State of the Art Imaging in Pancreatic Cancer: What Does Borderline Resectable and Locally Advanced Mean?

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CLINICAL PRESENTATION AND WORKUP

Clinical suspicion of pancreatic cancer or evidence of dilated pancreatic and/or bile duct (stricture) → **Axial imaging:**
- **Pancreatic protocol CT or MRI[a] (abdomen) (PANC-A)**

→ **Multidisciplinary consultation[b]**

No metastatic disease →
- Chest and pelvis CT[c]
- Consider endoscopic ultrasonography (EUS)[d]
- Consider MRI as clinically indicated for indeterminate liver lesions
- Consider PET/CT or PET/MRI in patients with high-risk features[e]
- Consider endoscopic retrograde cholangiopancreatography (ERCP) with stent placement[f]
- Liver function test and baseline CA 19-9[g] after adequate biliary drainage
- Genetic testing for inherited mutations if diagnosis confirmed[h]

→
- **No mass or diagnosis not confirmed** → **Refer to high-volume center for evaluation**
- **Resectable disease (PANC-2)[k]**
- **Borderline resectable disease (PANC-4)[k]**
- **Locally advanced disease (PANC-5)**
- **Metastatic disease (PANC-10)**

Metastatic disease → **Biopsy[i] confirmation, from a metastatic site preferred** →
- Genetic testing for inherited mutations[h]
- Molecular profiling of tumor tissue is recommended[j]
- Complete staging with chest and pelvis CT[c]

→ **Metastatic disease (PANC-10)**

The Staging of Pancreatic Cancer Depends on Imaging

- MDCT
- MR
- PET/CT

Pancreas Protocol CT Scan

- Dual phase CT scan (arterial and venous phase at 30 and 70 seconds)
- Oral contrast (water 750-1000ml) and IV contrast (100-120 ML of Omniapque-350 injection at 4-5 cc/sec)
- Reconstruction with submillimeter scan thickness (.75 mm every .5mm)
- Reconstruction with axial, multiplanar and ideally 3D imaging

Other Pancreas Protocol Imaging

- MR is usually reserved for cases with indeterminate liver lesions or patients allergic to iodinated IV contrast
- PET/CT use is still a work in progress and may be helpful for adenopathy or other select questions

Pancreas Protocol report

- Use of a standardized report for staging has proven to be valuable both to the radiologist reporting the study and the referring clinician reviewing the report (Medical Oncologist, Surgeon or Radiation Oncologist)

Arterial Mapping

NCCN Guidelines Index
Table of Contents
Discussion

PRINCIPLES OF DIAGNOSIS, IMAGING, AND STAGING
PANCREATIC CANCER RADIOLOGY REPORTING TEMPLATE[a]

Arterial Evaluation				
SMA Contact	☐ Present	☐ Absent		
Degree of solid soft-tissue contact	☐ ≤180	☐ >180		
Degree of increased hazy attenuation/stranding contact	☐ ≤180	☐ >180		
Focal vessel narrowing or contour irregularity	☐ Present	☐ Absent		
Extension to first SMA branch	☐ Present	☐ Absent		
Celiac Axis Contact	☐ Present	☐ Absent		
Degree of solid soft-tissue contact	☐ ≤180	☐ >180		
Degree of increased hazy attenuation/stranding contact	☐ ≤180	☐ >180		
Focal vessel narrowing or contour irregularity	☐ Present	☐ Absent		
CHA Contact	☐ Present	☐ Absent		
Degree of solid soft-tissue contact	☐ ≤180	☐ >180		
Degree of increased hazy attenuation/stranding contact	☐ ≤180	☐ >180		
Focal vessel narrowing or contour irregularity	☐ Present	☐ Absent		
Extension to celiac axis	☐ Present	☐ Absent		
Extension to bifurcation of right/left hepatic artery	☐ Present	☐ Absent		
Arterial Variant	☐ Present	☐ Absent		
Variant anatomy	☐ Accessory right hepatic artery	☐ Replaced right hepatic artery	☐ Replaced common hepatic artery	☐ Others (origin of replaced or accessory artery) ________________
Variant vessel contact	☐ Present	☐ Absent		
Degree of solid soft-tissue contact	☐ ≤180	☐ >180		
Degree of increased hazy attenuation/stranding contact	☐ ≤180	☐ >180		
Focal vessel narrowing or contour irregularity	☐ Present	☐ Absent		

[a] Al-Hawary MM, Francis IR, Chari ST, et al. Pancreatic ductal adenocarcinoma radiology reporting template: consensus statement of the Society of Abdominal Radiology and the American Pancreatic Association. Radiology 2014;270:248-260.

Continued

Venous Mapping

PRINCIPLES OF DIAGNOSIS, IMAGING, AND STAGING
PANCREATIC CANCER RADIOLOGY REPORTING TEMPLATE[a]

Venous Evaluation			
MPV Contact	☐ Present	☐ Absent	☐ Complete occlusion
Degree of solid soft-tissue contact	☐ ≤180	☐ >180	
Degree of increased hazy attenuation/stranding contact	☐ ≤180	☐ >180	
Focal vessel narrowing or contour irregularity (tethering or tear drop)	☐ Present	☐ Absent	
SMV Contact	☐ Present	☐ Absent	☐ Complete occlusion
Degree of solid soft-tissue contact	☐ ≤180	☐ >180	
Degree of increased hazy attenuation/stranding contact	☐ ≤180	☐ >180	
Focal vessel narrowing or contour irregularity (tethering or tear drop)	☐ Present	☐ Absent	
Extension	☐ Present	☐ Absent	
Other			
Thrombus within vein (tumor, bland)	☐ Present ☐ MPV ☐ SMV ☐ Splenic vein	☐ Absent	
Venous collaterals	☐ Present ☐ Around pancreatic head ☐ Porta hepatis ☐ Root of the mesentery ☐ Left upper quadrant	☐ Absent	

[a] Al-Hawary MM, Francis IR, Chari ST, et al. Pancreatic ductal adenocarcinoma radiology reporting template: consensus statement of the Society of Abdominal Radiology and the American Pancreatic Association. Radiology 2014;270:248-260.

Continued

Staging Pancreatic Cancer in Multidisciplinary Conference

- Resectable
- Borderline resectable
- Unresectable (either locally advanced or metastatic)

Staging Pancreatic Cancer in Multidisciplinary Conference

- Resectable- If the cancer is only in the pancreas (or has spread just beyond it) and the surgeon believes the entire tumor can be removed, it is called resectable.
- Borderline resectable
- Unresectable (either locally advanced or metastatic)

Staging Pancreatic Cancer in Multidisciplinary Conference

- Resectable
- Borderline resectable- a pancreatic tumor that is touching and possibly surrounding a small part of nearby blood vessels. After initial chemo or a combination of chemo and radiation, the surgeon may still be able to remove the tumor completely.
- Unresectable (either locally advanced or metastatic)

Staging Pancreatic Cancer in Multidisciplinary Conference

- Resectable
- Borderline resectable
- Unresectable (locally advanced) cancer has not spread to distant organs but it still can't be removed completely with surgery, it is called locally advanced. Often this is because the tumor has grown into or surrounded nearby major blood vessels.

Staging Pancreatic Cancer in Multidisciplinary Conference

- Resectable
- Borderline resectable
- Unresectable (metastatic) cancer has spread to distant organs especially to the liver but other organ involvement (lung, ovary, bone) can occur.

NCCN Guidelines 2025

National Comprehensive Cancer Network®

NCCN Guidelines Version 2.2025
Pancreatic Adenocarcinoma

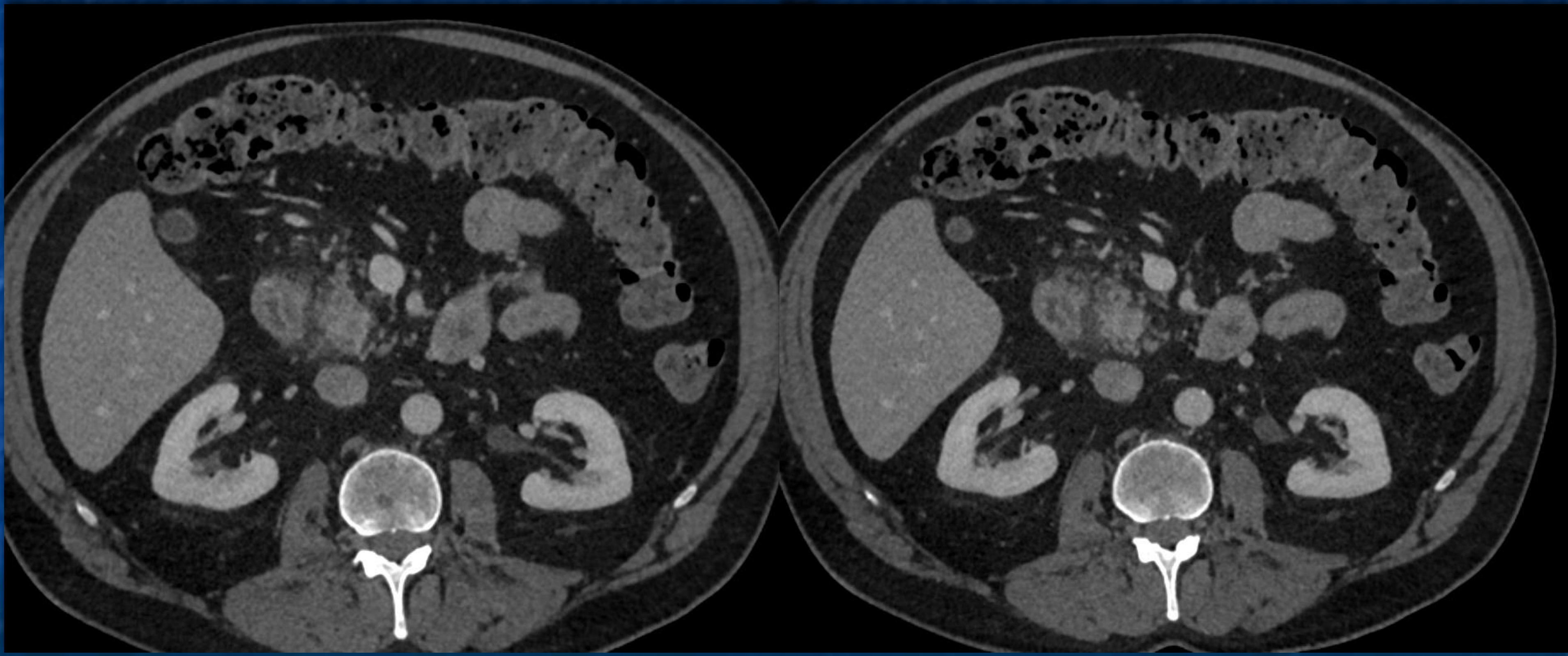
NCCN Guidelines Index
Table of Contents
Discussion

