OXFORD JOURNAL
OF STUDENT
SCHOLARSHIP

Integrating Conventional Imaging and Novel Techniques: A Framework for the Early Detection of Pancreatic Cancer

Kimaya Ranjan
kimayaranjan2010@gmail.com

ABSTRACT

One of the leading causes of death in pancreatic cancer is the late detection. Various imaging or screening techniques available today are not optimal for diagnosing PDAC cancer at an early stage. Earlier detection of pancreatic cancer would allow more patients to be eligible for surgery and get their tumors removed, which could lead to a dramatic improvement in the survival rate for pancreatic cancer patients. This paper is an analysis of available diagnostic techniques for Pancreatic Ductal Adenocarcinoma (PDAC) with the aim to further explore potential new or combination techniques for earlier diagnosis or prognosis of PDAC. The paper explores the most common imaging techniques, such as Computed Tomography (CT), Positron Emission Tomography (PET), Magnetic Resonance Imaging (MRI), and Ultrasound (US), before diving deeper into the US, its sub-type Endoscopic Ultrasound (EUS) and its variations, by reviewing their sensitivity, specificity, and accuracy, [13] when applied to PDAC. While EUS broadly happens to be the most favored type of imaging techniques today due to its high sensitivity; none of the EUS sub-types individually are optimal on all three test characteristics (sensitivity, accuracy, and specificity), so the paper proposes a combination approach to EUS along with other diagnostic techniques including modern imaging, and non-imaging techniques, and artificial intelligence (AI). The goal is to identify a combination diagnosis technology that can optimally identify PDAC at an early stage in a cost effective, and easy to deploy fashion.

INTRODUCTION

Although pancreatic cancer is currently the 11th most diagnosed cancer in the U.S., it is the third leading cause of cancer-related deaths, after lung and colorectal cancer. It is predicted to become the second leading cause of cancer-related deaths by 2030. An estimated 67,530 Americans will be diagnosed with pancreatic cancer in 2026, which continues a years-long trend of increasing incidences. And approximately 52,740 Americans are expected to die from the disease this year [1].

The pancreas is a gland in the abdomen, between the spine and the stomach, and it produces hormones that control blood sugar levels and enzymes that aid in digestion. Pancreatic cancer occurs when cells in

the pancreas start to mutate and grow out of control to form an unwanted tumor. Most of the pancreatic cancer cases start in the ducts of the pancreas. There are two main types of pancreatic tumors called:
Exocrine Tumor: Exocrine tumors are formed in exocrine cells of the pancreas. More than 94% of all pancreatic cancers are of the exocrine type [2], out of which 90% of exocrine cancers are adenocarcinoma, which begins in the cell lining of the organs [2].

Neuroendocrine Tumor: Less than 5% of all pancreatic cancers are of neuroendocrine [3]. As the name suggests, neuroendocrine tumors are formed in neuroendocrine cells that either transmit nerve signals and/or produce hormones.

Typically, exocrine cancers, including PDAC, are very aggressive in nature and PDAC makes up more than 90% of pancreatic cancer cases. Since the pancreas is located deep inside between the spine and the stomach, early detection of pancreatic cancer is very rare, as it is hard to detect through imaging until it becomes large enough. By then, the cancer metastasizes and spreads to other organs, while also being asymptomatic, never allowing patients to witness signs, and the diagnosis becomes too late, leading to a very low survival rate for PDAC. Surgery is the only option once diagnosed too late, which in itself has a quite low success rate [4]. The five-year relative survival rate for pancreatic cancer remains at 13% and is just 8% for people diagnosed with PDAC. By some estimates, PDAC has caused more than 495,773 deaths worldwide. Given this low survival rate of ~8% [5], early detection of PDAC tumors is extremely important to increase the chance of survival. PDAC is one of the leading causes of metastatic cancer deaths and is estimated to cause deaths to more than 495,773 people worldwide [5]. Early detection can be explored in several ways, including various imaging techniques, advanced genetic testing, composite imaging techniques, biomarkers, and/or some combination of these. Imaging has proven to be the best and most accessible way to approach early diagnosis and prevention, so this paper focuses on exploring ways to improve imaging technologies for early detection of PDAC.

As of the current year, the most common imaging techniques include CT (computed tomography), PET (Positron Emission Technology), MRI (magnetic resonance imaging), and finally US (ultrasonography) [6,7]. All these modalities are the most common due to their relatively positive results measured on a scale based on their specificity (how good the modality is at identifying the perfect negative diagnosis) , sensitivity (how easily the modality could detect tumors), and accuracy (judges the proportion of the false and true negatives/positives of the test). However, each of these imaging modalities has drawbacks and pitfalls, leading to the late diagnosis of PDAC and necessitating the need for optimizing these modalities or combining them together instead of relying on a single modality.

The paper first reviews some of the most common imaging modalities deployed in the detection and diagnosis of pancreatic cancer, providing a comparative analysis of their test characteristics, i.e. sensitivity, specificity, and accuracy. It then focuses on the superior diagnostic capabilities of endoscopic ultrasound (EUS) and its subtypes, ultimately arguing for exploring a combination approach of EUS techniques as the most promising path toward developing an optimal, cost-effective, and easy-to-deploy strategy for the early identification of PDAC.

REVIEW METHODOLOGY

This narrative review was conducted to synthesize and discuss the current literature available on PDAC, and existing imaging modalities used to diagnose it. A structured literature search was conducted, where both recent and foundational studies on PDAC and pancreatic cancer were reviewed and analyzed with specific focus on imaging modalities and novel techniques for diagnosis of PDAC. Relevant articles were identified through searches of databases like PubMed Central, Google Scholar, and some other cancer related journals and websites, with emphasis on peer reviewed articles from National Institute of Health and National Library of Medicine. Search terms included 'pancreatic ductal adenocarcinoma' 'PDAC', 'early detection of PDAC', 'PDAC and imaging modalities', 'computed tomography and PDAC', 'CT and PDAC', 'magnetic resonance imaging and PDAC', 'MRI and PDAC' 'endoscopic ultrasound and PDAC', 'EUS and PDAC', 'novel cancer detection techniques', 'application of artificial intelligence in PDAC', 'sensitivity, specificity, and accuracy for PDAC modalities', etc. The selection focus was on peer reviewed journals, and papers specifically discussing PDAC, diagnostic accuracy, limitations, and technical advancements in PDAC detection and early detection. The gathered literature was synthesized using a critical appraisal approach. Existing modalities (CT, MRI, EUS) were first evaluated for their sensitivity, specificity, and accuracy, in detecting early-stage lesions. These findings were then contrasted with identified clinical and technical limitations. Further deeper review and analysis was then conducted on the modalities and techniques that showed promise, to eventually provide a rationale to further explore the proposed combined and novel techniques.

REVIEW AND COMPARATIVE ANALYSIS OF COMMON IMAGING MODALITIES

Computed Tomography (CT)

A CT scan uses X-rays and computer image processing to create cross-sectional images of the body [7,8]. A special contrast agent (dye) is administered to make soft tissues, blood vessels, and tumors more distinct and visible. It is particularly useful in visualizing and creating 3D images of the internal organs of the body, which is helpful in case of pancreatic cancer, especially in determining if the cancer has spread to the lymph nodes and other organs. CT scans are less invasive than some of the other imaging techniques, so they are relatively easy to perform. CT scans also lead to relatively lower radiation exposure per scan as compared to some of the other imaging techniques, but the advantage is counterbalanced as typically multiple different scans are needed to put together the final image and diagnosis.

Limitations of CT scan for PDAC

While CT scans are the primary tool for diagnosing and staging pancreatic cancer, they have several critical limitations that can impact early detection and surgical planning. CT scans frequently miss early-stage tumors. Approximately 27% to 40% of tumors smaller than 2 cm are missed on standard abdominal CT scans [9]. For tumors less than 1.5 cm, CT scans sensitivity has been reported to be as low as 67% [10]. This could be for several reasons, for example, about 5% to 14% of pancreatic cancers are 'isoattenuating' [11], meaning they have the same density as normal pancreatic tissue. These lesions are invisible on CT unless secondary signs such as ductal dilation or glandular atrophy are present. Secondly,

routine abdominal CTs often use a single-phase protocol, which is less effective than a dedicated pancreatic protocol CT or multiphase imaging for highlighting the differences between a tumor and healthy tissue. And lastly, CT cannot reliably distinguish benign from malignant lymph nodes based on size alone. Its sensitivity for identifying lymph node involvement is reported as low as 37% [12]. In addition to above, since CT scans also involve ionizing radiation, and the iodinated contrast material required for high-quality scans carries a risk of kidney damage (nephrotoxicity). This limits their use for frequent surveillance and cannot be used in patients with severe renal failure or allergies.

Magnetic Resonance Imaging (MRI)

In the MRI technology, the scanner generates strong magnetic and radio-frequency fields that are used to generate comprehensive images of tissues [6,7]. A coil is placed around the abdomen to transmit strong magnetic and radio waves that align with hydrogen atoms in your body. The radio waves temporarily knock these hydrogen atoms out of alignment, and as these atoms fall back in line, they emit signals that are used to create detailed images of the body's internal structure. MRI imaging could be of type T1-Weighted, where normal pancreatic tissue appears bright, whereas cancerous cells appear darker, creating a contrast to detect the tumor, or it could be of type DWI (Diffusion Weighted Imaging), where movement of water molecules is tracked, and since cancerous cells are highly cellular, they restrict water movement, and hence light up in the scans. Typically, doctors prefer CT scans to MRIs for the pancreas, but MRI is generally better than CT for early detection in many cases. For example: some early tumors that may be invisible under CT scan because of isoattenuating structure, could be revealed by MRI due to the superior soft-tissue resolution of MRI. MRI is also superior to CT in detecting cystic lesions early on, which may have the potential to eventually become cancer. MRIs also don't have high radiation risks, which come along with CT due to ionizing radiation.

