high DSC of 0.84 on the internal test subset and demonstrated excellent generalizability across two public datasets: Medical Segmentation Decathlon (MSD) (DSC: 0.82) and The Cancer Imaging Archive (TCIA) (DSC: 0.84) (Fig. 3). The model's ability to generalize across public datasets further validates its potential for clinical adoption.

The authors attribute the model's success to its use of a bounding box, which narrowed the computational focus to the tumor's spatial boundaries and reduced the processing load. By homing in on the most relevant anatomical region, the CNN was able to effectively learn the tumor's spatial dimensions, yielding a more precise segmentation. The semi-automated nature of this model also means it can be integrated into clinical workflows with minimal input from radiologists, reducing time spent on manual segmentation while improving consistency.

While DL-based segmentation methods have advanced, challenges remain. The main limitation is the low-to-moderate performance, even in highly specialized models. PDAC segmentation is constrained by the small tumor size relative to the larger non-tumor area of the pancreas, which poses computational difficulties for AI algorithms. Further efforts should focus on improving volumetric slab-based approaches, where segmentation is initiated based on pre-determined spatial regions, offering a more streamlined method for identifying tumor boundaries.

### Therapy Response Assessment and Prognostication

Integrating multi-domain data from various sources, such as imaging and clinico-pathologic variables, has emerged as a powerful method for predicting patient outcomes. By merging diverse data sources, AI models can extract complex, multidimensional patterns, offering a more enriched dataset than unimodal approaches. For instance, recent studies that integrated radiomic features with clinical variables such as age, CA19-9 levels, tumor morphology, and metastatic status demonstrated superior performance in survival prediction compared to models relying on radiomics or clinical features alone [9]. In one study, a ML model

based on clinical data and a DL model utilizing pre-operative CT scans were integrated into an ensemble approach. This combined model achieved an AUC of 0.76 for predicting two-year post-operative survival in PDAC patients, highlighting the potential of multi-modal approaches [15]. Future approaches will incorporate multiparametric data, including text extracted from electronic medical records (EMRs), pharmacy utilization patterns, and concurrent diagnostic code-based billing information.

Radiomic signatures have also been evaluated for their utility in predicting early recurrence in post-surgical patients. A recent model achieved an AUC of 0.73 in the training dataset and 0.67 in the validation dataset for predicting early recurrence. Multivariate analysis confirmed that radiomic signatures were independent predictors of early recurrence, supporting the robustness of AI-driven approaches in this context [62]. Similarly, radiomics-based models have demonstrated high performance in predicting liver and lymph node metastasis, with AUCs of 0.7 and 0.85, respectively [63, 64].

Longitudinal changes in radiomic features, such as Delta Radiomic Features (DRFs), have shown potential for assessing treatment response to chemoradiation therapy. DRFs allow for the evaluation of significant changes in radiomic characteristics before and after treatment. In a recent study, 13 DRFs demonstrated significant alterations in response to treatment, enabling classification of patients into good or poor responders. The ability to predict treatment response was underscored by an AUC of 0.94, suggesting that DRFs could play a pivotal role in refining therapeutic strategies [65].

## Limitations

Despite advancements in computational power and machine learning, integrating AI into routine clinical practice remains limited. A key challenge is that AI model effectiveness depends heavily on the quality and depth of training data. For early PDAC detection, a major hurdle is the scarcity of pre-diagnostic imaging data, which hampers the development and validation of screening models. This issue is compounded by the absence of established surveillance protocols for high-risk populations, unlike in other cancers. Additionally, inconsistencies in data collection and annotation across institutions complicate the creation of robust, generalizable models. Publicly available datasets, vital for external validation, often lack quality and completeness, further limiting AI implementation in clinical practice. For instance, a recent study [66] assessing these datasets identified substantial quality gaps, including suboptimal imaging, incomplete annotations, and inherent biases. A significant proportion of CTs lacked essential details about the tumor histopathology, and approximately 25% include biliary stents. The presence of biliary stents introduces bias in AI models, as these models may erroneously associate the presence of stents with a PDAC diagnosis [67]. This leads to the misinterpretation of imaging data and affects the reliability of the model's predictive outcomes. Consequently, CT scans with biliary stents are unsuitable for AI-driven analyses in pancreas applications. Published studies using such datasets often overlook these limitations, resulting in an artificial inflation of the models' performance metrics. This oversight highlights the need for more meticulous documentation, dataset curation, and bias mitigation strategies in AI model training and validation. Developing robust and generalizable AI tools requires well-annotated datasets that

accurately reflect clinical conditions and enhance diagnostic reliability. Overcoming these barriers necessitates multi-institutional collaboration and the deep expertise of physicians to ensure that the datasets accurately capture nuanced diagnostic features and clinical context that AI models alone may overlook. Their insights are crucial for identifying relevant imaging markers and addressing potential biases that could skew model performance. Comprehensive datasets, including pre-diagnostic imaging, are vital for improving AI generalizability and clinical relevance to support seamless integration into routine practice. Moreover, creation of international, multi-institutional datasets with standardized imaging protocols and annotations is critical. Collaborative efforts to harmonize data acquisition, such as consistent imaging phases, contrast timing, and resolution, can mitigate variability and improve model robustness. Additionally, initiatives like open-access repositories can play a pivotal role in curating high-quality datasets, fostering external validation, and ensuring AI tools are generalizable across diverse populations and clinical settings. These solutions are essential for overcoming current challenges and facilitating the integration of AI into routine practice.