CRITERIA DEFINING RESECTABILITY STATUS AT DIAGNOSIS[a]

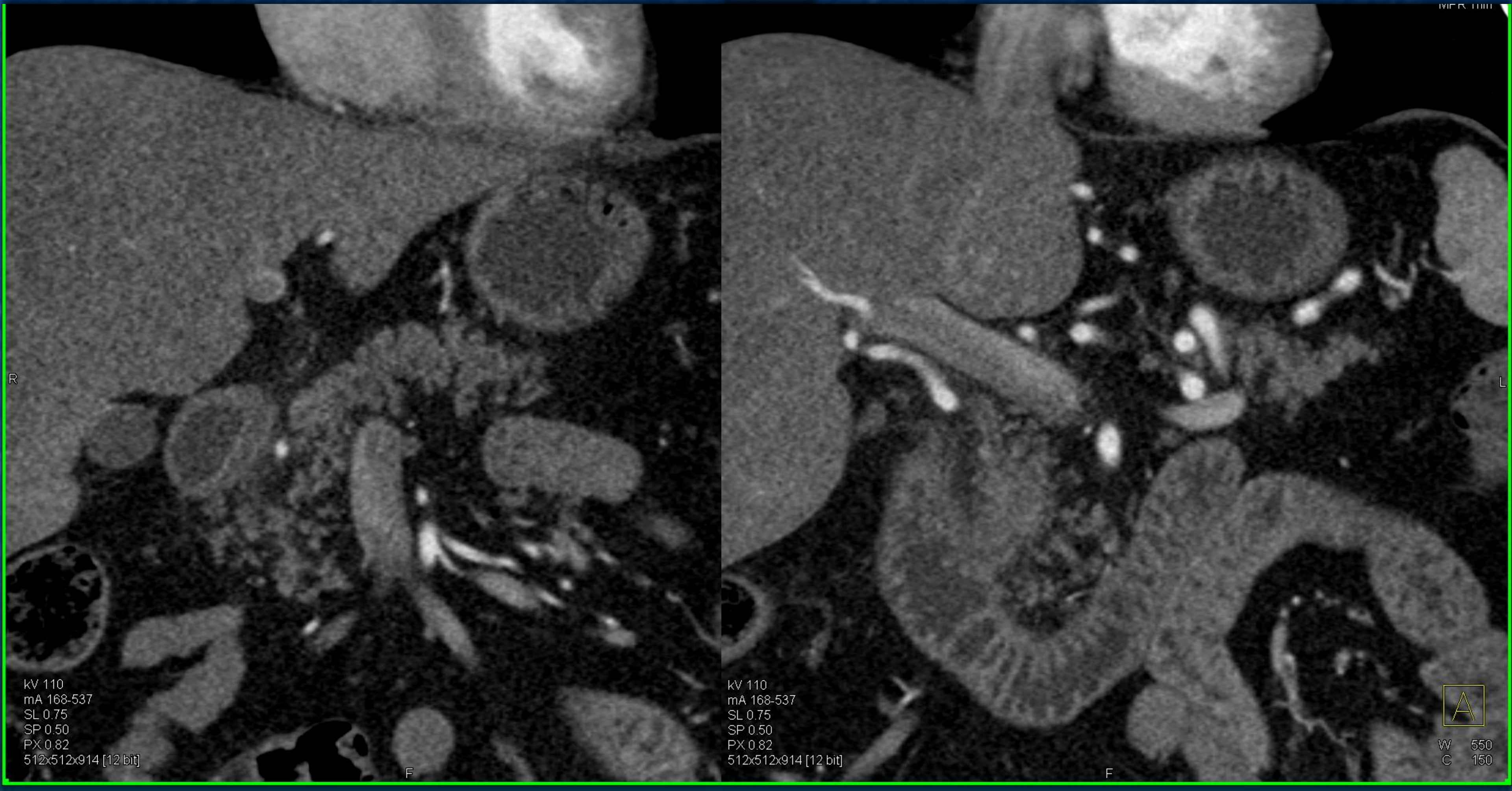
• Decisions about resectability status should be made in consensus at multidisciplinary meetings/discussions.

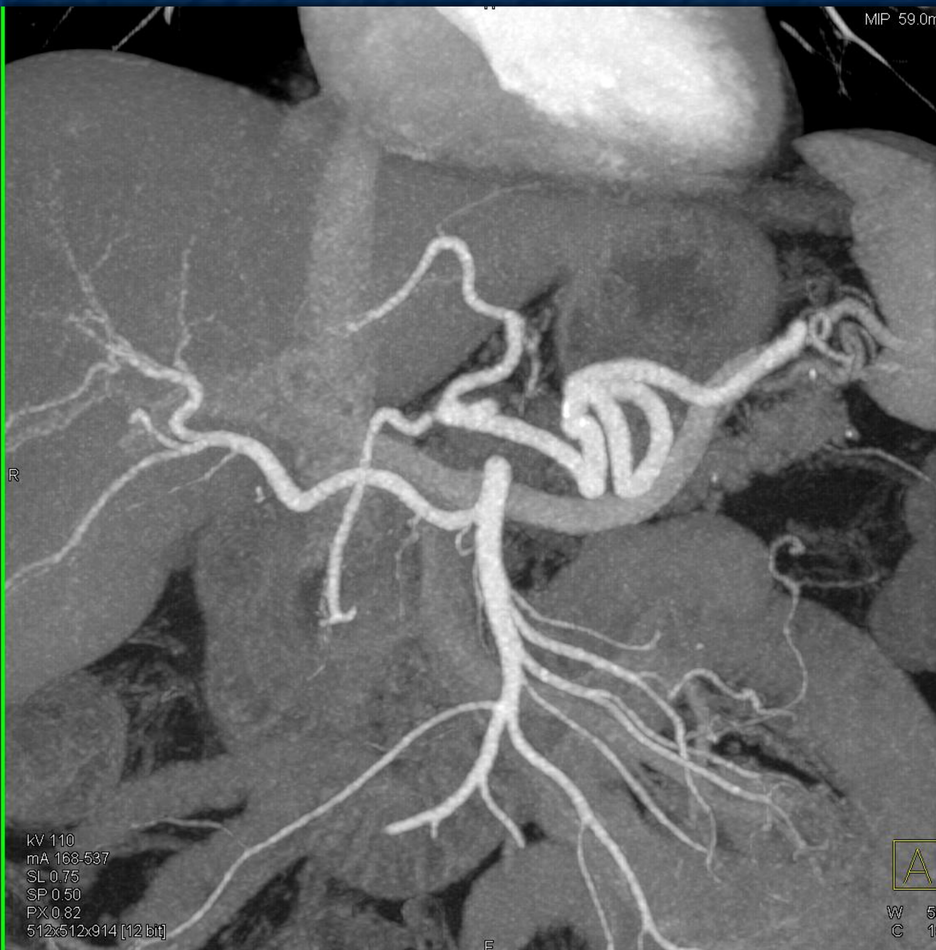
Resectability Status	Arterial	Venous
Resectable	• No arterial tumor contact (celiac axis [CA], superior mesenteric artery [SMA], or common hepatic artery [CHA]).	• No tumor contact with the superior mesenteric vein (SMV) or portal vein (PV) or ≤180° contact without vein contour irregularity.
Borderline Resectable[b]	Pancreatic head/uncinate process: • Solid tumor contact with CHA without extension to CA or hepatic artery bifurcation allowing for safe and complete resection and reconstruction. • Solid tumor contact with the SMA of ≤180°. • Solid tumor contact with variant arterial anatomy (eg, accessory right hepatic artery, replaced right hepatic artery, replaced CHA, and the origin of replaced or accessory artery) and the presence and degree of tumor contact should be noted if present, as it may affect surgical planning. Pancreatic body/tail: • Solid tumor contact with the CA of ≤180°.	• Solid tumor contact with the SMV or PV of >180°, contact of ≤180° with contour irregularity of the vein or thrombosis of the vein but with suitable vessel proximal and distal to the site of involvement allowing for safe and complete resection and vein reconstruction. • Solid tumor contact with the inferior vena cava (IVC).
Locally Advanced[b,c,d]	Head/uncinate process: • Solid tumor contact >180° with the SMA or CA. Pancreatic body/tail: • Solid tumor contact of >180° with the SMA or CA. • Solid tumor contact with the CA and aortic involvement.	• Not currently amenable to resection and primary reconstruction due to complete occlusion of SMV/PV