Limitations of MRI for PDAC

That said, MRI still has many limitations. First, performing MRI scans take longer than CT scans, which can lead to inaccuracies due breathing movements, bowel activity, etc. that can blur the images, potentially hiding small lesions. Secondly, MRI can sometimes underestimate how much the tumor has spread to blood vessels or lymph nodes, which is very important for planning surgeries. More importantly, MRIs can confuse the dark spots from T1-weighted images as cancer vs. chronic pancreatitis and vice versa, which makes it difficult to distinguish the cancer. Finally, the MRI scanning procedure takes a lot longer than CT, which is relatively easier to use.

Positron Emission Tomography (PET)

Positron Emission Tomography (PET) detects pancreatic cancer by identifying areas of high glucose metabolism [6,7]. So, PET technology is used to measure metabolic activity as opposed to physical structural changes to detect cancer. PET is typically used to track the progression of the disease, but its success in the initial detection of pancreatic cancer has been found to be limited. This is due to several technical and biological limitations. .

Limitations of PET for PDAC

Since PET is mainly focused on measuring metabolic activity instead of physical changes, it provides lower spatial resolution images as compared to MET, CT, US, etc. which lack the necessary detail to pinpoint the exact location and boundaries of the tumor and make it difficult to see if the tumor has invaded blood vessels or not. In addition, PET scans use a radioactive sugar called FDG, which typically accumulates in the area of high energy use. Inflamed pancreatitis tissues also consume sugar rapidly, which can cause it to light up like cancer, thus generating high false positives and leading to potential misdiagnosis. Lastly, because PET scans rely on glucose analogs, high blood sugar and diabetes can also interfere with the results.

Comparative Summary of Different Imaging Modalities

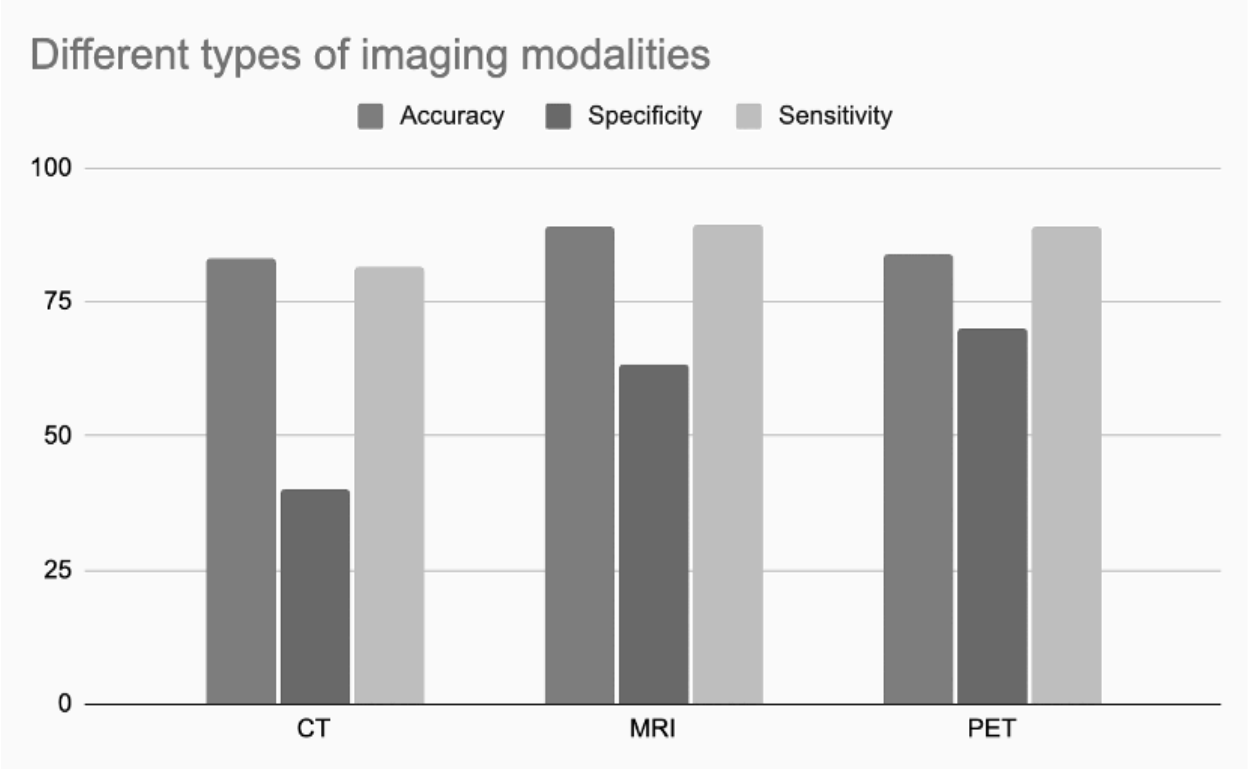
The table (Table 1) below summarizes the pros and cons of each technology along with their performance on various test characteristics. The 'sensitivity' measures how easily the modality could detect tumors, the 'specificity' measures how good the modality is at identifying the perfect negative diagnosis, and finally, the 'accuracy' judges the proportion of the false and true negatives/positives of the test [13]. Compared to ultrasound and its subtypes, discussed in the next sections, the rates for CT, MRI, and PET are much lower (Figure 1).

Table 1: Comparative Summary of Common Imaging Modalities used for PDAC

Modality	**Pros**	**Limitations**	**SE/SP/A**
CT	Non-invasive Global vein image with high spatial resolution Lower cost	Exposure to ionizing radiation Lack of real-time information Difficulties identifying intraluminal abnormalities. Requires contrast, may cause allergies/toxicity Has inferior soft tissue contrast resolution.	SE - 81.4% SP -40-50% A - 83.3%

MRI	Non-invasive Radiation-free High resolution Operator independent.	Limited sensitivity Extensive scan Post-processing durations Large probe need No real-time information Difficulties identifying intra-luminal abnormalities.	SE - 89.5% SP - 63.4% A - 89.1%
PET	Non-invasive Real-time information Detect aberrant metabolic activity Identifies small lesions Determines metastasis Measures cancer therapy efficacy Beneficial over CT & MRI in certain cases - detects metabolic changes at cellular levels.	Exposure to ionizing radiation	SE - 89% SP - 70% A - 84%

Figure 1: Test Characteristics of Key Imaging Modalities for PDAC



Ultrasonography and Its Subtypes for Pancreatic Cancer Detection

Ultrasound is another commonly used imaging modality for the diagnosis of PDAC. Ultrasonography (US) is the pivotal imaging technique as of 2025. A transducer or probe is used to send sound waves into the body, which reflect off tissues, organs, blood flow, tumors, and other structures, and a software then listens for echoes to form the images, called sonograms, based on the time and intensity of the echoes. These images are then analyzed and compared to detect tumors.

Standard Ultrasound is the most common US imaging modality. It is typically performed in a radiology lab with full-sized systems to detect abnormalities, as opposed to the portable units. Some advantages of ultrasound include that it is non-invasive, enables real-time scanning, emits non-ionizing radiation, and is easy to perform. Certain specific subtypes of US have proven to be superior as compared to MRI, CT, and PET scans [8]. The specificity, sensitivity, and accuracy of all the US sub-types stay relatively near 60-90%, 85%-98%, and 70%-94%, respectively [14,15,16] across all. Across all the US sub-types, Endoscopic ultrasonography (EUS), has been the most successful and most widely used technique for diagnosing PDAC. Some of the most common and modern modalities of EUS include conventional EUS, contrast-enhanced EUS (CE-EUS), EUS elastography, and EUS fine-needle aspiration (EUS-FNA) [16] that are discussed below in more detail.

Conventional EUS

Conventional Endoscopic ultrasound (EUS) has emerged as an invaluable tool for the diagnosis, staging, and treatment of PDAC. It combines two different techniques, endoscopy and ultrasound, to diagnose diseases and abnormalities, especially around the gastrointestinal tract and nearby organs and tissues such as the bile ducts, pancreas, lymph nodes, etc. EUS provides a detailed and high-resolution spatial imaging of the pancreas compared with CT or MRI through the addition of an ultrasound transducer on the tip of the flexible endoscope. Since EUS uses endoscopy to create the images from inside, it is minimally invasive, but not completely non-invasive. EUS also has an added advantage that it delivers high-resolution imaging along with magnification even for small pancreatic masses and cysts due to proximity of EUS transducer to the pancreas by positioning the transducer in the gastro-esophageal junction, bulb and second portion of the duodenum, and by eliminating the effect of intestinal gas and fat. The two main categories of EUS are Linear EUS (L-EUS) and Radial EUS (R-EUS) and each have their own respective advantages: Linear EUS performs imaging in the same plane as the shaft of the endoscope, whereas with radial EUS, circumferential viewing can be obtained in the plane perpendicular to the shaft of the endoscope. The L-EUS probes are more suitable for FNA as compared to R-EUS as L-EUS narrower sector longitudinal imaging is important to allow real-time tracking of a puncture needle, which is crucial for EUS-guided interventions. Due to this, L-EUS offers superior sensitivity (91-100%), especially for detecting small (<2 cm) lesions as compared to CT scans [17]. It also provides real-time, high-resolution imaging and guide fine-needle aspiration (FNA/FNB) to sample tumors. Linear EUS typically reveals PDAC as a heterogeneous hypoechoic, solid, irregular mass.