## Conclusion

AI has shown great potential in transforming the early detection, diagnosis, and prognostication of PDAC, often outperforming radiologists by identifying subtle imaging patterns imperceptible to the human eye. This capability can improve patient outcomes by detecting PDAC at treatable stages. Beyond early detection, AI aids in prognostication by predicting patient outcomes, early recurrence, and metastasis risk with precision. Integrating non-pixel-based data can further enhance predictive accuracy, advancing precision medicine. However, challenges like limited pre-diagnostic data and model generalizability must be addressed for broader clinical adoption, requiring collaborative efforts to standardize data and expand high-quality datasets. As AI evolves, it is poised to enhance diagnostic accuracy, support personalized treatment planning, and improve survival rates, revolutionizing PDAC detection and treatment.

## Data availability

No datasets were generated or analysed during the current study.

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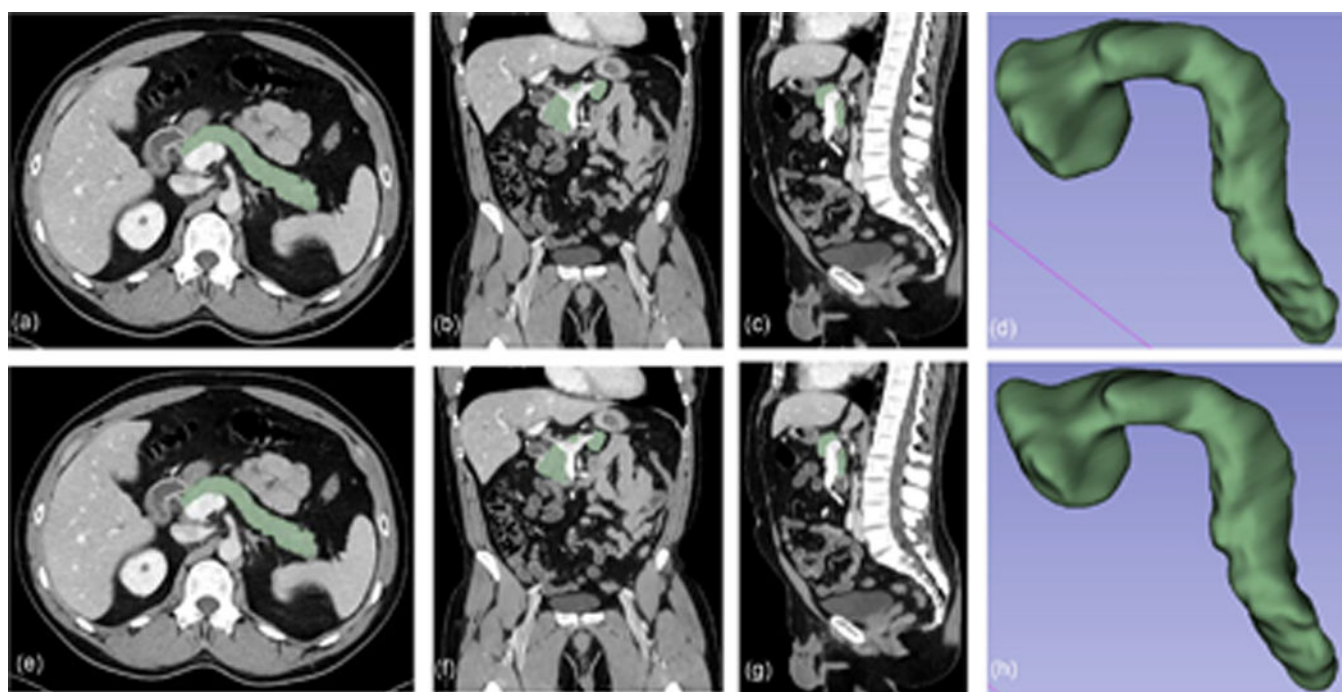
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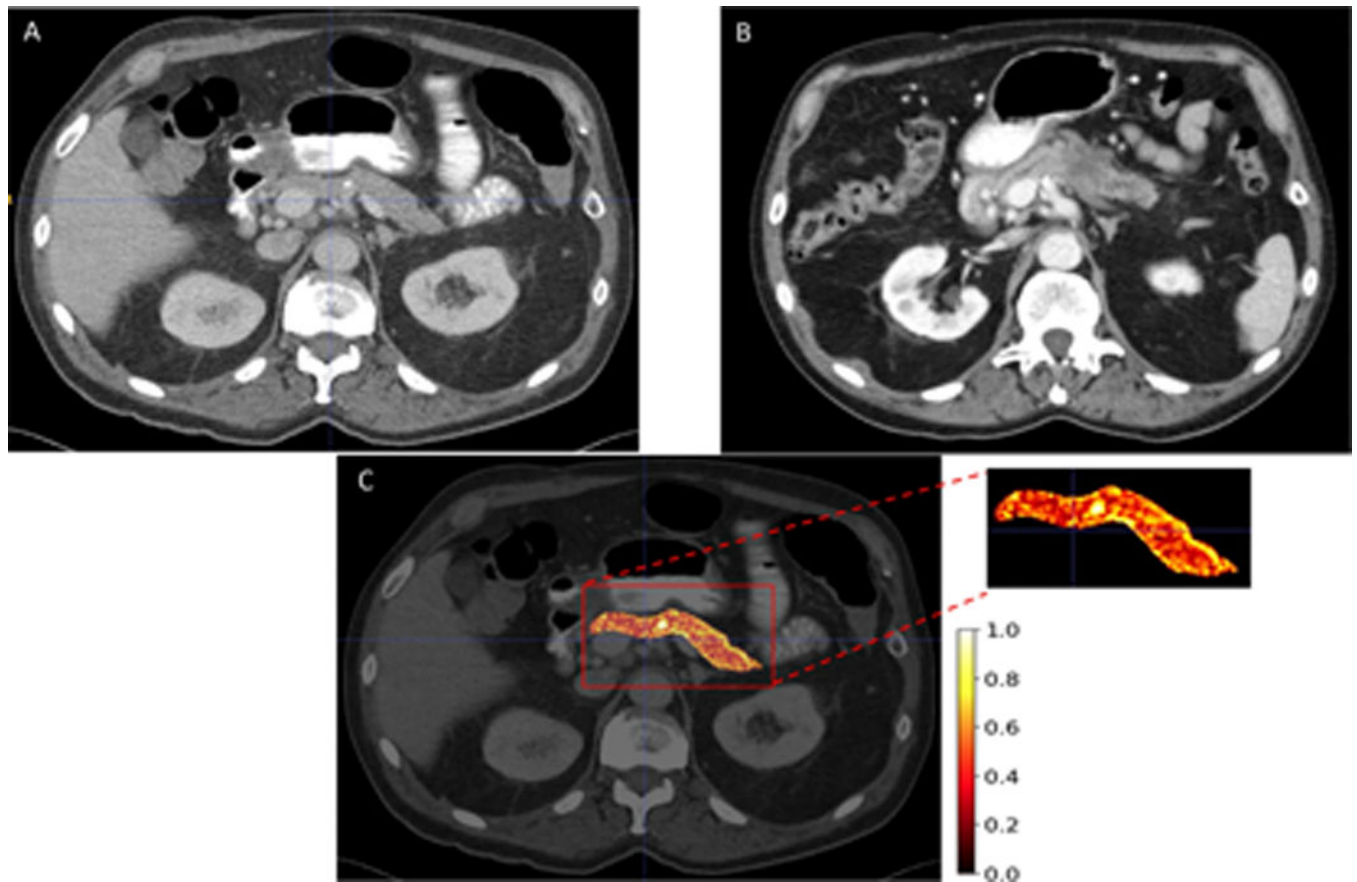
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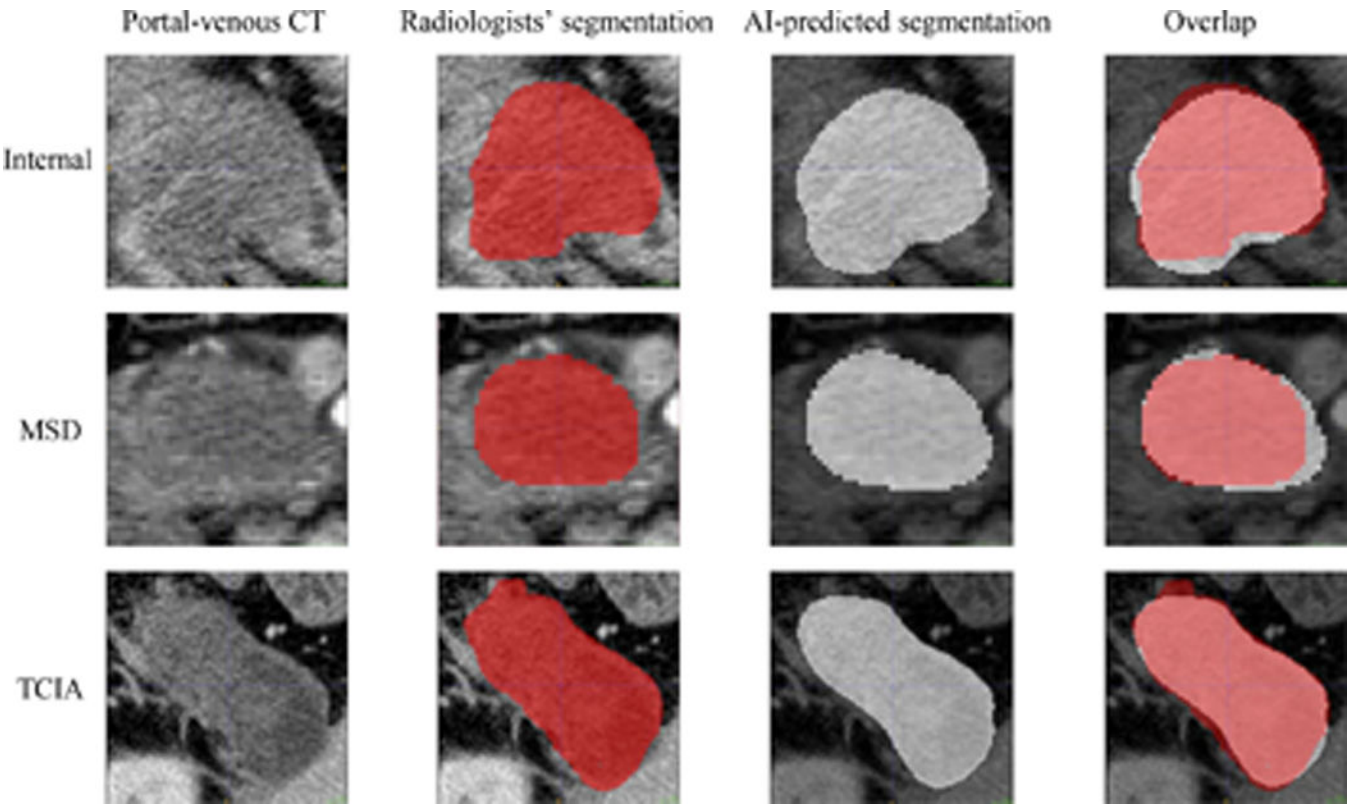
**Fig. 1. From: AI-Driven insights in pancreatic cancer imaging: from pre-diagnostic detection to prognostication**