1 Cm Adenocarcinoma Pancreas



1 Cm Adenocarcinoma Pancreas

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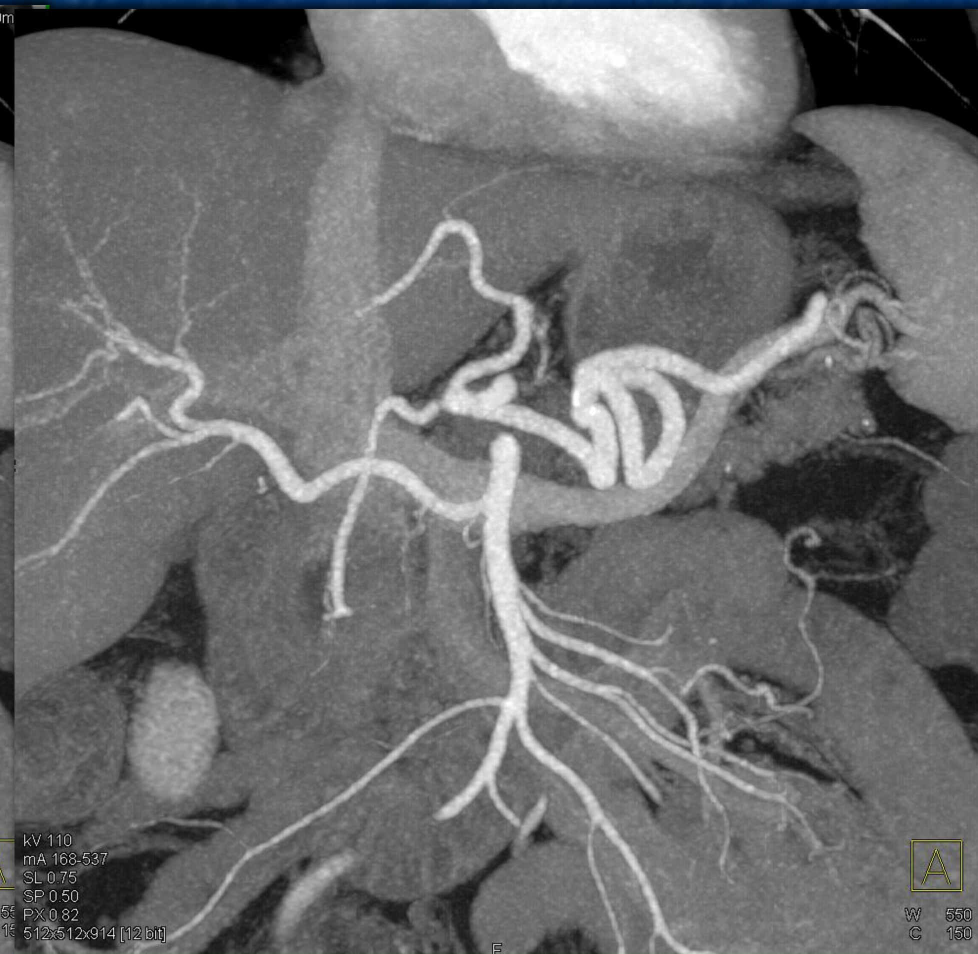
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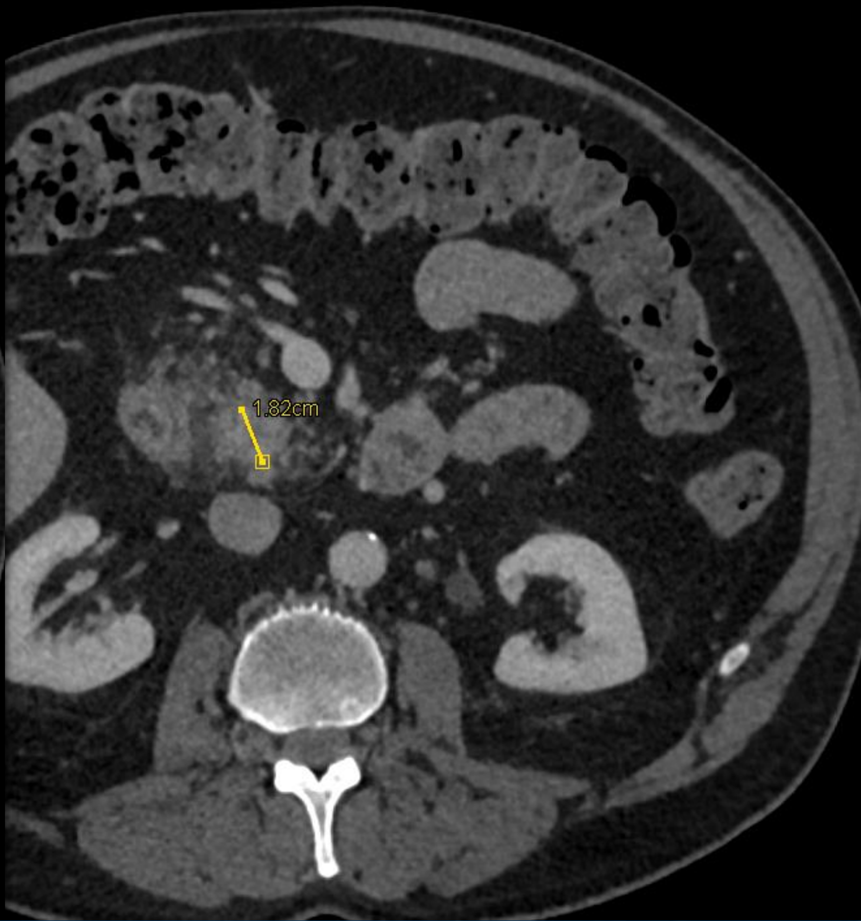
C 150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B 25
O 50
F
R
L
kV 110
mA 275-535
SL 0.75
SP 0.50
PX 0.82
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O 50 C 45
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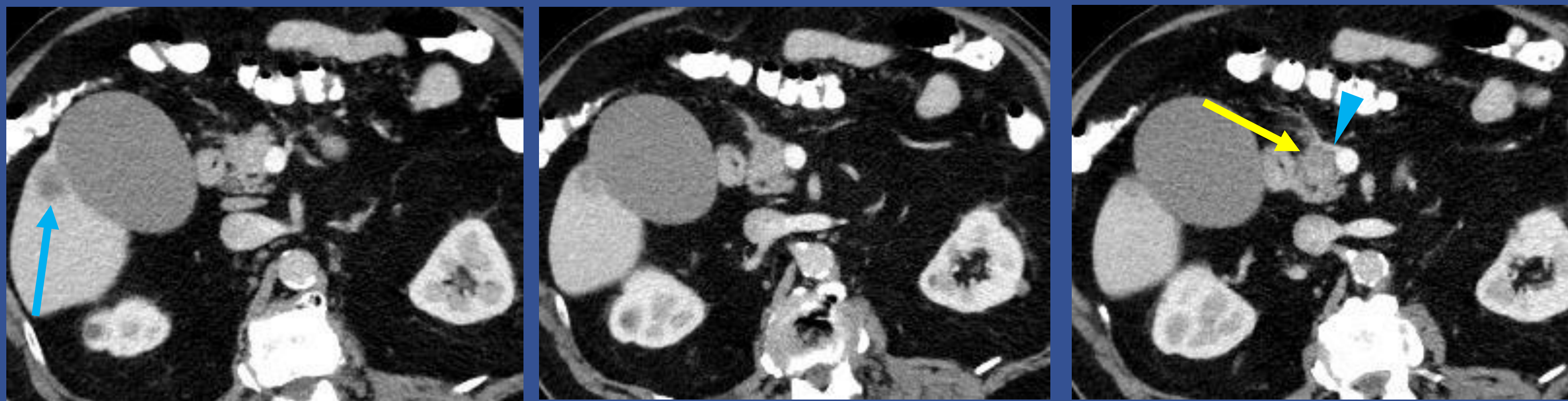
70’s-year-old man, incidental finding