R-EUS is superior when it comes to mapping anatomy, staging gastrointestinal tumors, and evaluating structural integrity. R-EUS probes are generally considered unsuitable for fine-need aspiration (FNA) applications as based on some studies when R-EUS is used for FNA, it may miss pancreatic lesions (up to 33% miss rate in some studies) more frequently than linear EUS (17.5% miss rate [18]).

EUS is currently the most sensitive imaging modality for detecting solid pancreatic tumors. Conventional EUS has evolved, and new imaging techniques, such as contrast-enhanced harmonics and elastography, have been developed to improve diagnostic accuracy while evaluating focal pancreatic lesions.

Contrast Enhanced EUS

To improve the image resolution and quality, Contrast-Enhanced EUS (CE-EUS) combines the high-resolution images of internal organs from the US with the administration of ultrasound contrast agents (UCAs), which improves the visibility of tissues, organs, and blood flow during the scan. 8. Contrast agents are made from gas-filled microbubbles that are 2-5 μm in diameter encapsulated by phospholipid/liquid shells, which are then administered through a peripheral vein. The microbubbles receive the ultrasound waves, producing the signal.

When it comes to PDAC, CE EUS allows for the characterization, differential diagnosis, and accurate staging of pancreatic lesions. CE EUS has also been shown to perform better compared to conventional EUS in characterizing vascular invasion by mass lesions. After contrast injection, portal vein borders can

be delineated better, resulting in higher accuracy compared to that of conventional EUS or CT scans. On CE EUS, lymph nodes can also be examined for enhancement patterns, with malignant lymph nodes showing a heterogeneous enhancement pattern compared to benign lymph nodes. A recent meta-analysis has shown pooled sensitivity and specificity of 91% and 86%, respectively, in the diagnosis of PDAC.[19] Apart from its diagnostic role, CE EUS also helps in the selection of the target area for EUS-guided FNA. In a recent meta-analysis involving six studies and 701 patients, the pooled sensitivity of CE EUS-guided FNA was higher than that of EUS-guided FNA (84.6% vs. 75.3%; $p < 0.001$) [20]. However, in a recent randomized trial comparing CE EUS-guided FNB and conventional FNB with fanning techniques, both arms had a similar diagnostic accuracy with similar requirements for the median number of passes [21]. So, with the advent of newer EUS FNB (fine-needle biopsy) needles, the routine use of CE EUS before EUS tissue acquisition (EUS TA) remains questionable. Given that CE-EUS-FNA does not have a significantly better accuracy or sensitivity than standard FNA, it typically finds its primary applications for identifying optimal needle paths in complex cases such as suspected vasculatures, difficult locations, or previous inconclusive FNAs.

EUS elastography

EUS-guided Elastography is an imaging modality that is used to differentiate malignant pancreatic tissues vs. benign tissues by evaluating tissue stiffness or elasticity in real time. Malignant pancreatic tissue, such as PDAC, is typically found to be more stiff or harder than the normal, inflamed, or benign pancreatic tissue due to increased fibrosis and desmoplasia. When the EUS probe applies pressure to the tissue by using vascular pulsation/respiration, it presses/strains the tissue with the pressure. This tissue strain or deformation is then measured and analyzed with the help of software to determine if the tissue is benign or malignant. EUS is typically used to characterize pancreatic masses and lymph node metastases of pancreatic cancer, as well as to judge the severity of chronic pancreatitis with evaluation of lesion elasticity.

There are two types of EUS elastography Strain Elastography (SE) and Shear Wave Elastography (SWE), both of which measure or estimate stiffness of the target issue to distinguish between cancerous and non-cancerous tissues EUS Elastography was first reported in 2006, and it is typically used to distinguish PDAC from chronic pancreatitis. It is also used for targeted biopsies by employing EUS elastography to identify the hardest areas and then using FNA to collect the samples in those targeted areas. EUS elastography has shown high sensitivity (above 90% in many cases), but the specificity is typically variable and in the range 67%-76% [22]. It usually requires further confirmation with the use of EUS-FNA/FNB.

EUS-FNA (Fine-Needle Aspiration) [23]

In addition to getting high-resolution and more accurate images in real-time, Endoscopic ultrasound-guided fine-needle aspiration (EUS-FNA) combines ultrasound and endoscopy along with a very fine needle at the tip used to obtain tissue or fluid samples from deep-seated organs like the pancreas, lymph nodes, or digestive tract lining. EUS-FNA was first reported in 1992 and has been used since then. EUS-FNA is used to acquire tissue from mucosal/ submucosal tumors, as well as peri-intestinal structures including lymph nodes, pancreas, adrenal gland, gallbladder, bile duct, liver, kidney, lung, etc.[24] Based

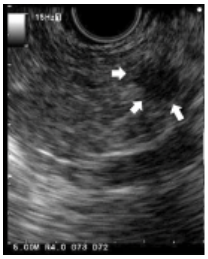
on the published literature, the pancreas and lymph nodes (intra-thoracic and intra-abdominal) are the most common organs targeted in EUS-FNA

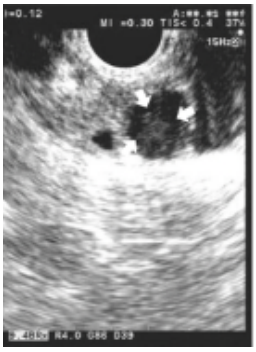
Typically, 19G-25G caliber needles are inserted under EUS guidance, The needle scouts for pancreatic cancer, lymph nodes, and/or hepatic metastatic pancreatic cancer.

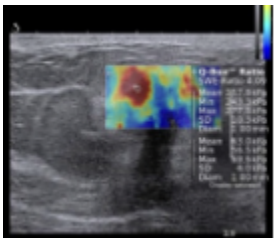
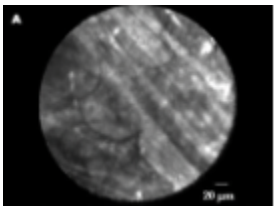
EUS-FNA has become an important method of diagnosing pancreatic tumors, especially for small tumors or early diagnosis, due to its high safety, cost-effectiveness and accuracy. EUS-FNA demonstrates high sensitivity for histological diagnosis (75–94%) and a specificity approaching 100% in majority of the studies. However, false-negative, atypical and suspicious cytopathological diagnoses remain relatively frequent.

EUS-FNA has been proven highly accurate in detecting very small pancreatic lesions (<2 mm) that might be missed by other imaging modalities such as CT and MRI. It also helps in determining resectability, by evaluating local tumor spread and lymph node involvement. EUS-FNA also provides a more definite, pre-operative diagnosis, which is necessary before starting neoadjuvant chemotherapy. The samples obtained via EUS-FNA/FNB are used for next-generation sequencing (NSG) to identify actionable genetic mutations and guided personal therapy. And lastly, EUS-FNA is used for diagnosing both solid masses and cystic lesions, often preventing the need for more invasive diagnostic surgeries.

Table 2: Comparative Summary of EUS sub-types

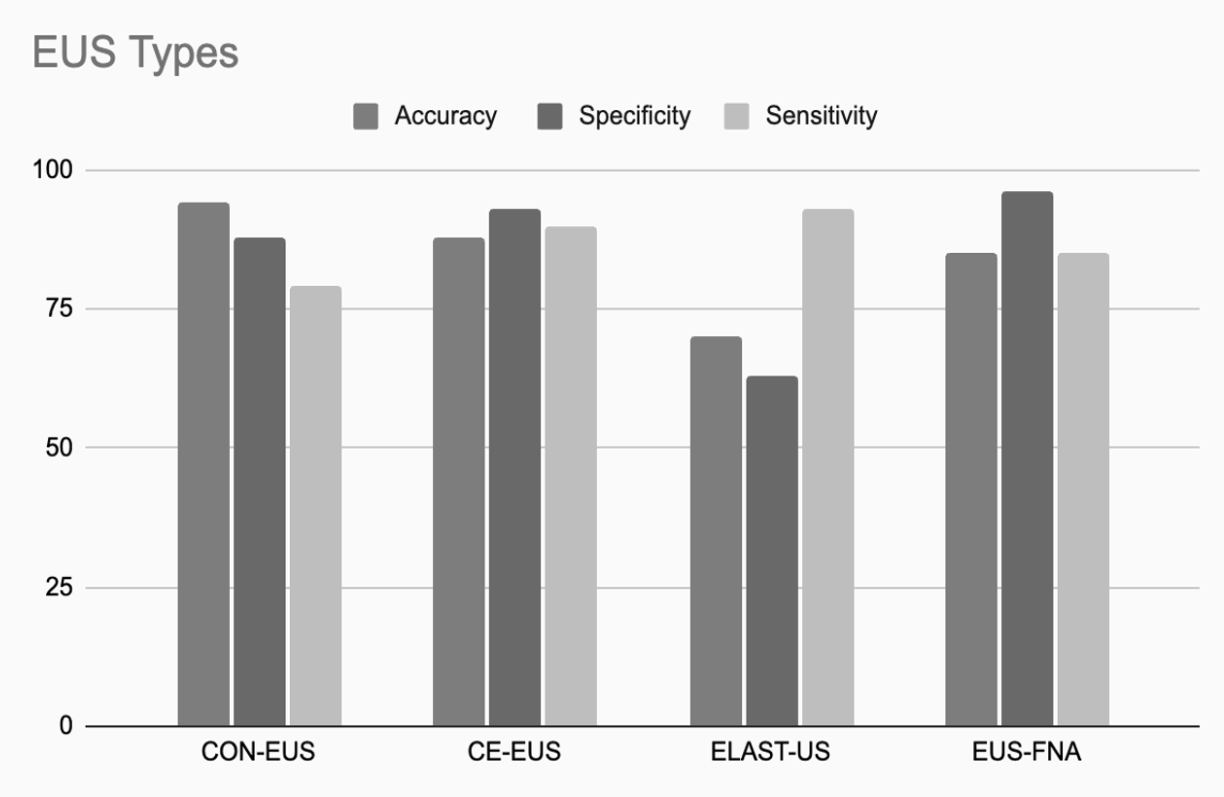
US Type	Pros	Cons	Sensitivity, Specificity, & Accuracy	Imaging photos
Conventional EUS [8]	EUS has better spatial & time resolution opposed to the other imaging methods. Plays an important role in detection of small lesions and characterization of cystic lesions. Highest sensitivity for detecting pancreatic cancer especially for tumors from 20-30 mm. Superior to CT, MRI, and transabdominal for small lesion detection. The imaging technique is able to provide real-time imaging unaffected by bowel gas	Low specificity for distinguishing benign vs. malignant tumors. It heavily depends on the operator's skills in handling the machine. Can't detect non-massing forming cancer. Provides no tissue diagnosis.	Sensitivity = 94% (79%-100%) Specificity = 88%-89% Accuracy = 94%	

