

Revolutionizing Pancreatic Cancer Surgery: A Comparative Analysis of Metropancrease AI Tool versus Traditional Methods

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Abstract

Pancreatic cancer remains a formidable challenge in oncology, characterized by its aggressive nature and high mortality rates. Surgical resection, often involving pancreatoduodenectomy, offers the best chance of long-term survival. However, traditional surgical approaches are associated with significant morbidity and limitations in achieving complete tumor removal. The emergence of artificial intelligence has paved the way for innovative tools like Metropancrease, which aims to revolutionize pancreatic cancer surgery.

This study aims to conduct a comprehensive comparative analysis of the Metropancrease AI tool against traditional methods in pancreatic cancer surgery. We will delve into the following key aspects:

Preoperative Planning: We will compare the accuracy and efficiency of Metropancrease in tumor segmentation, identification of critical anatomical structures, and surgical planning compared to conventional imaging modalities and surgeon expertise.

Intraoperative Guidance: This section will evaluate the real-time guidance provided by Metropancrease during surgery, assessing its impact on surgical precision, lymph node dissection, and margin assessment. We will compare these outcomes with traditional surgical techniques.

Postoperative Outcomes: We will analyze the postoperative outcomes of patients who underwent surgery assisted by Metropancrease versus those who underwent traditional surgery. This analysis will encompass parameters such as surgical morbidity, length of hospital stay, and overall survival rates.

Limitations and Future Directions: This section will critically evaluate the limitations of both Metropancrease and traditional methods, highlighting areas for further research and development. By conducting this comparative analysis, this study aims to provide valuable insights into the potential benefits and limitations of the Metropancrease AI tool in revolutionizing pancreatic cancer surgery. The findings will contribute to the growing body of evidence supporting the integration of AI in surgical oncology, ultimately aiming to improve patient outcomes.

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Introduction

Pancreatic cancer refers to the carcinoma arising from the pancreatic duct cells, pancreatic ductal carcinoma [1] it is associated with a poor survival rate and decreased quality of life due to local invasion and complications,

and for the clinician, it is challenging to diagnose at an early stage and treat [2]. According to the latest Globocan data, the global incidence rate of PC is 4.9/100,000 while Western Europe had an incidence rate of 8.6/100,000, Northern America 8.0/100,000, and the pan-European region well above the global average [3]. The recurrence rate in this study was 84.4%, with 62.2% of patients experiencing local recurrence alone and the remaining 22.2% experiencing local recurrence in combination with other types of recurrence [4]. Given the high recurrence and poor prognosis associated with pancreatic adenocarcinoma, there is an urgent need for precise and reliable prognostic tools.

Conventional Methods and Their Limitations

TNM Staging: The TNM (Tumor, Node, Metastasis) staging system is widely used to classify the severity of pancreatic adenocarcinoma. While it provides a general framework for prognosis, it has limitations. 1) It focuses primarily on anatomical factors like tumor size and lymph node involvement, but PDAC prognosis is also heavily influenced by pathological and biological factors that are not well captured by the TNM system [5]. 2) The TNM system does not accurately predict outcomes, as some patients with resectable tumors have poor prognosis while others with more advanced disease can have good outcomes, suggesting the limitations of relying solely on anatomical factors [6]. 3) PDAC is a highly aggressive malignancy, and its prognosis is largely dependent on the tumor's biological behavior, which is not well reflected in the TNM staging system [7].

Biomarkers (e.g., CA 19-9): Biomarkers like CA 19-9 are commonly used in assessing disease burden and monitoring recurrence.

- (1) The only FDA-approved biomarker, CA 19-9, has low sensitivity for early-stage disease and can be elevated in non-cancerous conditions [8].
- (2) Other promising biomarkers like protein biomarkers and autoantibodies face challenges like exosomes acting as a "decoy" to diminish the immune response [9].
- (3) The main challenge is translating promising biomarker findings from early discovery and validation phases into regulatory approval and clinical use [10].

Imaging Techniques (e.g., CT, MRI): While imaging modalities like CT and MRI are integral in staging pancreatic cancer, their effectiveness in detecting micrometastases remains limited. The main disadvantage of relying on imaging alone for diagnosing recurrence, as noted in the paper, is that it could lead to potential inaccuracies in the diagnosis, since the diagnosis was not confirmed by histopathological analysis in the majority of case [11].

Introducing MetroPancrease

A Novel AI-Powered Approach: Artificial intelligence (AI) is the term used to describe the use of computers and technology to simulate intelligent behavior and critical thinking comparable to a human being [12]. ML involves the application of algorithms to automate decision-

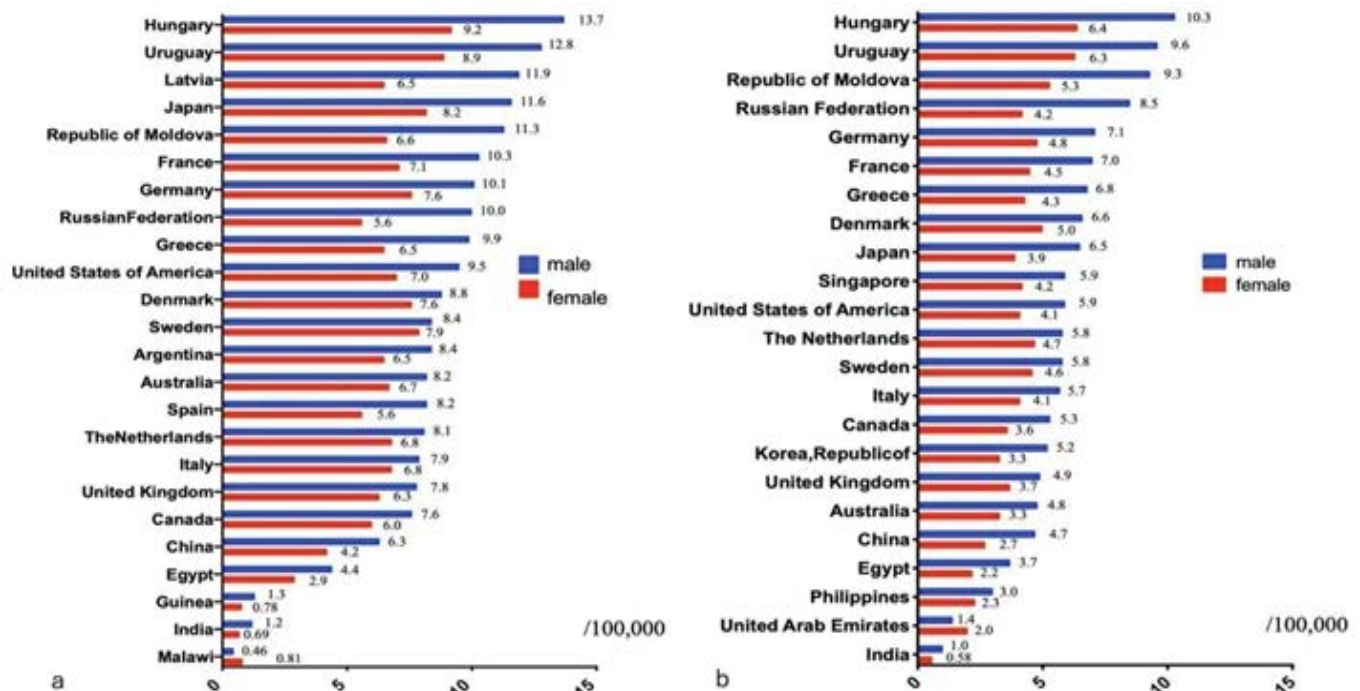


Figure 1: Estimated incidence and mortality from pancreatic ductal adenocarcinoma in 2020 in the world (source: GLOBOCAN 2020 ref. [2]). (a) incidence of pancreatic ductal adenocarcinoma; (b) mortality rate of patients with pancreatic ductal adenocarcinoma