Small, nearly isodense PDAC

(A) Initial CT for evaluation of painless hematuria



(B) 9 month later

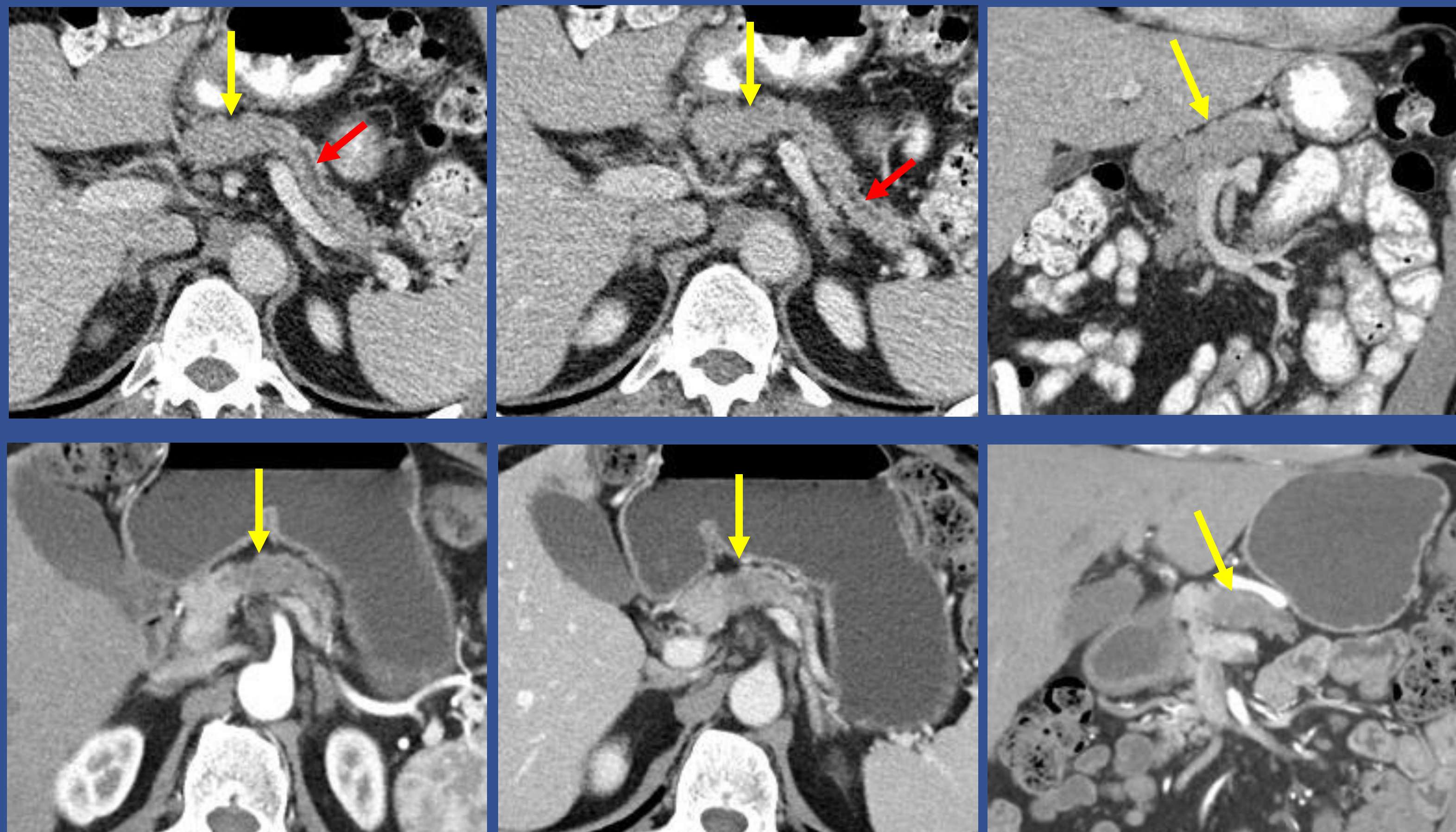
(A) Small, nearly isodense lesion in the head abutting the superior mesenteric vein (SMV) and its branch (blue arrowhead), with subtle fat stranding in retrospect. The patient had multiple known liver hemangiomata, and liver metastasis (blue arrow) was initially thought to be one of hemangiomata. (B) 9 month later, apparent hypodense mass (yellow arrow) is appearing compressing the SMV and obstructing the SMV branch, and encasing the gastroduodenal artery (GDA) (red arrowhead). Interval development of upstream pancreatic duct dilatation (red arrow).

50's-year old man with abdominal pain

Isodense PDAC in pancreatic neck with mild upstream pancreatic duct dilatation

(A) Initial CT

(B) 4 month later



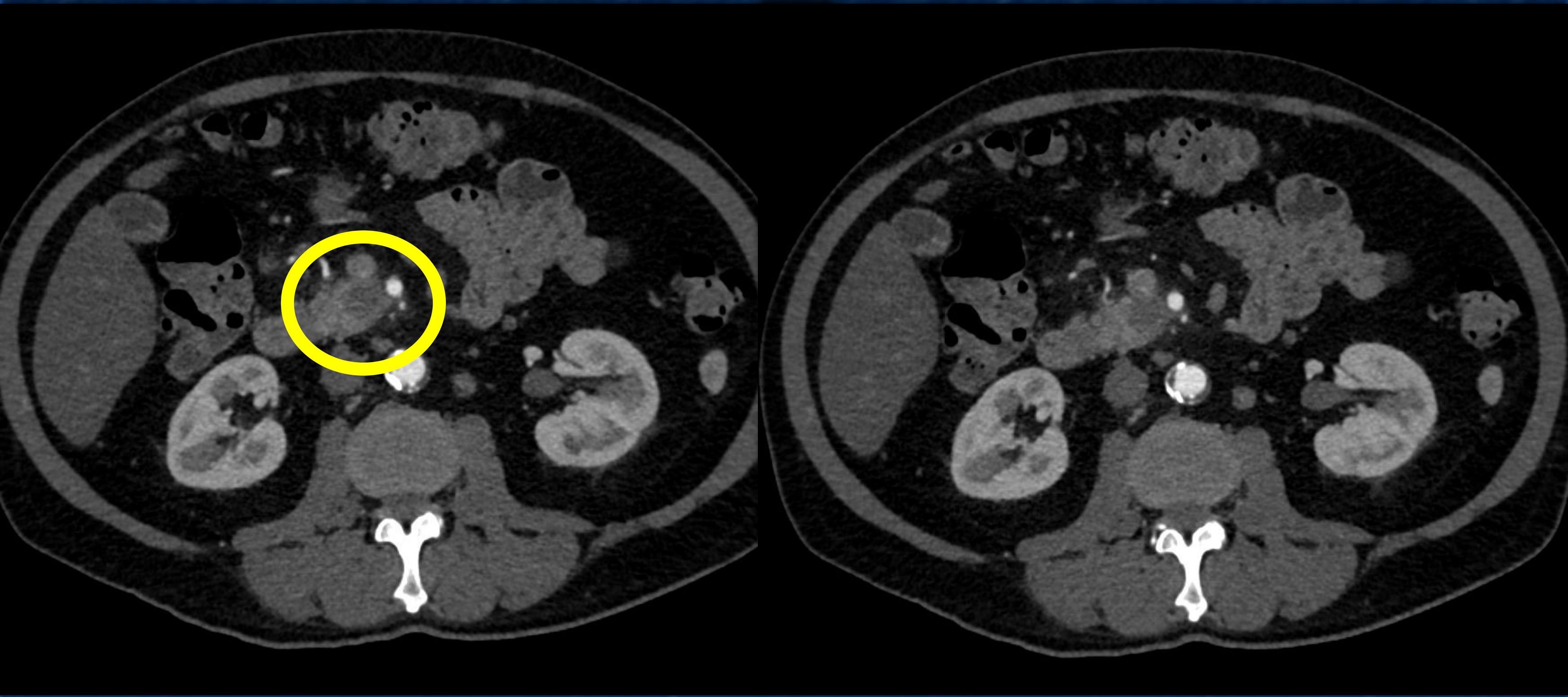
Arterial phase | Venous phase | Arterial phase

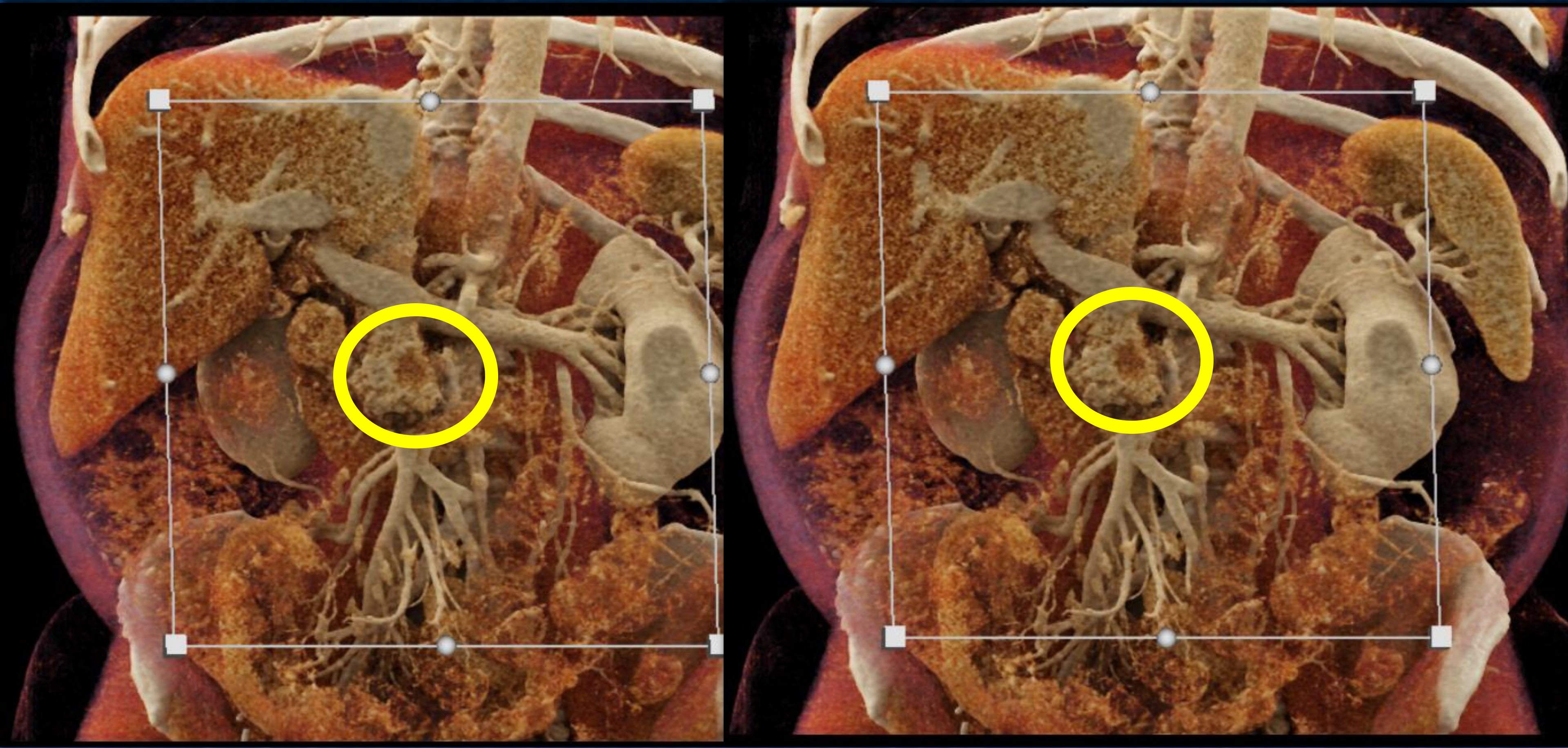
(A) Initial CT was read as negative, but isodense mass (yellow arrows) in the pancreatic neck with narrowing of the pancreatic duct at this level and mild upstream pancreatic duct dilation (red arrows) with parenchymal atrophy in retrospect. (B) 4 month later, hypodense mass is apparent (yellow arrow).