	Can evaluate ductal changes, cyst morphology, and parenchymal texture. No radiation exposure.			
CE-EUS (Contrast-Enhanced) [15]	Critical for characterization of solid/cystic lesions and the staging of pancreatic cancer with evaluation of lesion vascularity. Lesion vascularity - An abnormal growth or malformation of blood vessels. High specificity for identifying malignancy. Guides FNA targeting and reduces sample errors.	Also heavily dependent on the operator. Requires contrast agents and special equipment. Interpretation is harder in severely affected pancreas.	Sensitivity = 90%- 94% Specificity = 93% Accuracy = 88%-97%	

EUS elastography [14,25]	Can be coupled with conventional EUS with no additional devices. High sensitivity for detecting malignancy. Useful for differentiating hard cancers from the surrounding tissues.	Strain elastography is much more available, shear is extremely advanced. No reports for T-staging, R-staging, or N-staging of pancreatic cancer. No significant data on detection of cystic lesions/	Sensitivity = 93%- 99% Specificity = 63%-67% Accuracy = 70%-90%	
EUS-FNA (fine-needle aspiration) [26,27]	Superior to other methods in terms of tissue acquisition and safety. High sensitivity and specificity Delivers tissue diagnosis.	Overall complication rate is 0.82%, including complications such as: -0.38% stemming from pain -0.10% from bleeding -0.4% pancreatitis. Not useful for non-mass forming cancer.	Sensitivity = 85%- 92% Specificity = 96%-98% Accuracy = 85%-92%	

		Also depends heavily on operator skills. False negatives are common.		

Figure 2: Test Characteristics Comparison of Various EUS Sub-types



CRITICAL ANALYSIS OF EXISTING MODALITIES AND MAKING A CASE FOR COMBINATION TECHNIQUES

Due to the limitations of the existing imaging modalities, none of the existing modalities are ideal for early diagnosis of PDAC. While EUS has some limitations [Table 2] such as reduced accuracy for very small tumors, false negatives due to fibrosis capture in FNA samples, and lack of ROSE (Rapid On Site Evaluation) leading to reduced sensitivity, EUS-FNA/FNB superiority over other imaging modalities still makes it the most promising candidate to be further explored and combined with other imaging and non-imaging techniques to improve early detection of PDAC. CT scan, while cheap and easily accessible [Table 1], has not been very effective for early stage detection due to low specificity and accuracy [Figure 1] and low specificity, especially for early stage small lesions under 1cm. Because they are isoattenuating at an early stage, it is hard to distinguish between cancerous and non-cancerous tissues, which leads to low accuracy. While CT has an advantage to be non-invasive, early-stage cancers are hidden deep inside the body, which makes it difficult to be detected by CT. Given this, multiple CT scans are typically required just to detect the tumor, while still having low accuracy, which can lead to high costs, risks of overexposure to radiation, and patient anxiety. Even after that, due to the low accuracy and specificity [Figure 1], there may be a need for further invasive procedures, which makes CT a less viable technique for early diagnosis of PDAC. While MRI is superior to CT due to its ability to provide high contrast resolution for soft tissue and thus identifying the tissues that may appear isoattenuating or isodense in CT scan, it still has several limitations like high sensitivity to even minute respiratory motions, which can

degrade the image quality and even mask or blur the tumor, making it hard to detect. MRI also has a very high false positive rate, wherein it can identify small cystic benign lesions also as tumors, leading to low specificity, and potentially require further follow-ups and lead to patient anxiety. MRI is also significantly time consuming and costly, making it less efficient for rapid screening. Another common imaging modality, PET, has its own set of limitations, due to the fact that it relies on metabolic changes, as opposed to physical changes in tissues. For very small tumors, common during early stages, PET's spatial resolution is even less reliable to CT or MRI. Given that PET relies on metabolic changes, PET can lead to both a high number of false negatives and false positives, because due to high blood sugar levels, which is very common in PDAC cancer patients, tumors may not take enough FDG tracer, leading to false negatives. On the other hand, the non-cancerous immune cells can take up FDG, leading to the non-cancerous pancreatic tissues to look like hyper metabolic cancer tissues resulting in false positives. Certain specific pancreatic tumors, such as mucinous and highly necrotic tumors may not show up on PET due to low metabolic activity. And lastly, since PET does not rely on physical changes, it does not provide fine anatomical details that may be required to determine surgical resectability. All these factors along with the cost, and implementation or procedural complexities of PET [Table 1] may reduce PET's suitability as the stand-alone modality for early detection of PDAC.

While EUS has its own limitations, it addresses many of the limitations of CT, MRI, and PET discussed above, making it a potential candidate to explore combining it with other modalities and techniques for early detection. As US probes are placed in stomach or duodenum, right next to pancreas, EUS can capture superior high-resolution images of the inside of the digestive tract, detecting even small tumors (2-5 mm) that are often missed by cross sectional imaging of CT or MRI. EUS is also superior at visualizing and distinguishing isoattenuating tumors that are generally invisible in CT and MRI scans. This leads to EUS having superior sensitivity (~94%) as compared to CT and MRI. Not all the EUS sub-types are equally effective. CON-EUS has relatively low sensitivity, and EUS Elastography (EUS-Elast), while having superior sensitivity, struggles with specificity [Figure 2]. In addition, EUS-Elast is not very effective in distinguishing the cancer from chronic pancreatitis (specifically mass-forming pancreatitis) or some neuroendocrine tumors, as they can also appear stiff (hard) on elastography. EUS- Elast has relatively high operator dependency, requiring high skill for very specific manual pressure application by the operator, and can also lead to false signals due to respiratory interference, which can make analyzing the images difficult. Eventually EUS- Elast and CON-EUS, still require tissue samples to be definite. Given that tissue samples are required in most cases to be definite, EUS-FNA and FNB being only EUS techniques that allow for taking the tissue samples, providing a definitive cytological and histological diagnosis that cannot be obtained by imaging alone.

COMBINING IMAGING MODALITIES

Although each of the EUS types discussed above have their own merits, when it comes to early detection of PDAC, none of them is optimal across all test characteristics of sensitivity, specificity, and accuracy. Hence, some combination of screening methods may be the most optimal form of diagnosis. Extensive research has been going on this topic not just combining various imaging technologies, but also sometimes combining imaging modalities with other techniques, such as combining biomarkers with

classic imaging modalities [28].

Given high scores on all test characteristics, EUS-FNA makes a great candidate for early detection for PDAC, but it has some areas where it falls short. For example: EUS-FNA has not been very successful in distinguishing between cancer and non-cancer cells. So, if the drawbacks can be addressed by combining EUS-FNA with other imaging techniques, a potentially optimal diagnosis can be achieved. Combination imaging ideas that may have potential and can be further explored include EUS-FNA + CE-EUS, EUS-Elastography + EUS-FNA, and EUS-Elastography + CE-EUS.

EUS-FNA + CE-EUS: To start with combining EUS-FNA with CE-EUS should be further explored, because it fills a critical gap: its ability to differentiate malignancy from benign lesions based on vascularity complements EUS-FNA, which often falls short in cases of acute/chronic pancreatitis. CE-EUS may have shown lower specificity compared to its accuracy and sensitivity, yet is strong when it comes to differentiating malignancy from benign based on the lesion vascularity or pancreatitis [29,30, Figure 2]. On the other hand, EUS-FNA is a prominent imaging modality that has relatively high specificity, sensitivity, and accuracy; specificity being its highest aspect. but it falls short when it comes to patients with acute/chronic pancreatitis and fails to identify infiltrating adenocarcinomas in the pancreas [31]. CE-EUS is found to greatly complement EUS-FNA as it fills the gap that EUS-FNA has when it comes to differentiating between lesions. The contrast agents in CE-EUS are able to further observe the lesion, allowing for EUS-FNA to correctly identify said lesion [32,33]. When used together, they are able to easily identify harmful lesions, identify lesion vascularity, have relatively high sensitivity, specificity, and accuracy, and are able to differentiate malignancy.

EUS-FNA + EUS elastography: Secondly, a combination of EUS elastography and EUS-FNA could have merits as well. EUS elastography, compared to other EUS techniques, is relatively new, resulting in low specificity and accuracy, but very high sensitivity. So combining EUS-elastography with EUS-FNA, which has high specificity and accuracy, yet it has low sensitivity; can result in a combination that would be optimal [34, Figure. 2]. EUS elastography can identify lesions and more thoroughly check the consistency of tissues surrounding the affected area, and using fine needles would allow this to be much more specific [35]. EUS elastography is typically much more optimal for non-mass forming cancers than EUS-FNA is, and EUS-FNA has a high chance of false negatives, which can be balanced out by EUS elastography's low chance for this [36]. Based on tests, these two imaging methods combined allow for little to no distortion in images, as well as, making it easier to target the harder tissues [37]. Though it has been shown that EUS elastography is better at remaining a tool for malignancy diagnosis and may even be a better pairing with modalities like MRI, rather than being used with FNA [38,39]. But as previously discussed, EUS elastography is relatively new and is still being figured out, allowing for much open to interpretation.