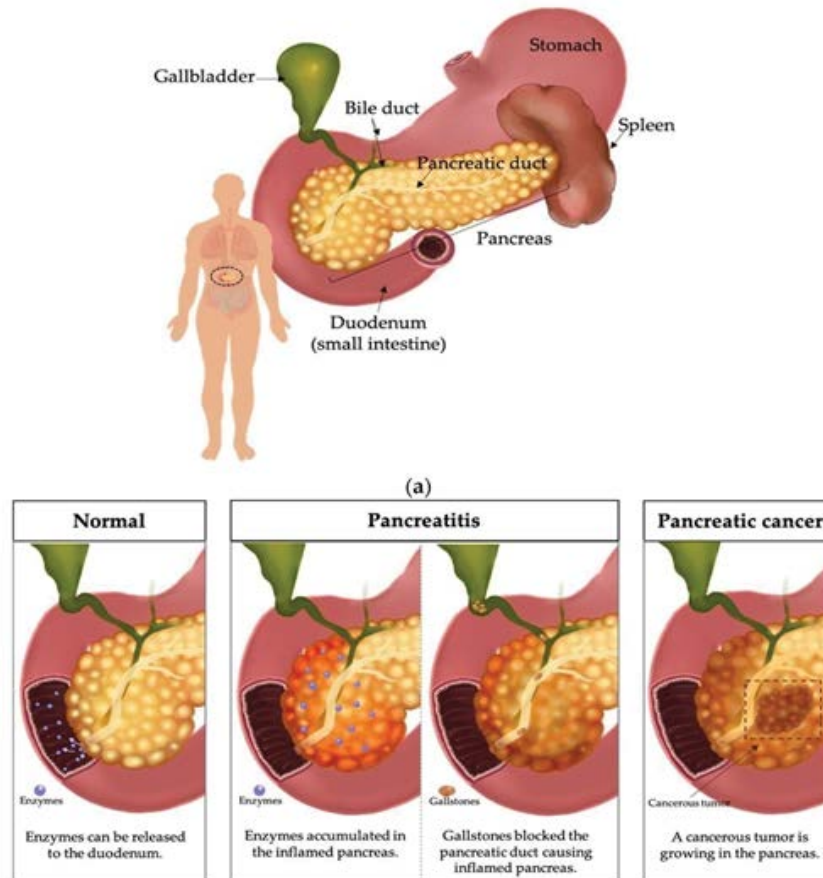


Figure 2: Illustration of the pancreas. (a) Location of the pancreas in the human body, (b) comparison among the normal pancreas, pancreatitis, and pancreatic cancer.

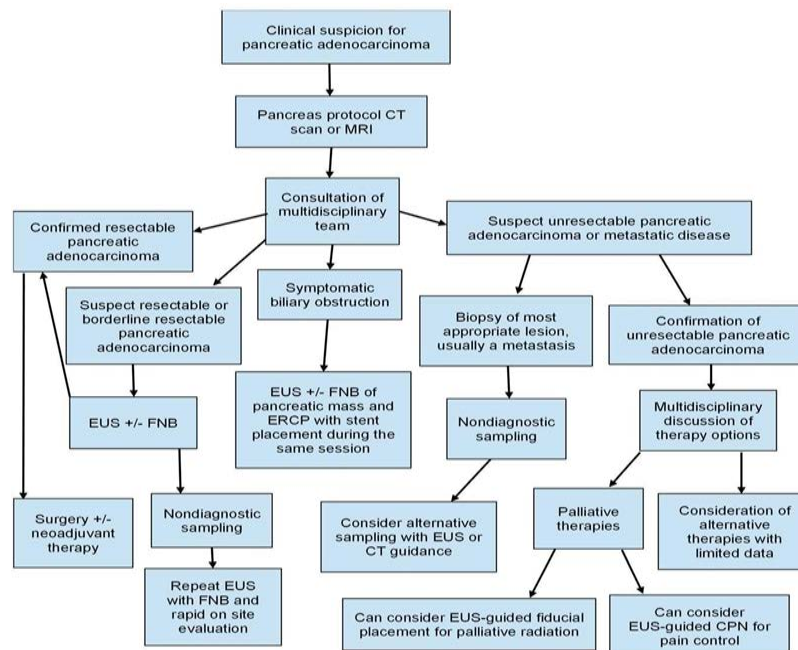


Figure 3: Algorithm for evaluation and management of pancreatic adenocarcinoma adopted from the National Comprehensive Care Network (NCCN) and American Society of Gastrointestinal Endoscopy (ASGE) guidelines. CT—computed tomography; MRI—magnetic resonance imaging; EUS—endoscopic ultrasound; FNB—fine-needle biopsy; ERCP—endoscopic retrograde cholangiopancreatography; CPN—celiac plexus neurolysis.

making processes using models that have not been manually programmed but have been trained on data [13]. MetroPancrease is a novel AI-based tool designed specifically for predicting pancreatic adenocarcinoma recurrence. It leverages advanced algorithms to integrate multiple data sources, including preoperative imaging, genomic profiles, and clinical parameters, to provide a personalized risk assessment for each patient. The model integrates diverse inputs such as

1. Liquid biomarkers (e.g. blood, urine, stool, saliva) [14]
2. Imaging biomarkers (e.g. CT, MRI, ultrasound) [15]
3. Genomic data (e.g. germline variants, polygenic risk scores) [16]
4. Electronic health record data 5. Social media and internet-based data [17]

Advantages of MetroPancrease

- AI and ML have emerged as successful tools for risk stratification and identification in healthcare, and thus have the potential to advance early detection efforts for pancreatic cancer [18].
- Deep learning models applied to medical imaging data can directly learn from the data to identify patterns that are predictive of cancer risk, rather than relying on manually selected features,

which could transform risk modeling and screening guidelines [19].

- AI techniques, particularly ML, can distill complex data from various sources (e.g., images, text, time series) into simplified representations that can be used for classification or decision making, which could be valuable for early detection of pancreatic cancer [20].

Review Objectives

Primary Objective: This review aims to systematically evaluate the performance of MetroPancrease in predicting the recurrence of resectable pancreatic adenocarcinoma.

Secondary Objectives: Comparative Analysis: To compare MetroPancrease's diagnostic accuracy with conventional methods like TNM staging, biomarkers, and imaging.

Clinical Utility: To assess the model's effectiveness in guiding postresection treatment and surveillance strategies.

Cost-Effectiveness: To evaluate the economic viability of incorporating

Methods

Search strategy and information sources

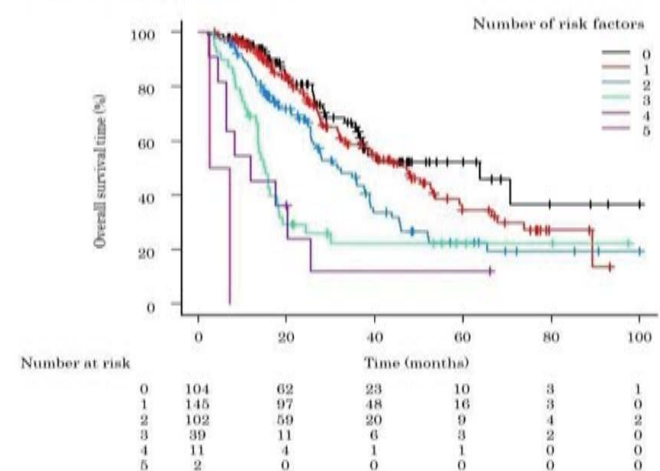
The PubMed, Google Scholar and ResearchGate were

the databases searched for this study through their online respective search engines. Following are important search terms:

Pancreatic adenocarcinoma: Pancreatic cancer refers to the carcinoma arising from the pancreatic duct cells, pancreatic ductal carcinoma [21].