Improve Lesion Detection

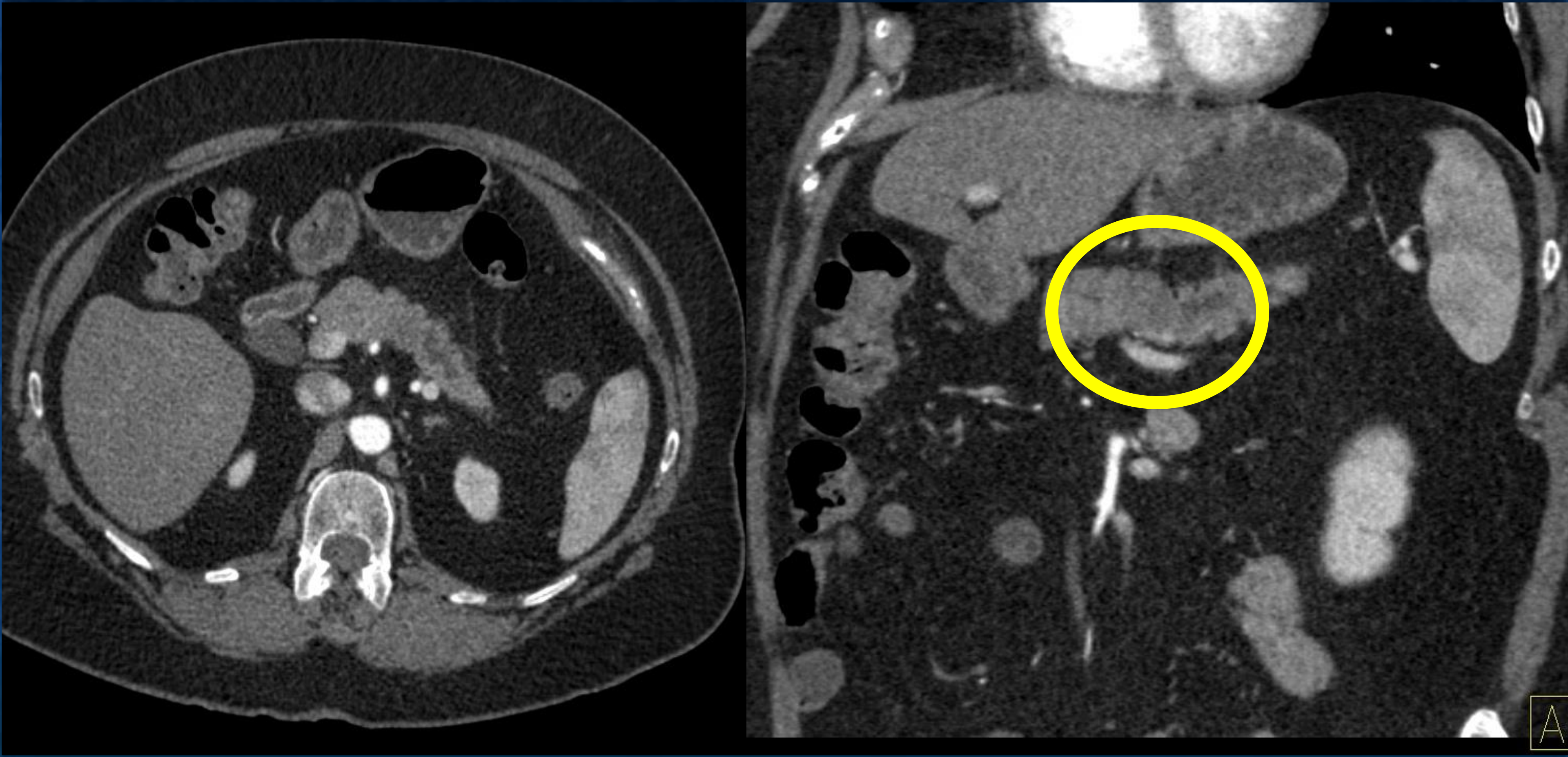
- 3D mapping to visualize volumes rather than slices
- Accentuate tissue differences rather than looking for a mass
- Cinematic Rendering for detection of early textural changes