EUS-FNA + EUS+FNB: Additionally, the combined use of EUS-FNA and EUS-FNB could be explored further, as the two techniques may offer complementary diagnostic outcomes as well. EUS-FNB is a fine needle biopsy that analyzes tissue samples to search for non-mass forming lesions or cancerous signs [40]. The combination should be explored because EUS-FNA is an advanced imaging method, though it's unable to have precise molecular profiling. This is shown through the lack of identifying certain

lymphomas/cells such as stroma lymphoma; mostly due to the fact that some tissues are much too complex to be able to identify without testing [41,42]. This is where EUS-FNB can complement EUS-FNA in combination screening. Several tests are done to pit EUS-FNB and EUS-FNA against each other, however many reviews of clinical trials suggest that, although FNB often is shown to have a higher diagnostic accuracy, it's rarely by a marginal difference that would prove FNA to be inferior [43]. In Mavrogenis et al. there's a test between EUS-FNA and EUS-FNB through usage of a 25-gauge histology (EUS-FNA) needle vs. a 22-gauge cytology (EUS-FNB) needle. In conclusions, the authors state that the needles shared similar results, with a high diagnostic yield [44]. But in this paper, we learn that the combination of EUS-FNB and EUS-FNA can combine histology with cytology providing for far more accurate and advanced results. Though, as mentioned previously, FNB always had an upside towards FNA, seen especially in its sensitivity and specificity, for lesions ranging from peri-hepatic and abdominal lymph nodes [45]. However, FNB and an FNA combination treatment has not been fully explored but is rather being inspected as of recent times. Though its potential is immense since it fixes the weaknesses of an already advanced FNA, which could allow for earlier diagnosis.

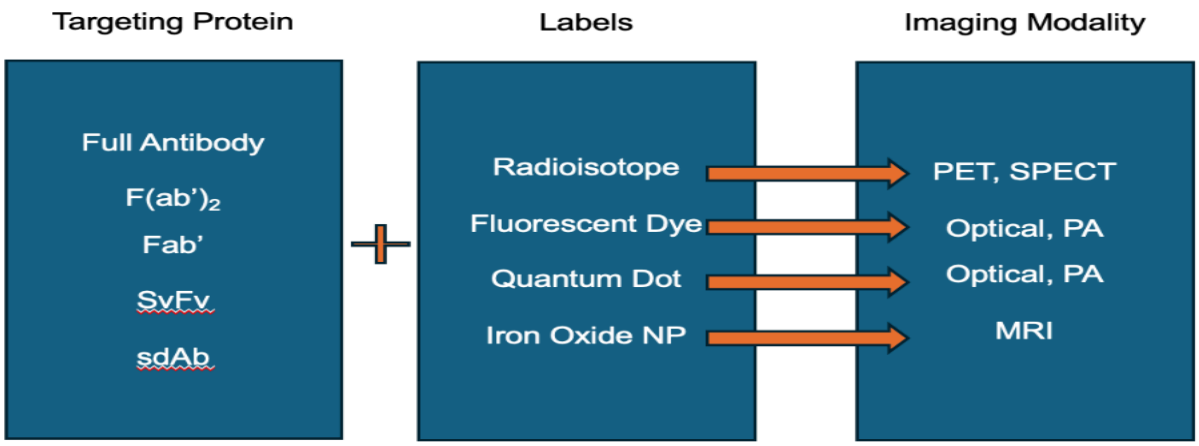
New imaging methods

While conventional imaging modalities and their combination are important tools in diagnosing PDAC today, they are not sufficient and are especially not very effective for early detection as they are mostly anatomical in the sense that they rely on mass effect, ductal dilation, and tissue density etc. These changes are not very efficient in early detection of PDAC as by the time lesion can be seen or detected, the tumor is already often grown >2 cm and micro metastatic spread may have already begun, which renders the treatment too late. So, there is room for much improvement due to this poor prognosis and asymptomatic activities of PDAC until later stages [46]. Hence, some of the new and emerging imaging technologies should be explored to leverage their inherent advantages such as detecting biology before the structural changes begin to appear, extracting several quantitative metrics and data points from these images, while the structural changes are still invisible to human eyes, and lastly helping eliminate some of the false positive scenarios.

Molecular & Targeted Imaging

To overcome these limitations of traditional imaging modalities when it comes to early detection of PDAC, several new techniques including molecular or targeted imaging modalities are being explored. Molecular or targeted imaging leverages the fact that the tumor cells produce certain specific antigens as compared to non-cancerous tissues, and since cancerous malignancies express atypical patterns of cell surface proteins in comparison to noncancerous tissues, novel antibody-based imaging agents can be constructed to target individual cancer cells or surrounding vasculature. These antigens can then act as markers for antibody- or peptide-based probes (e.g. integrins, EGFR, mesothelin) that are specially designed to lock on these biomarkers. (Figure 3)

Figure 3: Antibody based Antigens



These probes act like targeted scanners that bind these tumor cells thus making them visible during imaging or detect them in the blood as cancer signatures, thus potentially enabling earlier or more precise diagnosis. Typically, these probes can be attached to imaging agents (like radioactive tracers or fluorescent dyes) and injected into the body. They travel through the bloodstream, bind specifically to pancreatic cancer cells, and light up the tumor during scans (e.g., PET or fluorescence imaging), distinguishing it from healthy tissue. Currently, there are several imaging modalities commonly employed for molecular imaging. These imaging modalities include PET, single-photon emission computed tomography (SPECT), MRI, optical imaging (fluorescence and bioluminescence), and photoacoustic (PA) imaging. [47]

These methods generally offer higher sensitivity for early detection compared to conventional imaging and blood tests, reducing false negatives and enabling earlier intervention.

Novel PET Tracer

Several novel PET tracers are being studied/investigated lately due to their higher sensitivity and their ability to detect tumors earlier. Novel PET tracers are newly developed radioactive dyes that are injected into the body in very small quantities during a PET scan. They act as bio-markers by attaching to specific molecules within the body, such as sugar, proteins, or receptors, etc. By attaching to target molecules, these tracers accumulate in the area of interest and light up in the PET scan thus helping identify the tumor more effectively. Fluorodeoxyglucose (FDG) is one of the most common tracers used in PET scans. It tracks how cells in the body are being used, which can give an indication of various cancers.

When it comes to PDAC, in addition to FDG, several new tracers such as FLT-PET, FMISO / FASA, and FAPI-PET (Fibroblast Activation Protein Inhibitors-PET), etc. have been reviewed. These novel PET tracers, just like FDG, not only have higher sensitivity due their ability in identifying small tumors and metastases that are often missed by CT scans but also have improved accuracy with higher tumor-to-background ratios compared to FDG, reducing false negatives in early, small tumors. FAPI-PET

like 68-Ga-FAPI-46 or 68-Ga-FAPI-04 are surpassing traditional 18F-FDG, offering superior tumor-to-background ratios for detecting early-stage disease and metastases. This is due to the fact that FAPI-PET targets fibroblast activation protein, which is highly expressed in the cancer-associated fibroblasts (CAFs) that make up a large portion of PDAC's dense stromal microenvironment. In PDAC, these CAFs are abundant and relatively specific to tumor tissue, so FAPI tracers bind strongly to tumor-associated stroma but much less to most normal tissues, boosting contrast. Studies repeatedly show that FAPI tracers have higher SUV-max (uptake in tumor) than FDG in PDAC and lower background uptake in normal organs (e.g., liver), which enhances the detectability of small lesions and metastases. This leads to higher tumor-to-background ratios (TBR), which improves the visibility of tumors. In a total of seven studies, FAPI showed a higher sensitivity of 99% as compared to 84% sensitivity for FDG [48].
In addition to FAPI-PET and 18F-FDG, a couple of other common PET Tracers being studied, especially for PDAC, are FLT-PET and FMISO / FASA. FAPI-PET has proven to be more superior than those, as FAPI-PET has higher sensitivity as compared to FLT which has a lower sensitivity of 84%. FAPI also does a better job at reducing the background noise as it has very low uptake for the normal tissues, making the tumor cells stand out, whereas FLT has a high uptake of bone marrow and liver as well, which makes the images less clear and hard for tumor images to stand out. When it comes to FMISO/FAZA vs. FAPI-PET, FAPI-PET again turns out to be more superior as FMISO/FAZA relies on the hypoxia imaging technique, that is, it detects low oxygen areas inside tumors and generates images based on those low oxygen areas. Since it only tracks poor oxygen areas, as opposed to tumor stroma, it has lower sensitivity, as it may miss tumors that are not significantly hypoxic. Also, tumors FMISO/FAZA are slower to accumulate.