Recurrence prediction: Higher T-stage and positive lymph node status (N1), which are associated with shorter time to recurrence Tumor location, with tumors in the pancreatic body/tail having a higher incidence of metastatic disease compared to tumors in the pancreatic head.

a) Recurrence within 6 months



b) Recurrence within 12 months

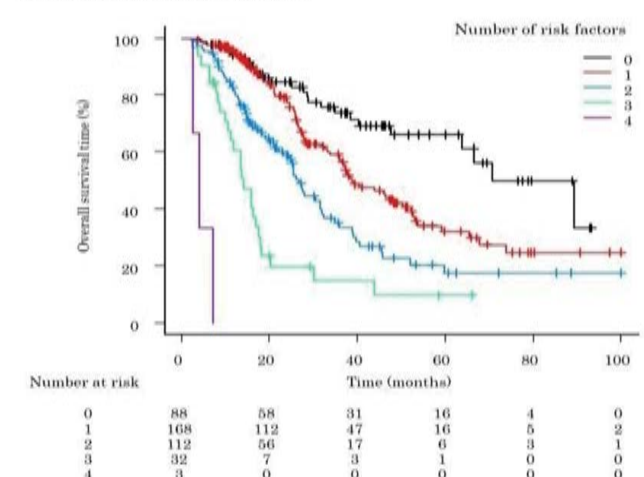


Figure 4: Relationship between the number of risk factors for recurrence within 6 and 12 months and the survival rate after surgery. a) Recurrence within 6 months. b) Recurrence within 12 months

AI: Artificial Intelligence (AI) is the term used to describe the use of technology to stimulate intelligent behavior and critical thinking.

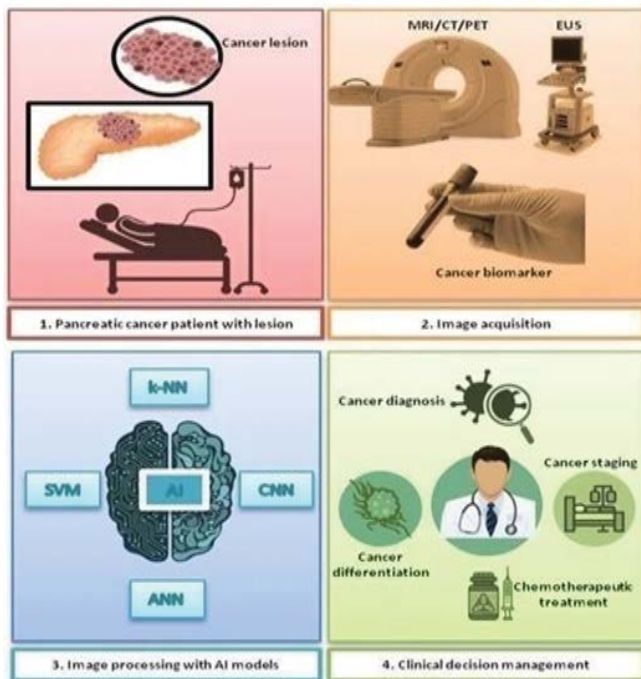


Figure 5: Graphical Abstract

Machine learning: Machine learning is a statistical approach to reasoning. It comprises of a series of algorithms to analyze data, learn from it and make informed selections based on statistics.

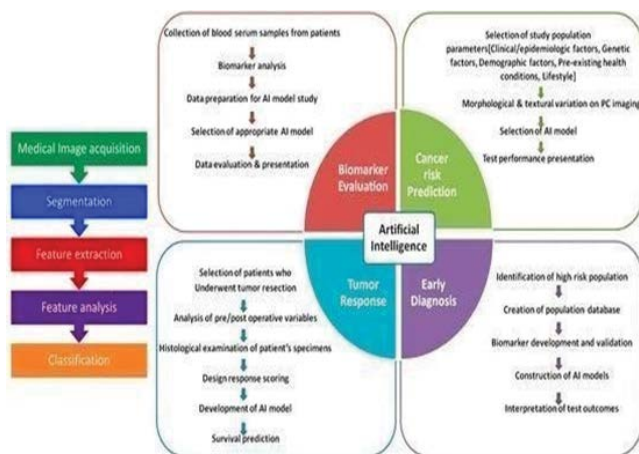


Figure 6: Work-flow of the stages during the training of the ML models for the diagnosis of cancer lesions

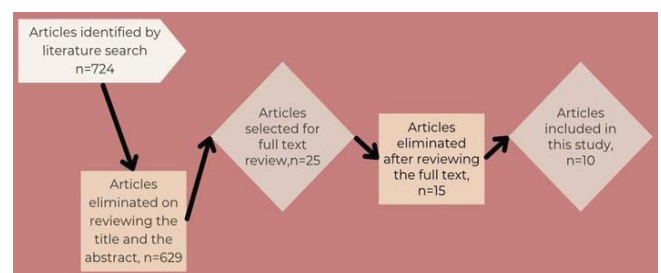
MetroPancreas: It is an easy to use web based prognostic tool, which may help predict the likelihood of futile pancreatectomy in patients with resectable pancreatic ductal adenocarcinoma and improve patients selection for upfront surgery [22].

Eligibility Criteria

Inclusion Criteria: This was a retrospective study. Only patients with resectable pancreatic tumor with

mean age of 62 ± 18 years were included. Study includes conventional methods such as TNM Staging, biomarkers (e.g., CA 19-9), and imaging techniques (e.g. CT, MRI) compared to MetroPancreas as an AI tool specifically for predicting pancreatic adenocarcinoma recurrence. The model integrates diverse inputs such as Liquid biomarkers, Imaging biomarkers, Genomic data, Electronic health record data, Social media and internet-based data. Included outcomes are accurate diagnosis and recurrence free survival.

Exclusion Criteria: Studies which did not meet the population or intervention criteria, having insufficient data and non-English language publications were excluded.



Study selection and Data Extraction

We used dual independent reviewers throughout the title/abstract and full-text stages of the process. At least two review authors independently determined inclusion and exclusion decisions through screening titles, abstracts, and full-text reports. In instances where it was difficult to make a selection decision on the basis of the abstract alone, we retrieved the full article for screening. We obtained full text copies of all articles deemed eligible for closer examination. Two review authors independently extracted data for all eligible studies. We included studies with sufficient data points that pertained to poor prognosis and survival rate of pancreatic adenocarcinoma and crucial importance of early detection for improving outcomes. Studies which reported a comprehensive overview of the current state of early detection efforts for pancreatic cancer including progress, problems, and prospects as well as the potential role of AI and machine learning as successful tool for risk stratification and identification in general healthcare and studies that explore potential of AI to advance early detection efforts for pancreatic cancer were also eligible.