Comparison of pancreas segmentations by radiologists and AI model: Panels (a-c) display the segmentations performed by the radiologists, while panels (e-g) show the segmentations predicted by the AI model. The Dice similarity coefficient (DSC) for this case is 0.96, reflecting a high degree of agreement between the two methods. The model's segmentations align well with those of the radiologists across all CT planes: axial (a, e), coronal (b, f), and sagittal (c, g), despite the pancreas's complex lobulated shape and curvature. Additionally, three-dimensional views of the segmentations from both the radiologists and the AI model are shown in panels (d) and (h), respectively



**Fig. 2. From: AI-Driven insights in pancreatic cancer imaging: from pre-diagnostic detection to prognostication**

Pre-diagnostic and diagnostic CT: A 66-year-old male with pancreatic ductal adenocarcinoma (PDAC). The pre-diagnostic CT (A) shows a normal pancreas, while approximately 1.5 years later, the patient was diagnosed with PDAC in the body of the pancreas, along with peritoneal carcinomatosis (B). Panel (C) displays a color-coded radiomics texture map overlaid on the pre-diagnostic CT, obtained from RED-MOD [5], highlighting the distribution of the gray level co-occurrence matrix informational measure of correlation 2 (GLCM-IMC2) texture feature across a single slice of the pancreas



**Fig. 3. From: AI-Driven insights in pancreatic cancer imaging: from pre-diagnostic detection to prognostication**

Comparison of AI model-predicted and reference PDA segmentations: Portal venous phase CT axial slices from the internal, Medical Segmentation Decathlon (MSD), and The Cancer Imaging Archive (TCIA) datasets. The AI model was trained on CT images that were cropped to focus on the tumor region using a 3D bounding box. Columns 1,2, and 3 display the original CT images, reference tumor segmentations, and AI- predicted tumor segmentations, respectively. Column 4 shows the overlay of the reference and AI- predicted segmentations. The bounding box-based approach demonstrates high accuracy in segmenting the tumor compared to the reference segmentations across all three cases. The volumetric Dice similarity coefficients (DSCs) between the AI-predicted and reference segmentations for the three cases were 0.91, 0.90, and 0.91, respectively