AI-Driven Imaging and PANDA CNN for PDAC

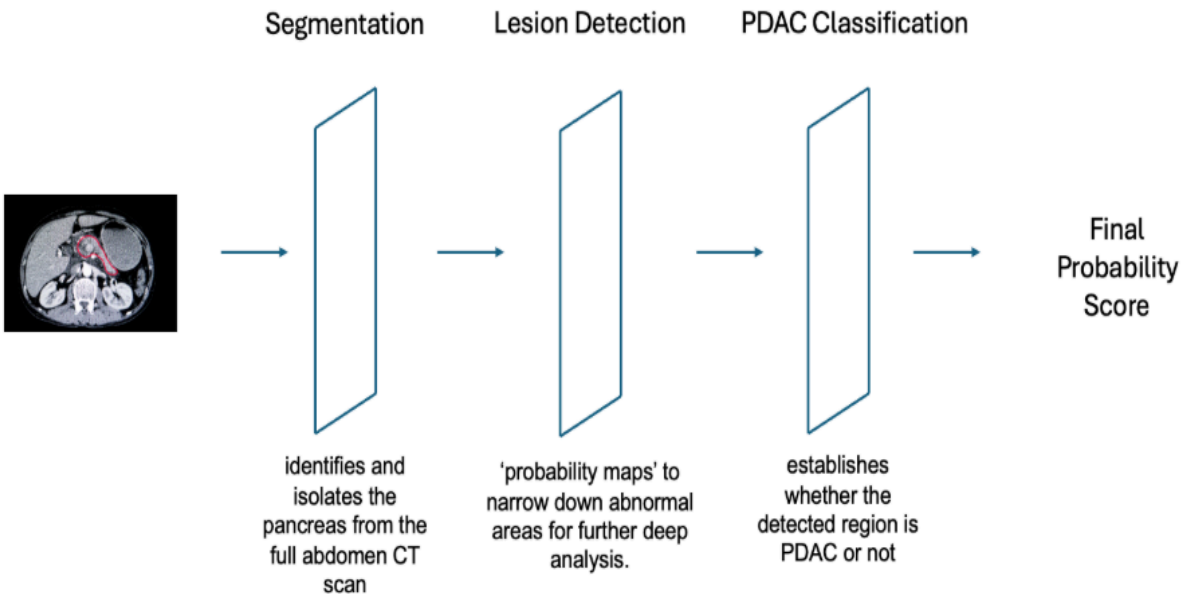
AI can be leveraged in multiple different ways when it comes to diagnosis of PDAC, including but not limited to improving imaging technologies and data for better scan analysis, tumor detection, and image classification, using deep learning models to integrate high dimensional molecular data such as genomics and proteomics to analyze blood-based markers like CA19-9 or cell-free DNA for subtle deviations from normal patterns to identify early PDAC signatures, EHR (Electronics Health Records) to detect risk patterns precursor to the onset of PDAC, or using of LLM models such as GPT-4, BioBert, ClinicalBert, PubMedBert, etc. for clinical notes analysis, and risk stratification from medical records etc.

While there is several AI applications as mentioned above, this paper and section focus only on reviewing the use of AI for imaging advancements towards early detection of PDAC. When it comes to the use of AI for 'detection' of PDAC, AI based Imaging models such as CNNs, ResNet, U-Net, and DenseNet, etc., are most commonly used. Among these, CNNs (Convolution Neural Networks) are currently dominating the research. A CNN is a deep learning model that analyzes visual images and learn to extract features like textures, shapes, edges, and other information using convolution layers. For early PDAC detection, CNNs analyze CT scans or endoscopic ultrasound (EUS) videos to identify subtle, early-stage tumors or tissue changes often missed by human eyes.

One of the common CNNs that has found success in early detection of PDAC is PANDA (Pancreatic Cancer Detection with Artificial Intelligence). PANDA is a multi-stage deep learning framework that heavily utilizes Convolutional Neural Networks (CNNs). PANDA is a three-stage system designed to

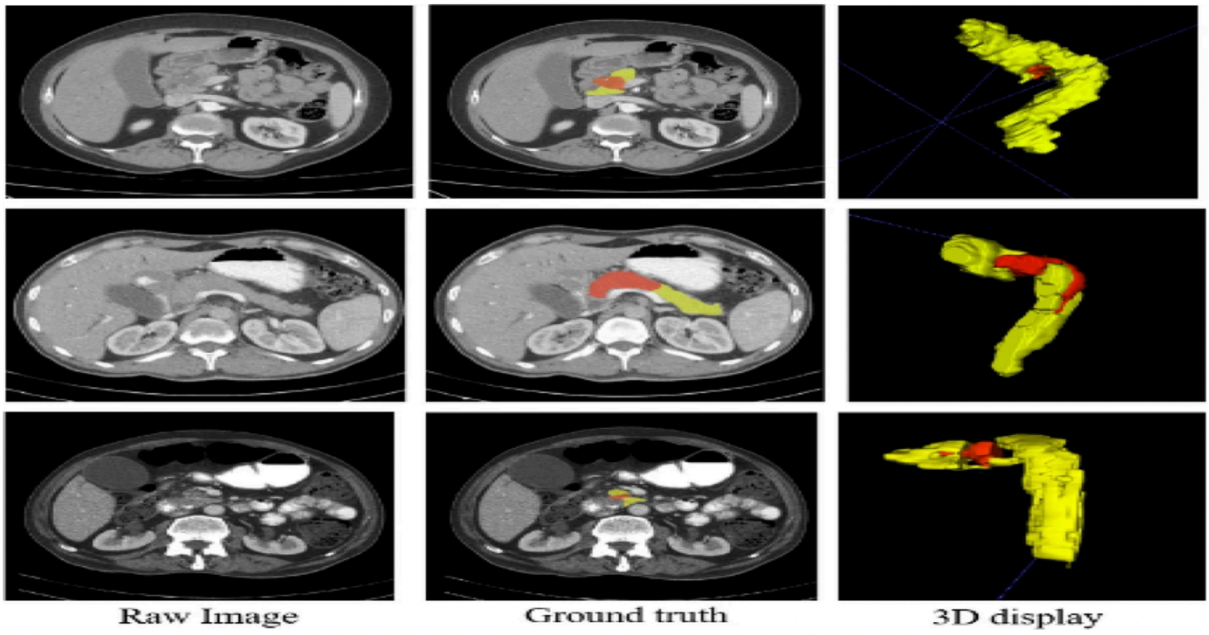
detect pancreatic cancer on non-contrast CT scans: Location, Detection, and Diagnosis [49].

Figure 4: A Simplified View of PANDA CNN for PDAC



Stage 1 is Pancreatic Localization, where the CNN system identifies and isolates the pancreas from the full abdomen CT scan using the segmentation model (typically U-net based). The output of this step is a 'pancreas mask' that removes irrelevant organs such as liver, stomach, spleen, etc. from the image, which helps reduce the search space and any false positives by ensuring the focus is only on the pancreatic tissue.

Figure 5: Segmentation of PDAC in CT scans [50]



Stage 2 is Lesion or Tumor detection, where a second deep learning CNN is applied to the isolated pancreas image in stage 1, to find textural, intensity, and structural abnormalities to identify potential PDAC lesions. The output of this state is 'probability maps' or 'bounding boxes' that narrow down abnormal areas identified for further deep analysis.

Stage 3 is PDAC classification, which establishes whether the detected region is PDAC or not. It does so by extracting high-level features and using a fully connected layer of binary classification of PDAC vs. non-PDAC to give a final probability score on whether the lesion is PDAC is not.

PANDA has demonstrated high sensitivity and specificity in detecting PDAC, outperforming average radiologist performance. The PANDA demonstrates high performance using non-contrast CT, with a reported sensitivity of 92.9% and specificity of 99.9% in a real-world, large-scale validation of over 20,000 cases, outperforming radiologists and showing significantly better results in identifying small lesions.

Some of the key performance metrics for the PANDA model include: [51]

- Sensitivity (Lesion Detection): 92.9% - 93.3%.
- Specificity (Lesion Detection): 98.8% - 99.9%.
- Performance vs. Radiologists: PANDA showed 34.1% higher sensitivity, and 6.3% higher specificity compared to the mean performance of radiologists.
- Small Lesion Sensitivity: 92.2% for T1 tumors.
- PDAC Detection Rate: 96.5% overall (95.6% for stage I).

CONCLUSION AND FUTURE DIRECTION

The paper analyzed various imaging modalities and their applications, diagnostic performance characteristics, and reasons for their varying success towards early detection of PDAC. Given the limitations identified in the existing imaging modalities, the paper proposes to further explore a combination of traditional and novel imaging, non-imaging modalities, and AI technology.

1. Among the various imaging modalities studied, Endoscopic Ultrasound (EUS), as a category, stood out as the most useful imaging technique for early PDAC diagnosis, given its relatively high sensitivity and specificity and overall success. While EUS and its sub-types demonstrated strong performance across these test parameters, its overall effectiveness across all three parameters varies across its subtypes. EUS-FNA is identified as potentially the most viable candidate to combine with other imaging and non-imaging techniques for further exploration towards early detection of PDAC. Various multimodal approaches, such as combining EUS-guided fine needle biopsy (EUS-FNB) with EUS-FNA, or FNA with contrast-enhanced EUS, or combining elastography with FNA, all present a significant opportunity and should be explored further. For example:
2. Combining EUS-FNB and EUS-FNA allows for both histologic and cytologic evaluation, thereby presenting an opportunity to enhance overall success for early detection.
3. Combining EUS-FNA with molecular imaging modalities such as novel PET tracer can also improve the overall success rate at early stages and should be explored further
4. Additionally, leveraging deep learning models such as CNNs (convolutional neural networks) and more specifically the PANDA CNN model for CT scans, has shown great success in the diagnosis of PDAC. In several studies, PANDA showed higher sensitivity for PDAC as compared to radiologists. This makes PANDA potentially a compelling candidate to explore its integration with EUS-FNA and FNB to further analyze the samples and improve the early detection.