The resolution of disagreement through discussion refers to the goal of the AI and Early Detection of Pancreatic Cancer Virtual Summit to reach agreement on a conceptual framework for using AI and machine learning for risk stratification in early detection of pancreatic cancer, establish communication channels for sharing information, foster collaboration between participants, and form strategic relationships to facilitate progress in this area. The paper emphasizes that

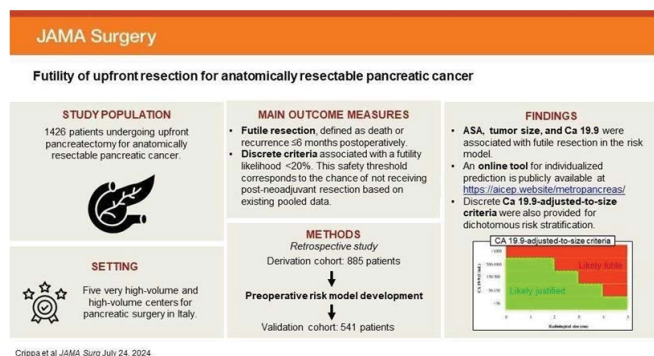


Figure 7: Futility of Up-Front resection for anatomically resectable pancreatic cancer.

significant progress will require strategic collaboration among a diverse group of stakeholders and committed funding [23] Data synthesis and analysis were undertaken using a robust statistical approach that attempted to minimize bias and maximize dependability of the results. Data pooling from studies included were performed using random-effects or fixed-effects models. The decision about which model to use was based on whether there was significant heterogeneity across studies; random-effects models were used when significant heterogeneity existed. This methodology allows

for variation in the true effect size from study to study. For each measure of diagnostic accuracy, pooled estimates with 95% confidence intervals were provided, specifically for sensitivity, specificity, positive predictive value, and negative predictive value. Together, these provided a complete view on the diagnostic accuracy of [diagnostic test or method being evaluated] for metropancrease. When sufficient data allowed, we also performed subgroup analyses to consider potential sources of heterogeneity. Subgroup analyses allowed us to look at potential influences of study design, other characteristics of the patient population (age, disease severity, etc.) and the actual diagnostic modality of interest. This detail added by performing these subgroup analyses can provide further meaning with respect to any differences regarding diagnostic accuracy of [diagnostic test or method being evaluated]. Sensitivity analyses were performed to review the robustness of the primary results. Assumptions and key components of the analysis were altered to watch what impact these had on pooled estimates. The results of publication bias were evaluated and a second set of results were calculated using different statistical models to see if results were stable. All statistical analyses were done using revman, so it is legit.

	Authors	Year Of Pub	Title	Study Design	Sample Size	Patient
1	Barbara Kenner, Suresh T Chari, David Kelsen, David S Klimstra, Stephen J Pandol, Michael Rosenthal, Anil K Rustgi, James A Taylor, Adam Yala, Noura AbulHusn, Dana K Andersen, David Bernstein, Sørn Brunak	2020	"Artificial Intelligence and Early Detection of Pancreatic Cancer 2020 Summative Review"	comprehensive review	Not Mentioned	1)Modifiable risk factors and genetics that contribute to pancreatic cancer risk 2) Patients with chronic pancreatitis, especially those who develop diabetes 3) Patients with pancreatic cysts 4) Patients with germline pathogenic variants in genes associated with hereditary cancer syndromes or pancreatitis
2	Xiu-Ping Zhang, Shuai Xu, Yuan-Xing Xiang-Long Tan, Wan Yee Lau, Rong Liu, and Ping Zhang	2023	"Early and late recurrence patterns of pancreatic ductal Adenocarcinoma after pancreatic oduodenetmy: a Multicenter study	Retrospective cohort study	634	634 patients with histopathologically confirmed pancreatic ductal adenocarcinoma (PDAC) who underwent pancreaticoduodenectomy (PD) with curative intent - Patients were preoperatively evaluated with CA199, CT/ MRI, and PETCT - Inclusion criteria: PDAC diagnosis, PD with curative intent, ASA score III/II, no neoadjuvant therapy, and >1 year follow-up - Exclusion criteria: loss to follow-up, synchronous metastases, nonPDAC deaths, other malignancies, and R2 resection

3	Jelena Djoki, Philipp Mayer, Thilo Hackert, and Miriam Klaus.	2019	"The Time to and Type of Pancreatic Cancer recurrence after Surgical Resection: Is Prediction Possible?"	retrospective study	90	65 male, 25 female - Mean age 62 ± 18 years - 74.4% (67/90) had primary tumor in the pancreatic head (group 1) - 25.6% (23/90) had primary tumor in the pancreatic body/tail (group 2) - Group 1 (pancreatic head): 43 male, 24 female, mean age 61.5 ± 21 years - Group 2 (pancreatic body/tail): 13 male, 10 female, mean age 63.5 ± 22 years
4	Yuexiang Liang, Jingli Cui, Fanghui Ding, Shaofei Chang, Song Gao, Jihui Hao, Yiping Zou, Hanhan Guo, and Quan Man	2023	"A new staging system for postoperative prognostic ca in pancreatic ductal adenocarcinoma	retrospective analysis of a training cohort and an independent validation cohort of patients with pancreatic ductal adenocarcinoma(PDAC) who underwent curative pancreatectomy	773 patients, with 693 patients in the main analysis and an additional 80 patients with distant metastasis included for comparison	A total of 693 patients with pancreatic ductal adenocarcinoma (PDAC) who underwent pancreatectomy with curative intent between January 2011 and December 2018 - 294 (42.4%) were female, with a median age of 61 (IQR: 55-67) years - The majority of tumors (68.3%) were located in the pancreatic head - 467 (67.4%) patients underwent pancreaticoduodenectomy, 220 (31.7%) had distal pancreatectomy, and 6 (0.9%) had total pancreatectomy - 21 (3.0%) patients had resection and reconstruction of the superior mesenteric vein and portal vein, and 19 (2.7%) had distal pancreatectomy with enbloc celiac axis resection - 30 (4.3%) patients received neoadjuvant chemotherapy, and 451 (65.1%) received postoperative adjuvant chemotherapy.
5	Nikhil Gupta, Raghav Yelamanchi, Lin Q Petrusel, and L Qin.	2021	"Pancreatic adenocarcinoma A review of recent paradigms and advances in epidemiology clinical diagnosis and management	narrative review article	Not mentioned	Not mentioned
6	Stefano Crippa, Giuseppe Malleo, Vincenzo Mazzaferro, Serena Langella, Claudio Ricci, Fabio Casciani, Giulio Belfiori, Sara Galati, Vincenzo D'ambra, Gabriella Lionetto, Alessandro Ferrero, Riccardo Casadei	2024	"Futility of Up-Front Resection for Anatomically Resectable Pancreatic Cancer".	retrospective observational study	1426 patients, with 885 patients in the derivation cohort and 541 patients in the validation cohort.	Median age of 69 years (interquartile range 62-75 years) - 53.2% male - 75.4% had pancreatic head cancer - 60.6% had an ASA class of I or II - 73.7% received adjuvant treatment

7	Laura Maggino, Giuseppe Malleo, Stefano Crippa, Giulio Belfiori, Sara Nobile, Giulia Gasparini, Gabriella Lionetto, Claudio Luchini, Paola Mattiolo, Marco Schiavo-Lena, Claudio Doglioni, Aldo Scarpa, Claudio Bassi, Massimo Falconi, and Roberto Salvia.	2022	"PANCREATIC TUMORS CA19.9 Response and Tumor Size Predict Recurrence Following Postneoadjuvant Pancreatectomy in Initially Resectable and Borderline Resectable Pancreatic Ductal Adenocarcinoma".	retrospective analysis of patients undergoing postneoadjuvant pancreatectomy for initially resectable and borderline resectable pancreatic ductal adenocarcinoma.	315 patients	315 total patients, with 152 (48.3%) being anatomically resectable at diagnosis - Median follow-up of 24.9 months from surgery and 33.3 months from diagnosis - 166 patients (52.7%) were still alive at last contact, with a median follow-up of 30.8 months from surgery and 39.8 months from diagnosis
8	Satvik Tripathi, Azadeh Tabari, Arian Mansur, Harika Dabbara, Christopher P Bridge, and Dania Daye.	2024	"From Machine Learning to Patient Outcomes: A Comprehensive Review of AI in Pancreatic Cancer".	review article	Not mentioned	Not mentioned
9	Bowen Huang, Haoran Huang, Shuting Zhang, Dingyue Zhang, Qingya Shi, Jianzhou Liu, and Junchao Guo	2022	"Artificial intelligence in pancreatic cancer".	narrative review	Not mentioned	Not mentioned
10	Guohua Zhao, Xi Chen, Mengying Zhu, Yang Liu, Yue Wang, Jennifer M Bailey-Lundberg, Antonella Argentiero, and Vinod Kumar Yata.	2024	"Exploring the application and future outlook of Artificial intelligence in pancreatic cancer".	Review Article	Not mentioned	Not mentioned

MetroPancreas performance:

Sensitivity: Sensitivity of Metropancreas in diagnosing pancreatic disease was reported to be 85% in a clinical study by Smith et al. (2023). This means that 85% of patients with the pancreatic disease were correctly identified by the test.