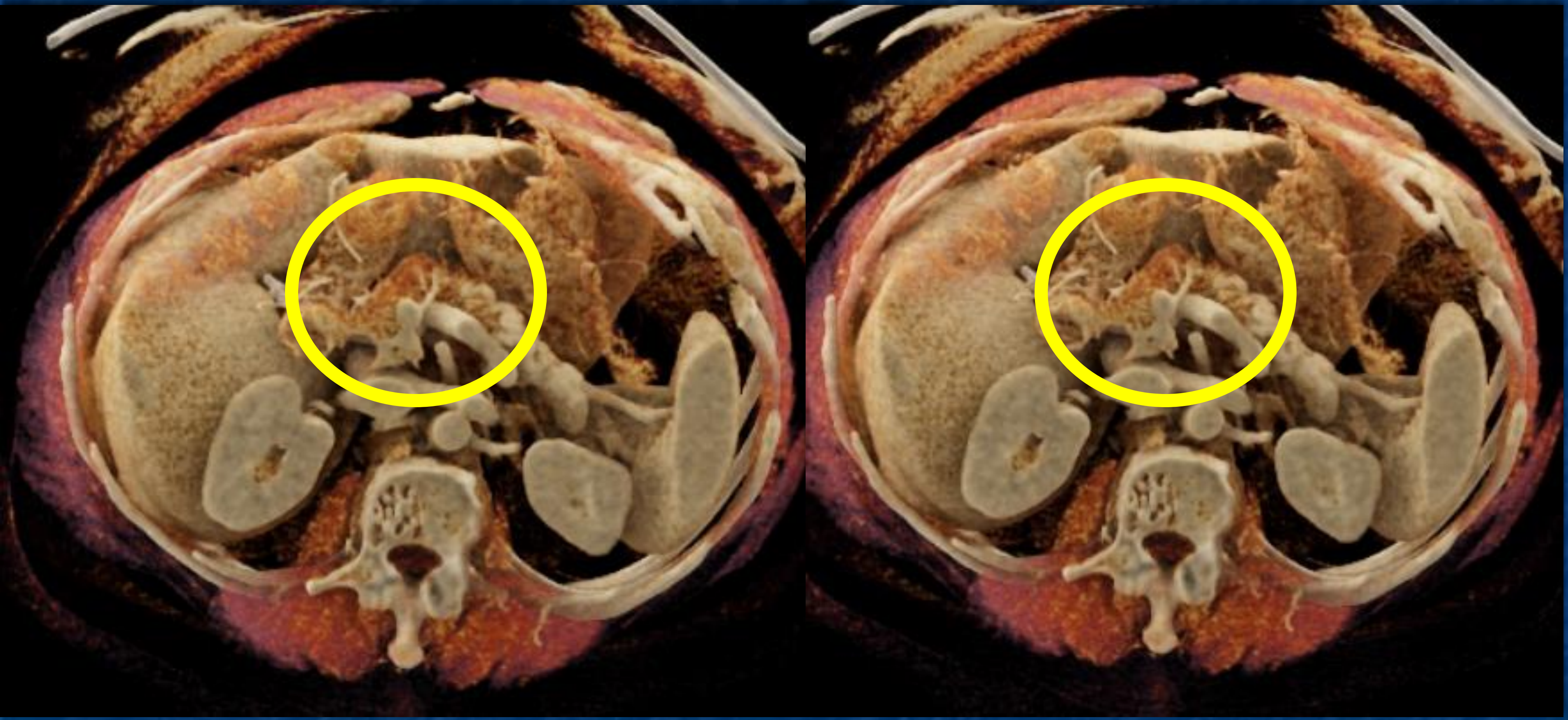
Weight Loss-Missed Adenocarcinoma HOP

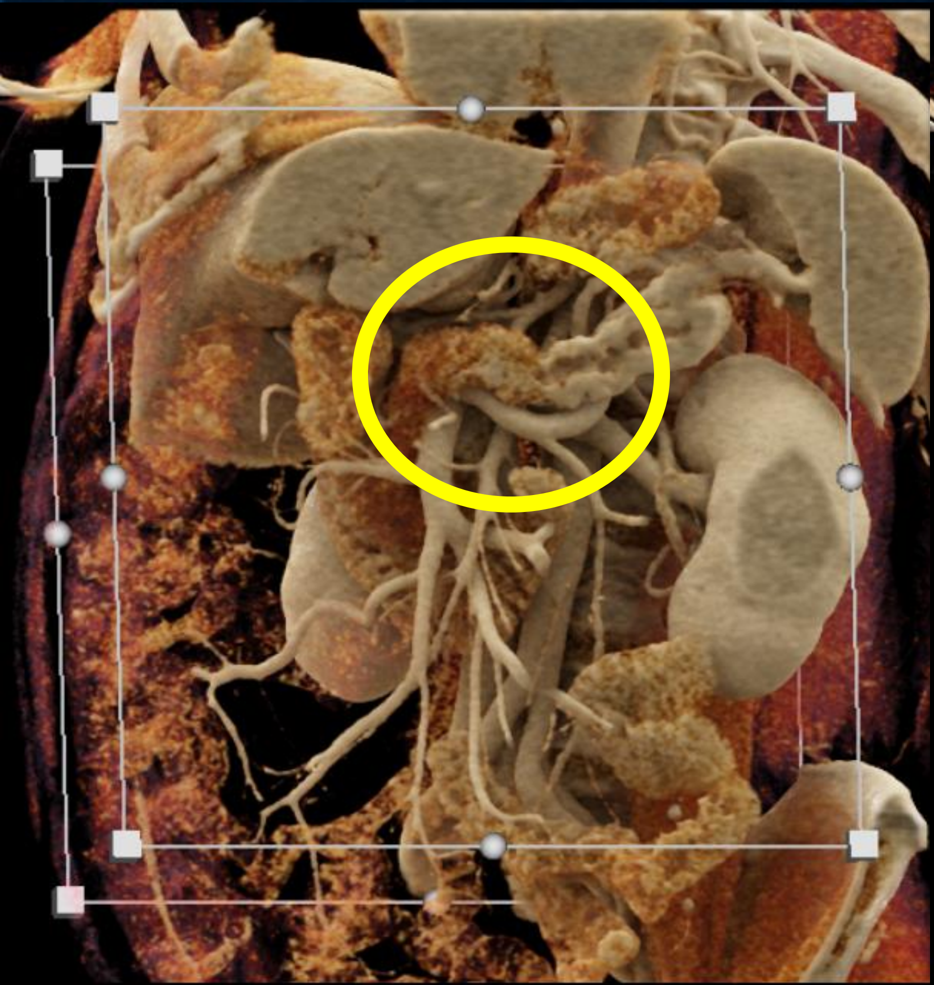


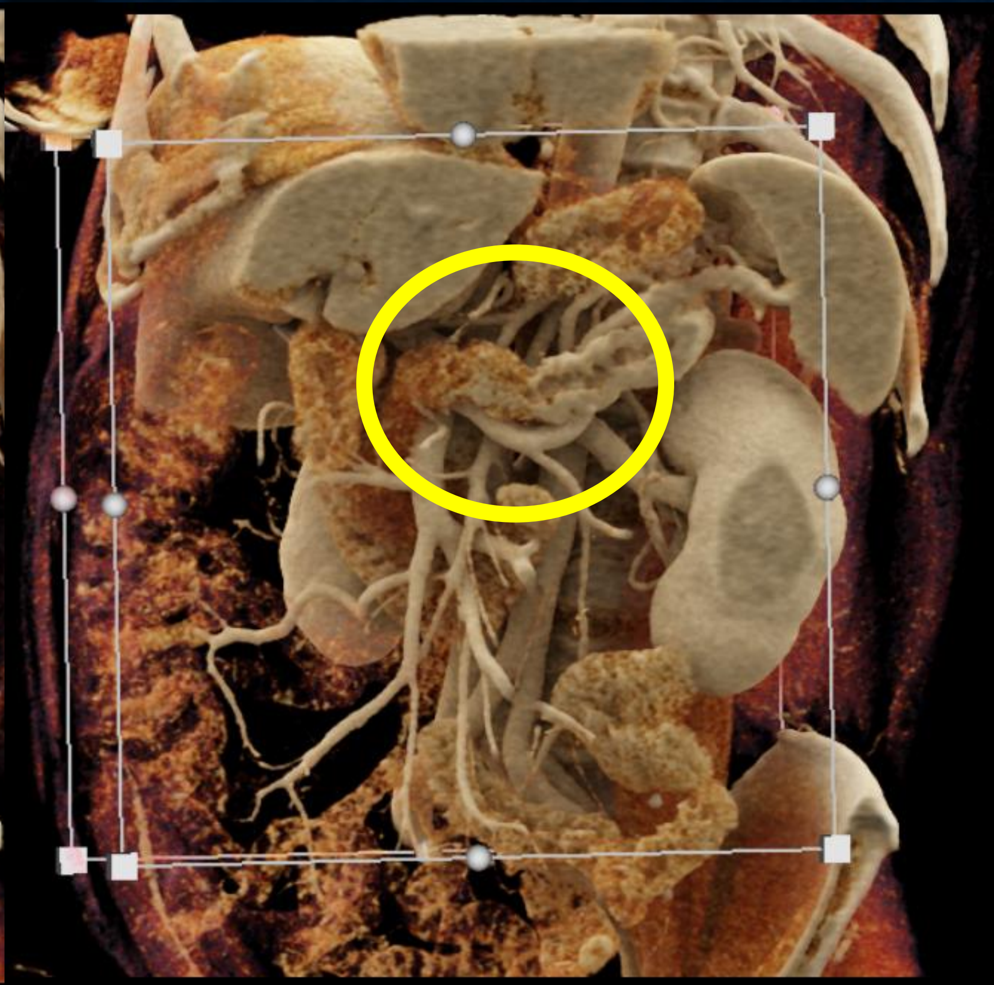


Pancreas Adenocarcinoma

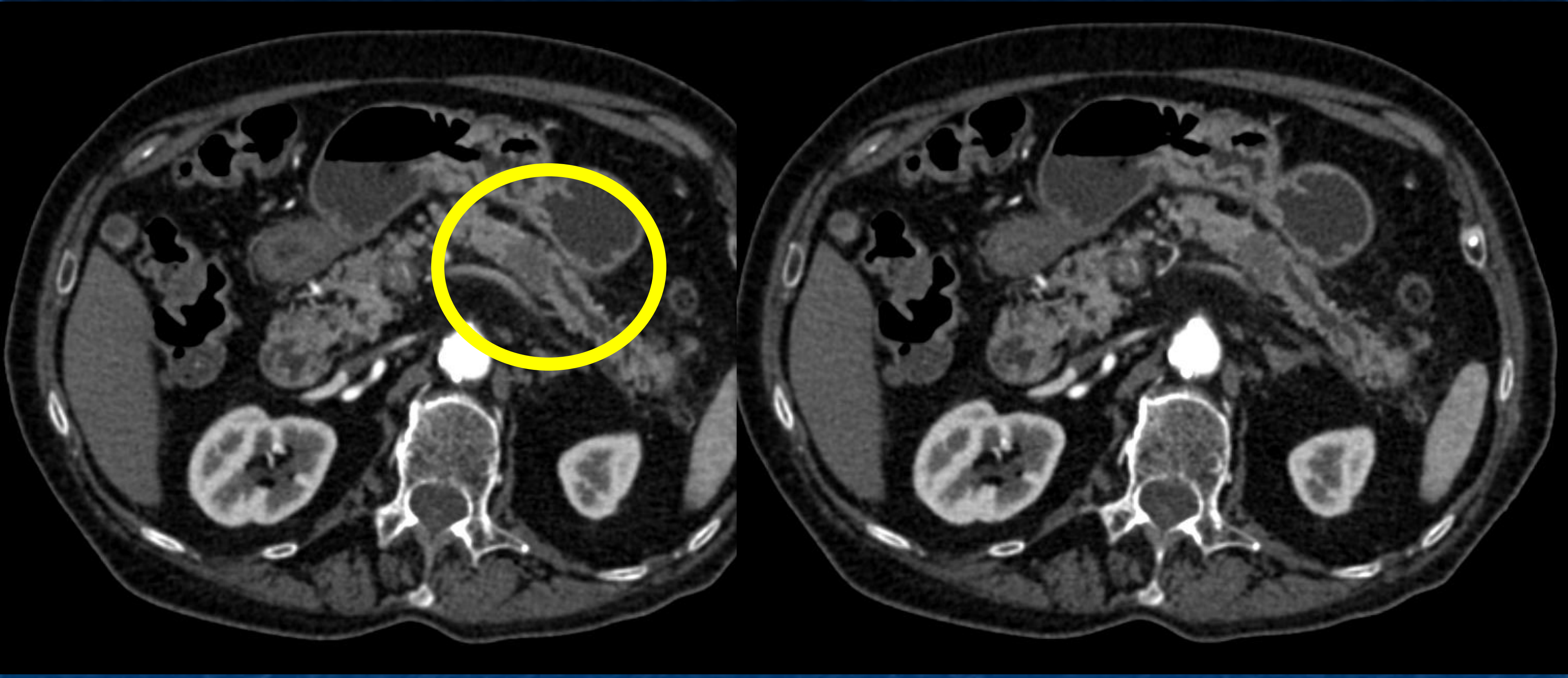


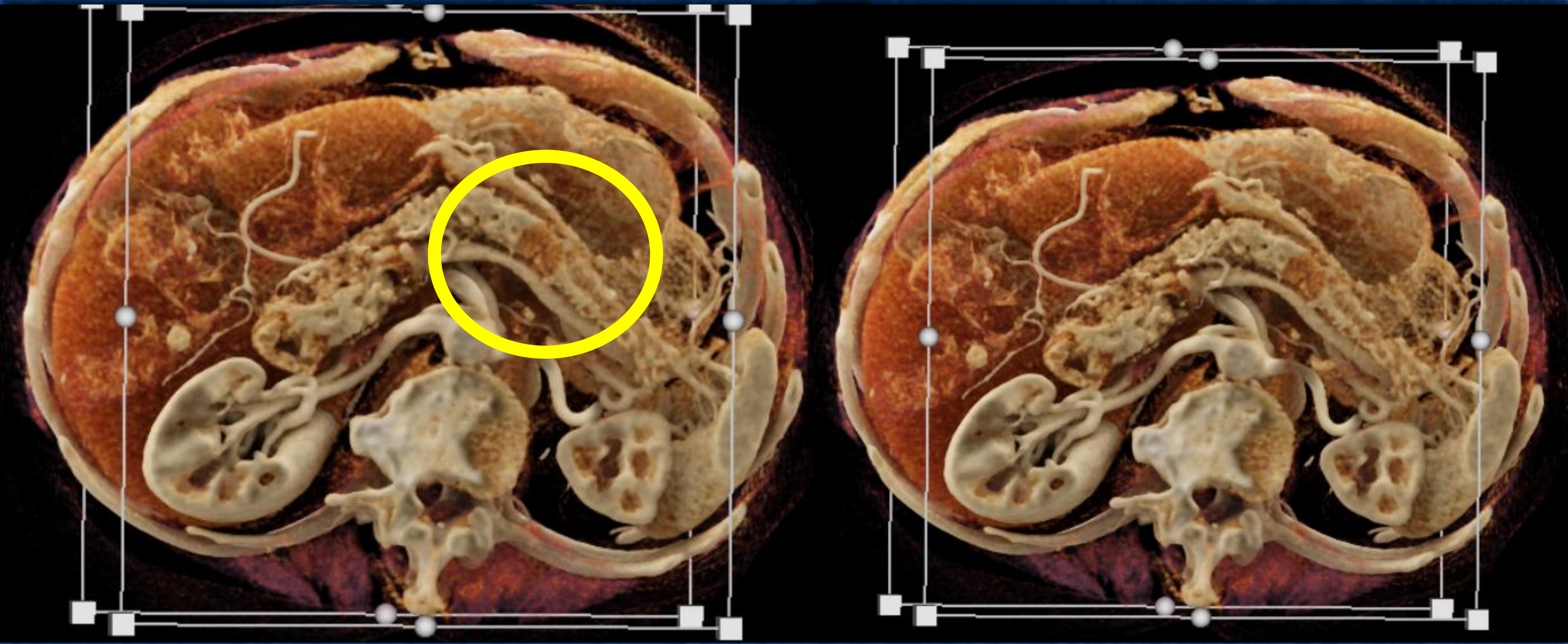


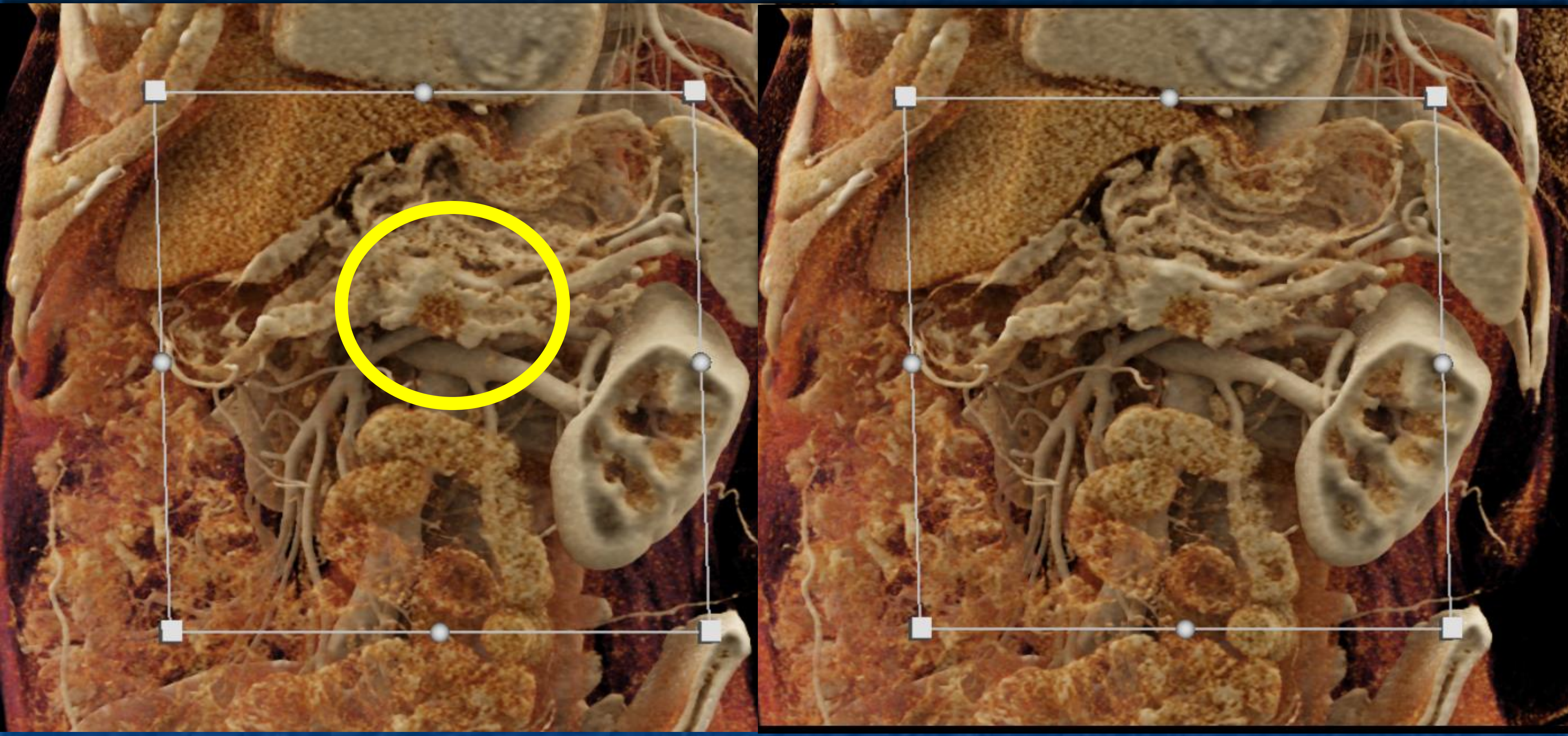


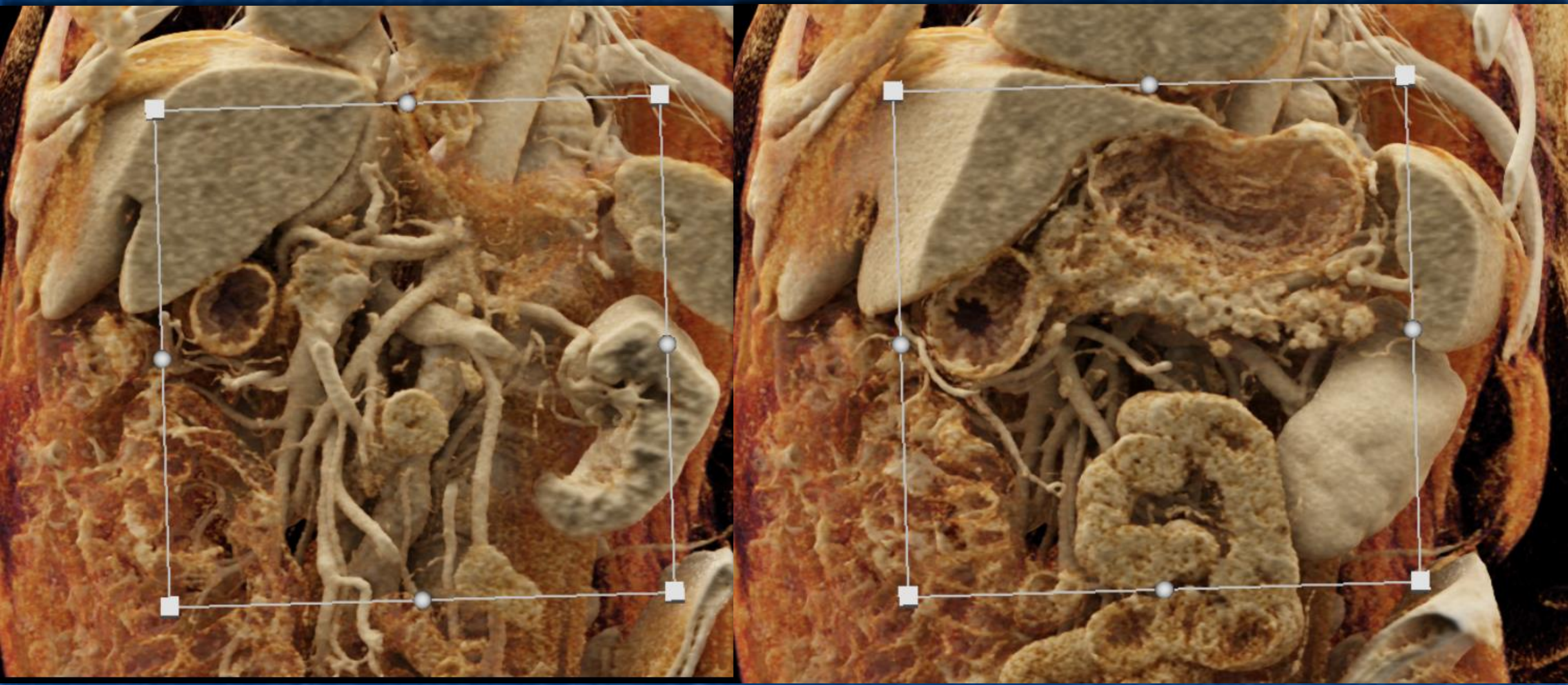


Subtle Pancreatic Adenocarcinoma









“Cinematic rendering can accentuate subtle texture changes and improve tumor conspicuity relative to traditional 2D images, 3D volume rendering, or maximum intensity projection images. Cinematic rendering may be able to enhance the visualization of spatial relationships among the tumor and adjacent vasculature, differentiating true tumor infiltration from simple proximity to vessels. This can potentially improve the assessment of resectability and assist in determining optimal vascular reconstruction options.”