Reference List

1. National Cancer Institute. “Cancer of the Pancreas - Cancer Stat Facts.” SEER, National Cancer Institute, 2024, seer.cancer.gov/statfacts/html/pancreas.html.
2. Niger, Monica, et al. “One Size Does Not Fit All for Pancreatic Cancers: A Review on Rare Histologies and Therapeutic Approaches.” *World Journal of Gastrointestinal Oncology*, vol. 12, no. 8, 15 Aug. 2020, pp. 833–849, www.ncbi.nlm.nih.gov/pmc/articles/PMC7443847/, https://doi.org/10.4251/wjgo.v12.i8.833.
3. Bartolini, Ilenia, et al. “Current Management of Pancreatic Neuroendocrine Tumors: From Demolitive Surgery to Observation.” *Gastroenterology Research and Practice*, vol. 2018, 22 July 2018, p. e9647247, www.hindawi.com/journals/grp/2018/9647247/, https://doi.org/10.1155/2018/9647247.
4. Kenner, B.J., Chari, S.T., Maitra, A., Srivastava, S., Cleeter, D.F., Go, V.L.W., Rothschild, L.J. and Goldberg, A.E. (2016). Early Detection of Pancreatic Cancer—a Defined Future Using Lessons From Other Cancers. *Pancreas*, 45(8), pp.1073–1079. doi:https://doi.org/10.1097/mpa.0000000000000701.

5. Ushio, J., Kanno, A., Ikeda, E., Ando, K., Nagai, H., Miwata, T., Kawasaki, Y., Tada, Y., Yokoyama, K., Numao, N., Tamada, K., Lefor, A.K. and Yamamoto, H. (2021). Pancreatic Ductal Adenocarcinoma: Epidemiology and Risk Factors. *Diagnostics*, [online] 11(3), p.562. doi:https://doi.org/10.3390/diagnostics11030562.
6. Costache, M.I., Costache, C.A., Dumitrescu, C.I., Tica, A.A., Popescu, M., Baluta, E.A., Anghel, A.C., Saftoiu, A. and Dumitrescu, D. (2017). Which Is the Best Imaging Method in Pancreatic Adenocarcinoma Diagnosis and Staging - CT, MRI or EUS? *Current Health Sciences Journal*, [online] 43(2), pp.132–136. doi:https://doi.org/10.12865/CHSJ.43.02.05.
7. Ahmad, I. and Fahad Alqurashi (2024). Early Cancer Detection Using Deep Learning and Medical Imaging: A Survey. *Critical Reviews in Oncology/Hematology*, 204(104528), pp.104528–104528. doi:https://doi.org/10.1016/j.critrevonc.2024.104528.
8. Costache, M.I., Costache, C.A., Dumitrescu, C.I., Tica, A.A., Popescu, M., Baluta, E.A., Anghel, A.C., Saftoiu, A. and Dumitrescu, D. (2017b). Which Is the Best Imaging Method in Pancreatic Adenocarcinoma Diagnosis and Staging - CT, MRI or EUS? *Current Health Sciences Journal*, [online] 43(2), pp.132–136. doi:https://doi.org/10.12865/CHSJ.43.02.05.
9. Claramae Shulyn Chia, Choon, L., Hennedige, T., Whee Sze Ong, Zhu, H., Hwei, G., Jin Wei Kwek, Chin Jin Seo, Si, J., Chin-Ann Johnny Ong, Choon Hua Thng, Khee Chee Soo and Ching, M. (2022). Prospective Comparison of the Performance of MRI Versus CT in the Detection and Evaluation of Peritoneal Surface Malignancies. *Cancers*, 14(13), pp.3179–3179. doi:https://doi.org/10.3390/cancers14133179.
10. Agostini, A., Borgheresi, A., Bruno, F., Natella, R., Floridi, C., Carotti, M. and Giovagnoni, A. (2020). New advances in CT imaging of pancreas diseases: a narrative review. *Gland Surgery*, 9(6), pp.2283–2294. doi:https://doi.org/10.21037/gs-20-551.
11. Ramaekers, M., Christiaan G. A. Viviers, Terese, Lotte, Tasios, N., Jacobs, I., Joost Nederend, van and Misha (2024). Improved Pancreatic Cancer Detection and Localization on CT Scans: A Computer-Aided Detection Model Utilizing Secondary Features. *Cancers*, 16(13), pp.2403–2403. doi:https://doi.org/10.3390/cancers16132403.
12. Torabi, M., Aquino, S.L. and Harisinghani, M.G. (2004). Current Concepts in Lymph Node Imaging. *Journal of Nuclear Medicine*, [online] 45(9), pp.1509–1518. doi:https://doi.org/10.1002/1097-0142(20010101)91:1.
13. Zhu, W., Zeng, N. and Wang, N. (2010). *Sensitivity, Specificity, Accuracy, Associated Confidence Interval and ROC Analysis with Practical SAS ® Implementations*. [online] Available at: https://lexjansen.com/nesug/nesug10/hl/hl07.pdf.
14. Iglesias-Garcia, J., de la Iglesia-Garcia, D., Lariño-Noia, J. and Dominguez-Muñoz, J.E. (2023). Endoscopic Ultrasound (EUS) Guided Elastography. *Diagnostics*, [online] 13(10), p.1686. doi:https://doi.org/10.3390/diagnostics13101686.
15. He, X.-K., Ding, Y. and Sun, L.-M. (2017). Contrast-enhanced endoscopic ultrasound for differential diagnosis of pancreatic cancer: an updated meta-analysis. *Oncotarget*, 8(39). doi:https://doi.org/10.18632/oncotarget.18915.
16. Kitano, M., Yoshida, T., Itonaga, M., Tamura, T., Hatamaru, K. and Yamashita, Y. (2018). Impact of endoscopic ultrasonography on diagnosis of pancreatic cancer. *Journal of Gastroenterology*, [online] 54(1), pp.19–32. doi:https://doi.org/10.1007/s00535-018-1519-2.

17. Zakaria, A., Al-Share, B., Klapman, J.B. and Dam, A. (2022). The Role of Endoscopic Ultrasonography in the Diagnosis and Staging of Pancreatic Cancer. *Cancers*, 14(6), p.1373. doi:https://doi.org/10.3390/cancers14061373.
18. Shin, E.J., Topazian, M., Goggins, M.G., Syngal, S., Saltzman, J.R., Lee, J.H., Farrell, J.J. and Canto, M.I. (2015). Linear-array EUS improves detection of pancreatic lesions in high-risk individuals: a randomized tandem study. *Gastrointestinal Endoscopy*, [online] 82(5), pp.812–818. doi:https://doi.org/10.1016/j.gie.2015.02.028.
19. Chatterjee, A. and Shah, J. (2024). Role of Endoscopic Ultrasound in Diagnosis of Pancreatic Ductal Adenocarcinoma. *Diagnostics*, [online] 14(1), p.78. doi:https://doi.org/10.3390/diagnostics14010078.
20. Chatterjee, A. and Shah, J. (2024). Role of Endoscopic Ultrasound in Diagnosis of Pancreatic Ductal Adenocarcinoma. *Diagnostics*, [online] 14(1), p.78. doi:https://doi.org/10.3390/diagnostics14010078.
21. Chatterjee, A. and Shah, J. (2024). Role of Endoscopic Ultrasound in Diagnosis of Pancreatic Ductal Adenocarcinoma. *Diagnostics*, [online] 14(1), p.78. doi:https://doi.org/10.3390/diagnostics14010078.
22. Chatterjee, A. and Shah, J. (2024). Role of Endoscopic Ultrasound in Diagnosis of Pancreatic Ductal Adenocarcinoma. *Diagnostics*, [online] 14(1), p.78. doi:https://doi.org/10.3390/diagnostics14010078.
23. Eri Kameta, Kazuya Sugimori, Kaneko, T., Ishii, T., Miwa, H., Sato, T., Ishii, Y., Sue, S., Sasaki, T., Yamashita, Y., Shibata, W., Matsumoto, N. and Maeda, S. (2016). Diagnosis of pancreatic lesions collected by endoscopic ultrasound-guided fine-needle aspiration using next-generation sequencing. *Oncology Letters*, 12(5), pp.3875–3881. doi:https://doi.org/10.3892/ol.2016.5168.
24. Saftoiu, Adrian, et al. "Endoscopic Ultrasound-Guided Fine Needle Aspiration: From the Past to the Future." Endoscopic Ultrasound, vol. 2, no. 2, 2013, p. 77, https://doi.org/10.4103/2303-9027.117691
25. Sigrist, R.M.S., Liau, J., Kaffas, A.E., Chammas, M.C. and Willmann, J.K. (2017). Ultrasound Elastography: Review of Techniques and Clinical Applications. *Theranostics*, [online] 7(5), pp.1303–1329. doi:https://doi.org/10.7150/thno.18650.
26. Yousaf, M.N., Chaudhary, F.S., Ehsan, A., Suarez, A.L., Muniraj, T., Jamidar, P., Aslanian, H.R. and Farrell, J.J. (2020). Endoscopic ultrasound (EUS) and the management of pancreatic cancer. *BMJ Open Gastroenterology*, 7(1), p.e000408. doi:https://doi.org/10.1136/bmjgast-2020-000408.
27. Saftoiu, A., Vilmann, P., Costache, M.-I., Iordache, S. and Karstensen, J. (2013). Endoscopic ultrasound-guided fine needle aspiration: From the past to the future. *Endoscopic Ultrasound*, 2(2), p.77. doi:https://doi.org/10.4103/2303-9027.117691.
28. Smith, L.M., Mahoney, D.W., Bamlet, W.R., Yu, F., Liu, S., Goggins, M.G., Darabi, S., Majumder, S., Wang, Q.-L., Coté, G.A., Demeure, M.J., Zhang, Z., Srivastava, S., Chawla, A., Izmirlian, G., Olson, J.E., Wolpin, B.M., Genkinger, J.M., Zaret, K.S. and Brand, R. (2024). Early detection of pancreatic cancer: Study design and analytical considerations in biomarker discovery and early phase validation studies. *Pancreatology*, [online] 28(8). doi:https://doi.org/10.1016/j.pan.2024.10.012.