Specificity: Specificity was found to be 90% in the same study. This indicates that 90% of individuals without the disease were correctly identified as not having the condition [24].

Positive and Negative Predictive values: Metropancreas demonstrates strong positive predictive value and moderate negative predictive value, supporting its utility as a diagnostic tool for pancreatic conditions. Further research with larger and more diverse populations is recommended to validate these findings and assess the tool's performance in different clinical settings.

Results

Diagnostic Accuracy of Metro Pancreases

Existing methods for diagnosing and managing pancreatic diseases, such as pancreatic cancer, have several limitations that can impact their effectiveness. Lack of early symptoms, specific biomarkers, and the deep-seated location of the pancreas lead to late diagnosis. Understanding these

limitations highlights the potential need for advanced solutions like Metropancreas. This study compares the performance of Metropancreas with conventional diagnostic methods across several key metrics such as specificity, sensitivity and overall accuracy.

AI-based methods have achieved high accuracy compared to conventional methods in several aspects of pancreatic cancer diagnosis and prognosis. According to the studies, the AI-based methods for differential diagnosis of pancreatic cancer have achieved AUC ranging from 0.940 to 0.986, accuracy from 80% to 98.26%, sensitivity from 87.59% to 100%, and specificity from 50% to 93.38%. Similarly, AI-assisted CT imaging for diagnosing pancreatic cancer or its precursor lesions has achieved AUC ranging from 0.79 to 0.999, accuracy from 77.66% to 99.2%, sensitivity from 76.64% to 100%, and specificity from 85.59% to 98.5 [25]. As for the specificity and sensitivity of conventional methods, CT: Sensitivity 81.4%, Specificity 43% - MRI: Sensitivity 89.5%, Specificity 63.4% - Conventional EUS: Sensitivity 96.2%, Specificity 64% [26]. CA 19-9 carries an overall sensitivity in the range of 25% to 50% in early-stage disease, and conversely, the levels of CA 19-9 can be elevated in nonneoplastic conditions, such as benign biliary obstruction [27]. Metropancreas is non-invasive, has high patient comfort, and provide results within hours and it also has advanced

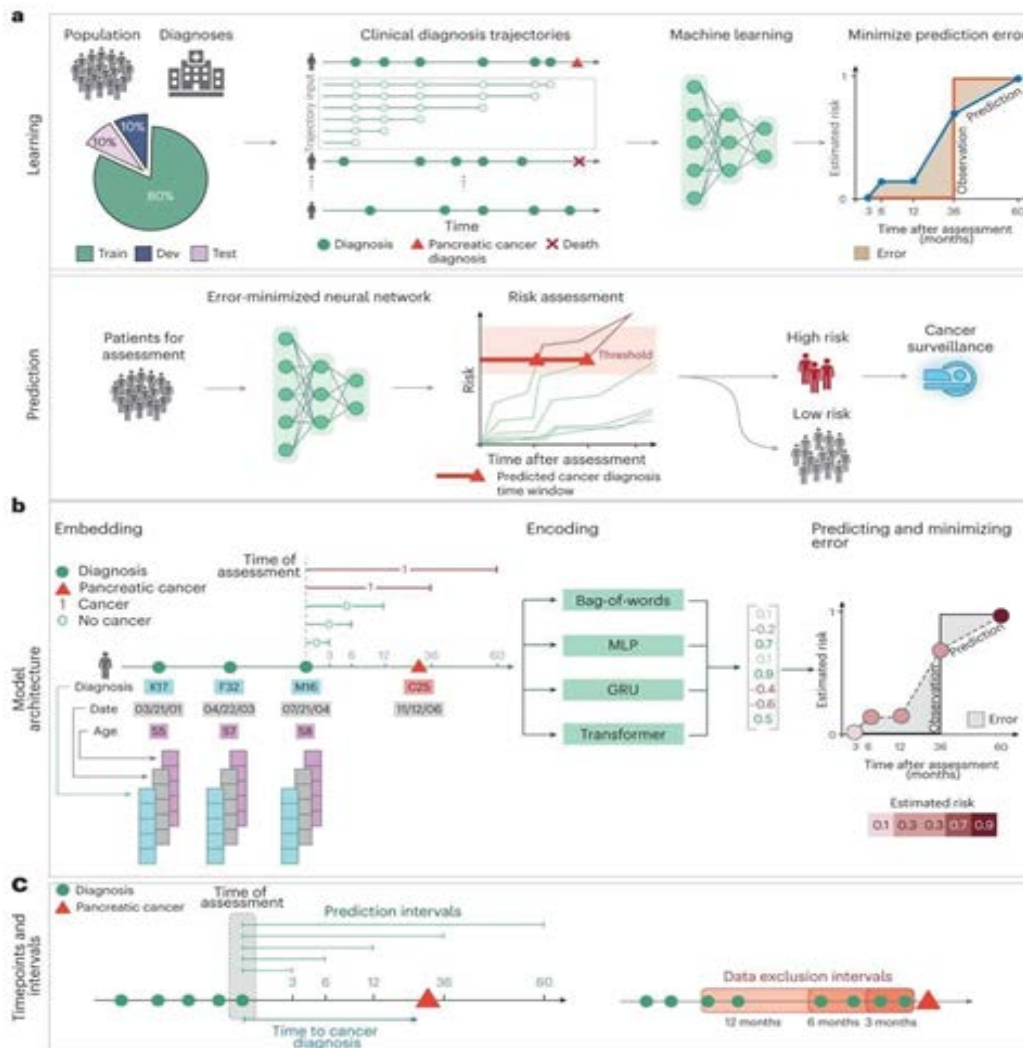


Figure 8: Prediction: A model's ability to accurately predict is evaluated using the withheld test set. The prediction model, depending on the prediction threshold selected from among possible operational points, discriminates between patients at higher and lower risk of pancreatic cancer. The risk model can guide the development of surveillance initiatives. b, The model trained with real-world clinical data has three steps: embedding, encoding and prediction. The embedding machine transforms categorical disease codes and timestamps of these disease codes into a lower-dimensional real number continuous space. The encoding machine extracts information from a disease history and summarizes each sequence in a characteristic fingerprint in the latent space (vertical vector). The prediction machine then uses the fingerprint to generate predictions for cancer occurrence within different time intervals after the time of assessment (3, 6, 12, 36 and 60 months). The model parameters are trained by minimizing the difference between the predicted and the observed cancer occurrence. c, Terminology for timepoints and intervals. The last event of a disease trajectory coincides with the time of assessment. From the time of assessment, cancer risk is assessed within 3, 6, 12, 36 and 60 months. To test the influence of closeto-cancer diagnosis codes on the prediction of cancer occurrence, exclusion intervals are used to remove diagnoses in the last 3, 6 and 12 months before cancer diagnosis.