29. Hocke M, Schulze E, Gottschalk P, Topalidis T, Dietrich CF. Contrast-enhanced endoscopic ultrasound in discrimination between focal pancreatitis and pancreatic cancer. *World J Gastroenterol* 2006; 12(2): 246-250 [PMID: 16482625 DOI: 10.3748/wjg.v12.i2.246]
30. Jang, S.I. and Lee, D.K. (2014). Contrast-enhanced endoscopic ultrasonography: advance and current status. *Ultrasonography*, 33(3), pp.161–169. doi:https://doi.org/10.14366/usg.14017.
31. Bhutani, M.S., Gress, F.G., Giovannini, M., Erickson, R.A., Catalano, M.F., Chak, A., Deprez, P.H., Faigel, D.O., Nguyen, C.C. and No Endosonographic Detection of Tumor (NEST) Study (2004). The No Endosonographic Detection of Tumor (NEST) Study: a case series of pancreatic cancers missed on endoscopic ultrasonography. *Endoscopy*, [online] 36(5), pp.385–389. doi:https://doi.org/10.1055/s-2004-814320.
32. Fusaroli, P., Spada, A., Mancino, M.G. and Caletti, G. (2010). Contrast Harmonic Echo–Endoscopic Ultrasound Improves Accuracy in Diagnosis of Solid Pancreatic Masses. *Clinical Gastroenterology and Hepatology*, 8(7), pp.629-634.e2. doi:https://doi.org/10.1016/j.cgh.2010.04.012.
33. Claudon, M., Cosgrove, D., Albrecht, T., Bolondi, L., Bosio, M., Calliada, F., Correas, J.-M., Darge, K., Dietrich, C., D'Onofrio, M., Evans, D., Filice, C., Greiner, L., Jäger, K., Jong, N., Leen, E., Lencioni, R., Lindsell, D., Martegani, A. and Meairs, S. (2008). Guidelines and Good Clinical Practice Recommendations for Contrast Enhanced Ultrasound (CEUS) - Update 2008. *Ultraschall in der Medizin - European Journal of Ultrasound*, 29(01), pp.28–44. doi:https://doi.org/10.1055/s-2007-963785.
34. Kongkam, P., Lakananurak, N., Navicharern, P., Chantarojanasiri, T., Aye, K., Ridtitid, W., Kritisin, K., Angsuwatcharakon, P., Aniwan, S., Pittayanon, R., Sampatanukul, P., Treeprasertsuk, S., Kullavanijaya, P. and Rerknimitr, R. (2015). Combination of EUS‐FNA and elastography (strain ratio) to exclude malignant solid pancreatic lesions: A prospective single‐blinded study. *Journal of Gastroenterology and Hepatology*, 30(11), pp.1683–1689. doi:https://doi.org/10.1111/jgh.13067.
35. Săftoiu, A., Vilmann, P., Gorunescu, F., Gheonea, D.I., Gorunescu, M., Ciurea, T., Popescu, G.L., Iordache, A., Hassan, H. and Iordache, S. (2008). Neural network analysis of dynamic sequences of EUS elastography used for the differential diagnosis of chronic pancreatitis and pancreatic cancer. *Gastrointestinal Endoscopy*, 68(6), pp.1086–1094. doi:https://doi.org/10.1016/j.gie.2008.04.031.
36. Sahai, Anand. "The Resectable Pancreatic Lesion: To FNA or Not to FNA? A Diagnostic Dilemma, FNA Cons." Nih.gov, 2024, pmc.ncbi.nlm.nih.gov/articles/PMC5774078/. Accessed 14 May 2026.
37. Itonaga, M., Ashida, R. and Kitano, M. (2020). Endoscopic Ultrasound-Guided Fine-Needle Aspiration (EUS-FNA) with Image Enhancement. *Diagnostics*, 10(11), p.888. doi:https://doi.org/10.3390/diagnostics10110888.
38. Gheorghiu, M., Sparchez, Z., Rusu, I., Bolboacă, S.D., Seicean, R., Pojoga, C. and Seicean, A. (2022). Direct Comparison of Elastography Endoscopic Ultrasound Fine-Needle Aspiration and B-Mode Endoscopic Ultrasound Fine-Needle Aspiration in Diagnosing Solid Pancreatic Lesions. *International Journal of Environmental Research and Public Health*, [online] 19(3), p.1302. doi:https://doi.org/10.3390/ijerph19031302.

39. Jang, S.I. and Lee, D.K. (2014). Contrast-enhanced endoscopic ultrasonography: advance and current status. *Ultrasonography*, 33(3), pp.161–169. doi:https://doi.org/10.14366/usg.14017.
40. Levine, I. and Trindade, A.J. (2021). Endoscopic ultrasound fine needle aspiration vs fine needle biopsy for pancreatic masses, subepithelial lesions, and lymph nodes. *World Journal of Gastroenterology*, 27(26), pp.4194–4207. doi:https://doi.org/10.3748/wjg.v27.i26.4194.
41. Ji Hwan Bang, Hebert-Magee, S., Trevino, J., Ramesh, J. and Shyam Varadarajulu (2012). Randomized trial comparing the 22-gauge aspiration and 22-gauge biopsy needles for EUS-guided sampling of solid pancreatic mass lesions. 76(2), pp.321–327. doi:https://doi.org/10.1016/j.gie.2012.03.1392.
42. Brand, B., Pfaff, T., Binmoeller, K.F., Parupudi V.J. Sriram, Fritscher-Ravens, A., Knöfel, W.T., Jäckle, S. and Nib Soehendra (2000). Endoscopic Ultrasound for Differential Diagnosis of Focal Pancreatic Lesions, Confirmed by Surgery. *Scandinavian Journal of Gastroenterology*, 35(11), pp.1221–1228. doi:https://doi.org/10.1080/003655200750056736.
43. Tian, L., Tang, A., Zhang, L., Liu, X., Li, J., Wang, F., Shen, S. and Wang, X. (2018). Evaluation of 22G fine-needle aspiration (FNA) versus fine-needle biopsy (FNB) for endoscopic ultrasound-guided sampling of pancreatic lesions: a prospective comparison study. *Evaluation of 22G fine-needle aspiration (FNA) versus fine-needle biopsy (FNB) for endoscopic ultrasound-guided sampling of pancreatic lesions: a prospective comparison study*, 32(8), pp.3533–3539. doi:https://doi.org/10.1007/s00464-018-6075-6.
44. Mavrogenis, G., Weynand, B., Sibille, A., Hassaini, H., Deprez, P., Gillain, C. and Warzée, P. (2014). 25-gauge histology needle versus 22-gauge cytology needle in endoscopic ultrasonography-guided sampling of pancreatic lesions and lymphadenopathy. *Endoscopy International Open*, 03(01), pp.E63–E68. doi:https://doi.org/10.1055/s-0034-1390889.
45. Levine, I. and Trindade, A.J. (2021). Endoscopic ultrasound fine needle aspiration vs fine needle biopsy for pancreatic masses, subepithelial lesions, and lymph nodes. *World Journal of Gastroenterology*, 27(26), pp.4194–4207. doi:https://doi.org/10.3748/wjg.v27.i26.4194.
46. Kikuyama, M. (2023). A Novel Diagnostic Imaging Method for the Early Detection of Pancreatic Cancer. *Diagnostics*, [online] 13(12), p.2080. doi:https://doi.org/10.3390/diagnostics13122080.
47. England, C.G., Hernandez, R., Eddine, S.B.Z. and Cai, W. (2015). Molecular Imaging of Pancreatic Cancer with Antibodies. *Molecular Pharmaceutics*, 13(1), pp.8–24. doi:https://doi.org/10.1021/acs.molpharmaceut.5b00626.
48. Hu, X., Li, X., Wang, P. and Cai, J. (2025). The Role of FAPI PET Imaging in Pancreatic Cancer: A Meta-analysis Compared with 18F-FDG PET. *Academic Radiology*, 32(1), pp.191–200. doi:https://doi.org/10.1016/j.acra.2024.07.032.
49. Lopez-Ramirez, F., Syailendra, E.A., Tixier, F., Kawamoto, S., Fishman, E.K. and Chu, L.C. (2025). Early detection of pancreatic cancer on computed tomography: advancements with deep learning. *Radiology advances*, [online] 2(5), p.umaf028. doi:https://doi.org/10.1093/radadv/umaf028.
50. Mahmoudi, T., Zahra Mousavi Kouzahkanan, Amir Reza Radmard, Rahele Kafieh, Aneseh Salehnia, Davarpanah, A.H., Hossein Arabalibeik and Ahmadian, A. (2022). Segmentation of pancreatic ductal adenocarcinoma (PDAC) and surrounding vessels in CT images using deep convolutional neural networks and texture descriptors. *Scientific Reports*, 12(1). doi:https://doi.org/10.1038/s41598-022-07111-9.

51. Clinicaltrials.gov. (2026). *Artificial Intelligence-powered Low-Dose Computed Tomography for Screening of Pancreatic Cancer (AI-LDCT-PC)*. [online] Available at: https://clinicaltrials.gov/study/NCT07117045?aggFilters=status [Accessed 18 Feb. 2026].

ABOUT THE AUTHOR

Kimaya Ranjan is a high school sophomore at Emerald High School in Dublin, CA. She takes interest in health and medicine, and aspires to pursue a career in oncology and global health administration to make healthcare accessible to underserved communities worldwide.