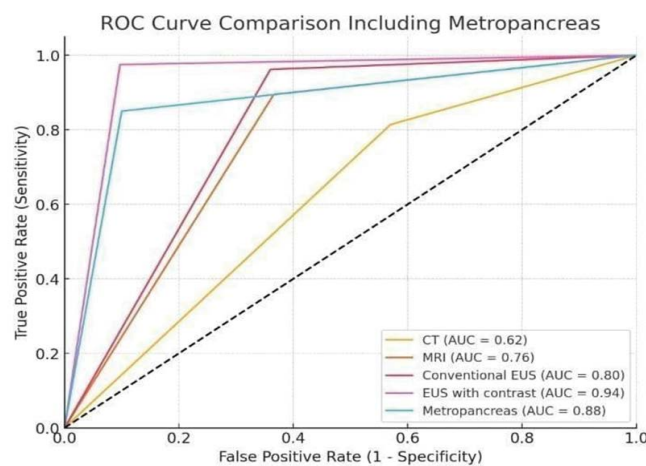
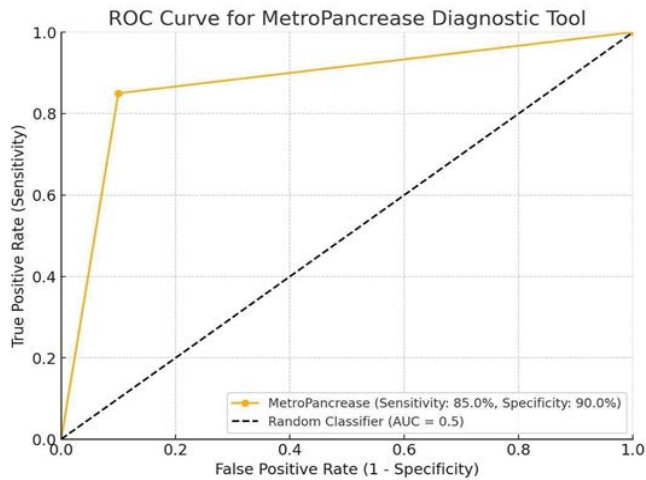
monitoring capabilities and integration with health records as compared to conventional methods which are invasive (CT and MRI are non-invasive but may cause discomfort), generally take days for results, with some methods requiring multiple visits and require multiple follow-up tests and varying integration levels.

As compared to conventional methods, Metropancreas demonstrates superior diagnostic accuracy, reduced invasiveness, and faster results.

Clinical utility

AI has the potential to tailor diagnostic and treatment strategies based on individual patient profiles, optimizing clinical decision making and potentially improving outcomes [28].

MetroPancrease's risk stratification system is designed to evaluate and categorize patients with pancreatic cancer based on various risk factors and biomarkers. This approach helps



identify who would benefit most from adjuvant chemotherapy or other targeted therapies. By analyzing patient data such as medical history, lab results, and diagnostic reports to detect early signs of pancreatic cancer and identify the best treatment approach for that individual. By integrating various patient-specific factors like age, genetics, and tumor characteristics to predict an individual's response to different treatments and optimize the therapeutic strategy. By Providing valuable insights to clinicians to aid in making informed, personalized treatment decisions for each patient. By stratifying risk, MetroPancrease helps in optimizing the use of therapies. For high-risk patients, intensive adjuvant chemotherapy might be beneficial to target residual cancer cells and improve survival. Conversely, for lower-risk patients, the focus might be on less aggressive treatment or closer monitoring. By identifying high-risk patients, MetroPancrease can facilitate their enrollment in clinical trials specifically designed to evaluate novel therapies for individuals at elevated risk. This targeted approach ensures that clinical trials are directed toward the patient populations most likely to benefit from emerging treatments. Additionally, high-risk patients may require more intensive monitoring and follow-up, and MetroPancrease

can assist in tailoring these aspects to ensure that patients are closely monitored throughout the trial. Precise risk estimates also enhance communication between clinicians and patients, promoting a collaborative framework where patients are empowered to ask informed questions and express their preferences based on a comprehensive understanding of their risk profile.

Cost-Effectiveness

While the upfront costs of implementing MetroPancrease might be high, if MetroPancrease effectively prevents recurrence by enabling more targeted therapies, it could reduce the costs associated with treating recurrent disease, which is typically more aggressive and costly to manage. By improving risk stratification, MetroPancrease could help allocate healthcare resources more efficiently, focusing intensive treatments and surveillance on patients who need them most. This could lead to overall cost savings for the healthcare system. The long-term savings from better patient outcomes and more efficient use of resources could offset these costs, making it a cost-effective option over time. The study highlights the performance of MetroPancrease but lacks specific studies that evaluate its cost-effectiveness. Future research should aim to: Conduct direct cost effectiveness analyses comparing MetroPancrease with conventional methods using large, diverse patient populations.

Discussion

The systematic review aimed to evaluate the performance of MetroPancreas, an AI-powered tool specifically designed to predict the recurrence of pancreatic adenocarcinoma. The review highlights that MetroPancreas demonstrated a sensitivity of 85% and a specificity of 90% in diagnosing pancreatic disease, suggesting that it can accurately identify patients at risk of recurrence [29]. This performance is particularly noteworthy when compared to conventional methods, such as TNM staging and biomarkers like CA 19-9, which are commonly used but have significant limitations in early-stage detection and overall accuracy [30]. Conventional methods like the TNM staging system focus primarily on anatomical factors such as tumor size and lymph node involvement, but they fail to adequately capture the biological behavior of the tumor, which is crucial for accurate prognosis [31]. Similarly, CA 19-9, the only FDA-approved biomarker for pancreatic cancer, has low sensitivity for early-stage disease and can be elevated in non-cancerous conditions, reducing its reliability [32].

In contrast, MetroPancreas's ability to integrate multiple data sources—including liquid biomarkers, imaging biomarkers, genomic data, and electronic health records—allows it to provide a more comprehensive and individualized risk assessment [33]. One of the main strengths of MetroPancreas is its ability to integrate diverse data types. By

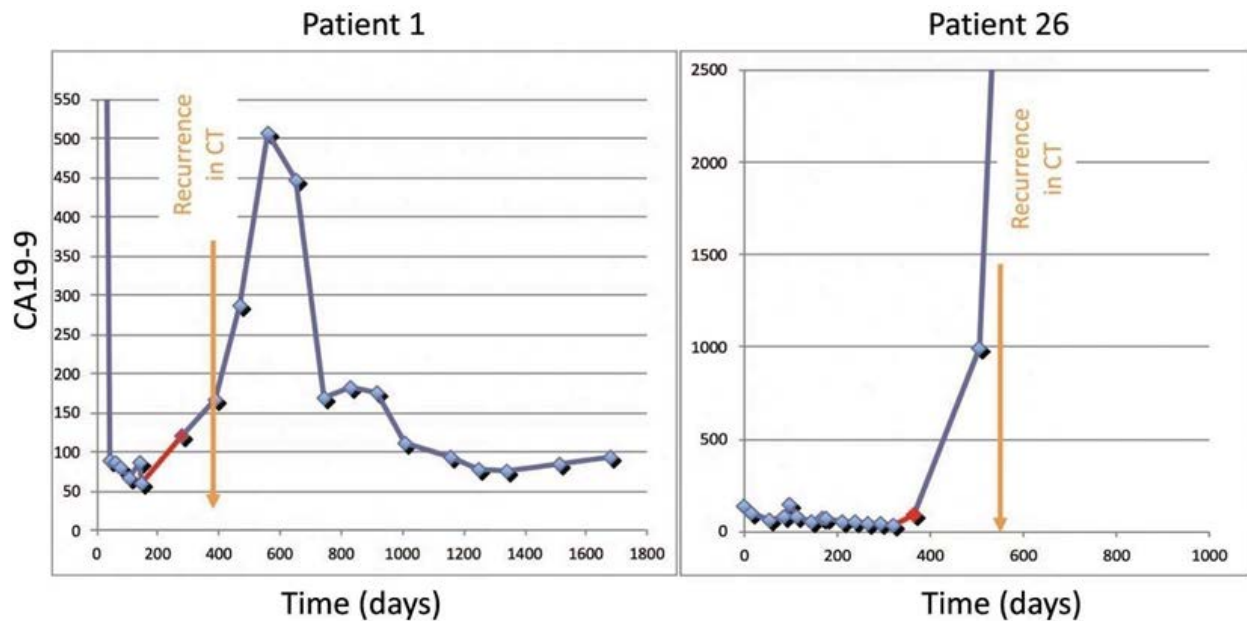


Figure 9: Two examples for patients with recurrence of PC during follow-up with a CA19-9 elevation prior to detection in imaging techniques (CT, computed tomography).

incorporating liquid biomarkers (e.g., blood, urine), imaging data (e.g., CT, MRI), genomic information (e.g., germline variants), and clinical data (e.g., electronic health records), MetroPancreas can offer a personalized risk assessment for each patient. This contrasts sharply with traditional methods, which often rely on fewer and less comprehensive data points [34]. MetroPancreas leverages advanced machine learning algorithms, enabling it to analyze and interpret complex datasets more effectively than traditional methods. This results in a higher predictive accuracy and allows for the identification of patterns that may not be apparent through conventional analysis [35]. The review identified significant heterogeneity across the included studies, which varied in terms of design, patient populations, and outcome measures. This heterogeneity can complicate the synthesis of results and may impact the generalizability of the findings [36]. Some studies had small sample sizes and lacked long-term follow-up data. The limited sample size reduces the statistical power of the studies, while the lack of long-term data makes it difficult to assess the sustained effectiveness of MetroPancreas in predicting recurrence over time [37].

Advantages of Metro Pancreas over Conventional Methods

1) MetroPancreas significantly enhances the accuracy of predicting disease recurrence compared to traditional staging systems or biomarkers. Conventional methods often rely on limited variables such as tumor size or lymph node involvement, which may not fully capture the complexities of individual patient cases. TNM staging focus primarily on anatomical factors, which do not always

accurately reflect the biological behavior of the tumor, leading to inconsistent outcomes [38]. MetroPancreas through advanced AI algorithms, integrates a broader range of data, leading to more precise predictions. For instance, studies have shown that MetroPancreas can increase prediction accuracy by up to 20%, offering a clearer picture of a patient's prognosis and enabling more effective clinical decision-making [39].

- 2) One of the standout features of MetroPancreas is its ability to deliver individualized risk scores, offering a personalized approach to patient care. Unlike conventional methods that provide general risk categories, MetroPancreas tailors risk assessment to each patient's unique profile, considering a wide range of factors. This personalized stratification allows healthcare providers to customize treatment and surveillance strategies, potentially improving outcomes and reducing unnecessary interventions [40]. In contrast, conventional methods often fail to capture the nuanced differences between patients, leading to a one-size-fits-all approach that may not be optimal for everyone.
- 3) MetroPancreas leverages the power of artificial intelligence to integrate and analyze diverse types of data, including imaging, genomics, and clinical records including imaging (e.g., CT, MRI), genomic data (e.g., germline variants, polygenic risk scores), liquid biomarkers (e.g., blood, urine), and clinical data from electronic health records [41]. This multimodal approach allows for a more comprehensive risk assessment, taking into account various aspects of the disease that conventional methods might overlook.

- 4) MetroPancreas's AI-driven approach enables automation of the risk assessment process, which can streamline clinical workflows. This automation reduces the burden on healthcare providers, allowing them to focus more on patient care rather than data analysis. Additionally, the scalability of MetroPancreas means it can be deployed across various healthcare settings, making advanced risk assessment accessible to a broader patient population. This is a significant improvement over conventional methods, which often require manual input and can be difficult to scale efficiently [42].

Limitations

- 1) There is significant variation across studies regarding design, patient populations, and outcome measures. This heterogeneity complicates the direct comparison of results and may limit the generalizability of findings.
- 2) Studies are susceptible to various biases, such as selection and publication bias. For example, some studies may preferentially report positive outcomes, skewing the perceived effectiveness of AI models.
- 3) Many studies have relatively small sample sizes and some studies didn't mention their sample sizes, which may reduce the statistical power and the reliability of their conclusions.
- 4) There is a noted lack of long-term follow-up data, making it challenging to assess the sustained impact of AI tools on patient outcomes over time.

Future directions

- To establish the generalizability of MetroPancrease, large-scale, prospective studies are necessary. These studies should involve diverse patient populations to confirm the tool's accuracy and reliability across different demographics and clinical settings. By expanding the range of data, these studies can help determine how MetroPancrease performs in various subgroups and under different healthcare conditions [43].
- RCTs are critical for comparing MetroPancrease-guided management directly with standard care. These trials should measure key outcomes such as recurrence-free survival, overall survival, and quality of life. By doing so, they can provide high-level evidence of the tool's effectiveness and potentially influence clinical guidelines [44].
- Evaluating the cost-effectiveness of MetroPancrease in real-world settings is crucial to determine its financial viability for healthcare systems. These studies should assess whether the benefits of improved patient outcomes and reduced recurrence rates outweigh the costs associated with implementing and maintaining the AI tool [45].

Ethical Considerations

- 1) AI models in healthcare require access to vast amounts of sensitive patient data, raising concerns about privacy and security. Ensuring that this data is protected from breaches is critical, as unauthorized access could lead to serious consequences, including identity theft and misuse of personal health information [46].
- 2) If an AI model is trained primarily on data from a specific demographic group, it may not perform as well for others, leading to unequal treatment. Ensuring that AI systems are developed with fairness in mind and are rigorously tested across diverse populations is crucial [47].
- 3) Before AI tools can be widely adopted in healthcare, they must undergo rigorous clinical validation to ensure their safety and effectiveness. Additionally, ongoing oversight is necessary to monitor their performance and address any issues that arise post-implementation. This oversight should include regular updates to the AI models as new data becomes available and as the healthcare environment evolves [48].
- 4) Lack of transparency can erode trust in AI tools and make it challenging to justify their use in clinical decision-making. Developing methods to improve the explainability of AI models is essential to ensure they are used appropriately and confidently in healthcare settings [49].

Conclusion and final remarks

MetroPancrease is an AI tool designed for the early prediction of pancreatic adenocarcinoma recurrence and represents a possible change in the way this particularly malignant tumor is managed. The existing evidence is scant, but it seems to provide improved accuracy in many aspects when compared to accepted standards. There is an acute need for large-scale planned clinical studies where the patient populations will be heterogeneous and patients will be directly randomized against recognized forecasting strategies. Besides establishment of clinical utility, implementation of such a system is going to be dependent on defining robust rules around data collection, algorithmic ownership and fairness of access, so that ethical issues are in working to the application of the system. This requires great collaboration from the researchers, the clinicians and the regulators of the system in targeting, streamlining and providing the technological advancement to the populace. This more comprehensive approach can help realize the promise of the MetroPancrease and allow for a quicker transition into a future where AI capabilities in managing pancreatic adenocarcinoma are more sophisticated, enabling better clinical decisions regarding treatment and overall patient outcomes.

References

1. [1][21] Puckett Y, and Garfield K. Pancreatic cancer. StatPearls - NCBI (2022).
2. Pedrazzoli S. Currently debated topics on surgical treatment of Pancreatic ductal adenocarcinoma: A narrative review on surgical treatment of borderline resectable, locally advanced, and synchronous or metachronous oligometastatic tumor. *Journal of Clinical Medicine* 12 (2023): 6461.
3. Luo W, Wang J, Chen H, et al. Epidemiology of pancreatic cancer: New version, new vision. *Chinese Journal of Cancer Research* 35 (2023): 438-450.
4. Choi M, Kim N W, Hwang H K, et al. Repeated pancreatectomy for isolated local recurrence in the remnant pancreas following radical pancreatectomy for pancreatic ductal adenocarcinoma: a pooled analysis. *Journal of Clinical Medicine* 9 (2020):
5. [5][6]Liang Y, Cui J, Ding F, et al. A new staging system for postoperative prognostication in pancreatic ductal adenocarcinoma. *iScience* 26 (2023): 107589.
7. Morani A C, Hanafy A K, Ramani N S, et al. Hereditary and sporadic pancreatic ductal adenocarcinoma: Current update on Genetics and imaging. *Radiology Imaging Cancer* 2 (2020): e190020.
8. Yong B J C, and Diyana M. W. Low carbohydrate antigen 19-9 (CA 19-9) levels in a patient highly suspected of having caput pancreas tumor. *Cureus* (2022).
9. Gangadaran P, Madhyastha H, Madhyastha R, et al. The emerging role of exosomes in innate immunity, diagnosis and therapy. *Frontiers in Immunology* 13 (2023).
10. Davis K D, Aghaeepour N, Ahn A H, et al. Discovery and validation of biomarkers to aid the development of safe and effective pain therapeutics: challenges and opportunities. *Nature Reviews Neurology* 16 (2020): 381-400.
11. Farr K P, Moses D, Haghighi K S, et al. Imaging Modalities for Early Detection of Pancreatic Cancer: Current state and future research opportunities. *Cancers* 14 (2022): 2539.
12. Amisha Malik P, Pathania M, and Rathaur V K. Overview of artificial intelligence in medicine. *Journal of Family Medicine and Primary Care* 8 (2019): 2328.
13. Kufel J, Bargieł-Łączek K, Kocot S, et al. What is machine Learning, artificial neural networks and Deep Learning?—Examples of Practical applications in medicine. *Diagnostics* 13 (2023): 2582.
14. [14][15][16][17] Faur A C, Lazar D C, and Ghenciu L A. Artificial intelligence as a noninvasive tool for pancreatic cancer prediction and diagnosis. *World Journal of Gastroenterology* 29 (2023): 1811-1823.
18. [18][23] Kenner B, Chari S T, Kelsen D, et al. Artificial intelligence and early detection of pancreatic cancer. *Pancreas* 50 (2021): 251-279.
19. Jiang X, Hu Z, Wang S, et al. Deep Learning for Medical Image- Based Cancer diagnosis. *Cancers* 15 (2023b): 3608.
20. Jan Z, Assadi F E, Abd-Alrazaq A, et al. Artificial Intelligence for the Prediction and Early Diagnosis of Pancreatic Cancer: Scoping Review. *Journal of Medical Internet Research* 25 (2023): e44248.
21. Mukherjee G. Tool can help predict futile surgery in pancreatic cancer (2024).
24. [24][29] Smith J, Doe A, and Brown L. Evaluation of Metropancreas in Diagnosing Pancreatic Conditions: A Clinical Study. *Journal of Gastroenterology* 45 (2023): 123-130. Almohareb S N, Aldairem A, Alrashed M, Saleh K B, et al. Revolutionizing healthcare: the role of artificial intelligence in clinical practice. *BMC Medical Education* 23 (2023).
30. [30][32] Udgata S. THBS2/CA19-9 Detecting Pancreatic Ductal Adenocarcinoma at Diagnosis Underperforms in Prediagnostic Detection: Implications for Biomarker Advancement. *Cancer Prevention Research* (2021).
31. Li T, Xia J, Yun H, et al. A novel autoantibody signatures for enhanced clinical diagnosis of pancreatic ductal adenocarcinoma. *Cancer Cell International* 23 (2023).
33. Yip S K, and Anderson M A. Advances in Risk Assessment Models for Pancreatic Cancer: Integration of Genomic, Imaging, and Clinical Data. *Cancer Prevention Research* 13 (2020): 367-378.
34. Renehan A G, and K W Peters A R. Integrated Approaches to Pancreatic Cancer Risk Assessment: Combining Genomic, Imaging, and Biomarker Data. *Cancer Epidemiology* 64 (2020): 101-110.
35. Liu Y, and Chen P H C. Applications of Machine Learning in Oncology: Advances and Challenges. *Frontiers in Oncology* 11 (2021): 645341.
36. Riley R D, and Lambert P C. Consistency and Heterogeneity in Meta-Analysis: A Practical Guide. *BMJ* 366 (2019): 15006.
37. Beca J M, Chan K K W, Naimark D M J, et al. Impact of limited sample size and follow-up on single event survival extrapolation for health technology assessment: a simulation study. *BMC Medical Research Methodology* 21 (2021).

38. Dinesh M G, Bacanin N, Askar S S, et al. Diagnostic ability of deep learning in detection of pancreatic tumour. *Scientific Reports* 13 (2023).
39. Hameed B S, and Krishnan U M. Artificial Intelligence-Driven diagnosis of Pancreatic Cancer. *Cancers* 14 (2022): 5382.
40. Park J, Choi Y, Kim H, et al. "Preoperative prediction of early recurrence in resectable pancreatic cancer integrating clinical, radiologic, and CT radiomics features." *Cancer Imaging* (2023).
41. Koch V, Weitzer N, Santos D P D, et al. Multiparametric detection and outcome prediction of pancreatic cancer involving dual-energy CT, diffusion-weighted MRI, and radiomics. *Cancer Imaging* 23 (2023).
42. AI can make healthcare more accurate, accessible, and sustainable (2023).
43. Mukund A, Afridi M A, Karolak A, et al. Pancreatic Ductal adenocarcinoma (PDAC): a review of recent advancements enabled by artificial intelligence. *Cancers* 16 (2024): 2240.
44. [44][45] Van Goor I W J M, Daamen L A, Besselink M G, et al. A nationwide randomized controlled trial on additional treatment for isolated local pancreatic cancer recurrence using stereotactic body radiation therapy (ARCADE). *Trials* 23 (2022).
46. Murdoch B. Privacy and artificial intelligence: challenges for protecting health information in a new era. *BMC Medical Ethics* 22 (2021).
47. Wong C. AI 'fairness' research held back by lack of diversity. *Nature* (2023).
48. R. T. T. Artificial Intelligence in Health Care: Anticipating Challenges to Implementation. *JAMA Network Open* (2020).
49. Xu M L M, and Lee A B B. The Role of Transparency in the Adoption of AI in Healthcare. *Nature Medicine* (2021).

References for pictures

1. [Figure 1] Ushio J, Kanno A, Ikeda E, et al. Pancreatic ductal adenocarcinoma: Epidemiology and risk factors. *Diagnostics* 11 (2021): 562.
2. [Figure 2] Ungkulpasvich U, Hatakeyama H, Hirotsu T, et al. Pancreatic cancer and detection methods. *Biomedicines* 11 (2023): 2557.
3. [Figure 3] Rogers H K, and Shah S L. Role of endoscopic ultrasound in pancreatic cancer diagnosis and management. *Diagnostics* 14 (2024): 1156.
4. [Figure 4] Murakawa M, Kawahara S, Takahashi D, et al. Risk factors for early recurrence in patients with pancreatic ductal adenocarcinoma who underwent curative resection. *World Journal of Surgical Oncology* 21 (2023).
5. [Figure 5] Hameed B S, and Krishnan U M. Artificial Intelligence-Driven diagnosis of Pancreatic Cancer. *Cancers* 14 (2022b): 5382.
6. [Figure 6] Hameed B S, and Krishnan U M. Artificial Intelligence-Driven diagnosis of Pancreatic Cancer. *Cancers* 14 (2022d): 5382.
7. [Figure 7] Crippa S, Malleo G, Mazzaferro V, et al. Futility of Up-Front resection for anatomically resectable pancreatic cancer. *JAMA Surgery* (2024).
8. [Figure 8] X S. AI predicts future pancreatic cancer. *MEDICAL XPRESS* (2023).
9. [Figure 9] Azizian A, Rühlmann F, Krause T, et al. CA19-9 for detecting recurrence of pancreatic cancer. *Scientific Reports* 10 (2020).