Pancreatic ductal adenocarcinoma staging: a narrative review of radiologic techniques and advances

Linda C. Chu, Elliot K. Fishman

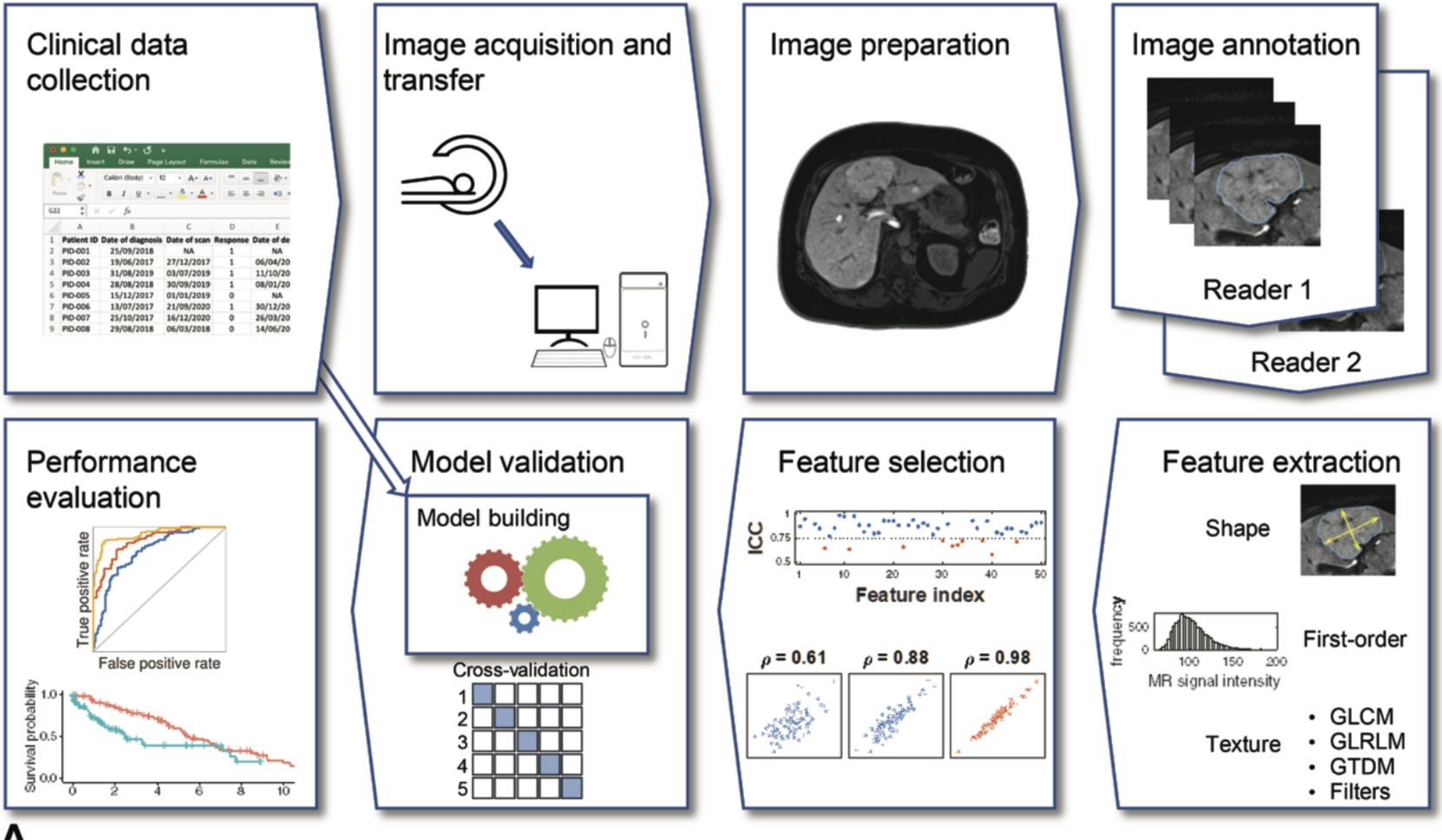
International Journal of Surgery (2024) 110:6052–6063

”Radiomics refers to the extraction of mineable high-dimensional data from radiologic images and has been applied within oncology to improve diagnosis and prognostication with the aim of delivering precision medicine. The premise is that imaging data convey meaningful information about tumor biology, behavior, and pathophysiology and may reveal information that is not otherwise apparent to current radiologic and clinical interpretation.”

Radiomics in Oncology: A Practical Guide

Joshua D. Shur, et al.

RadioGraphics 2021; 41:1717–1732



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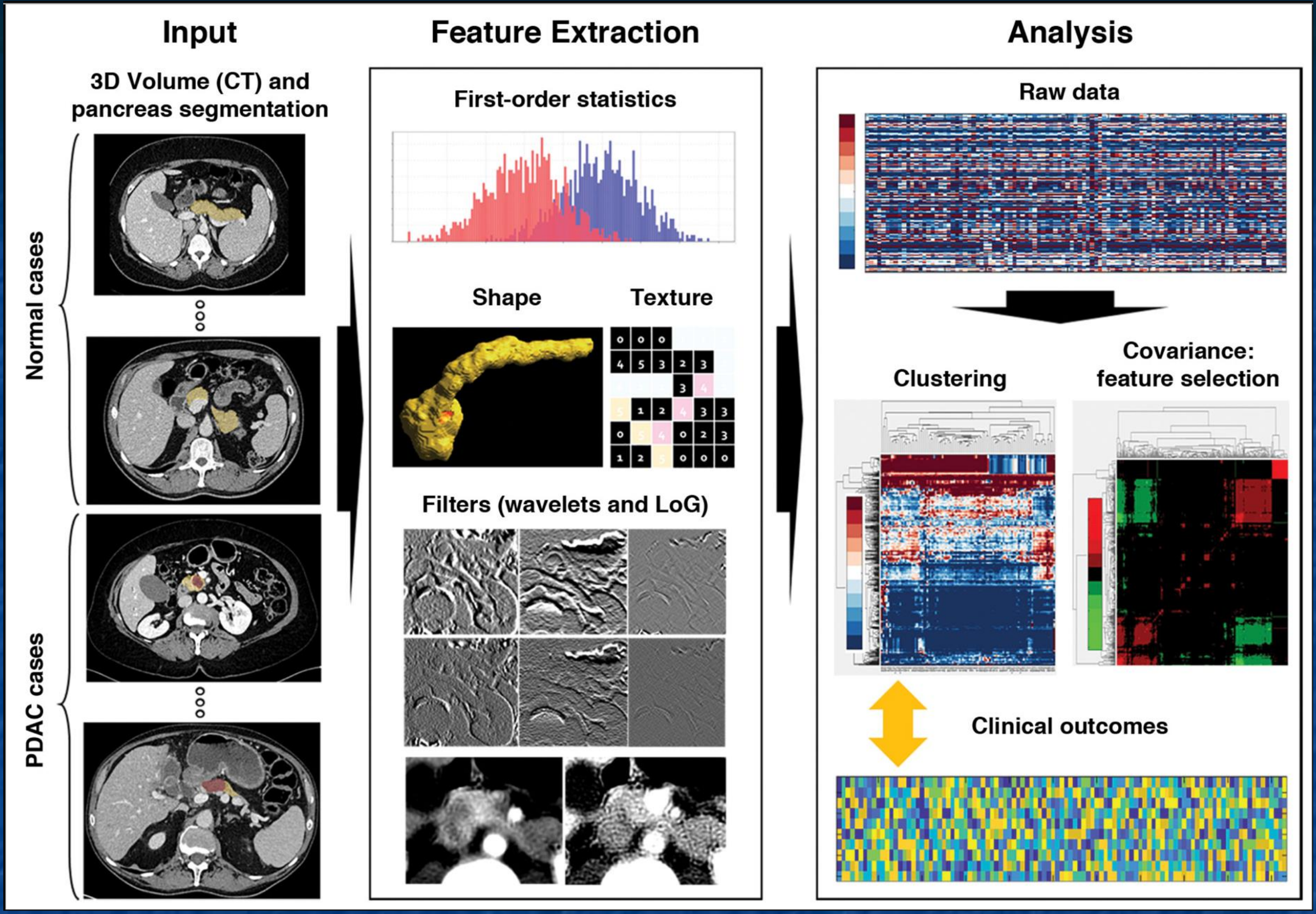


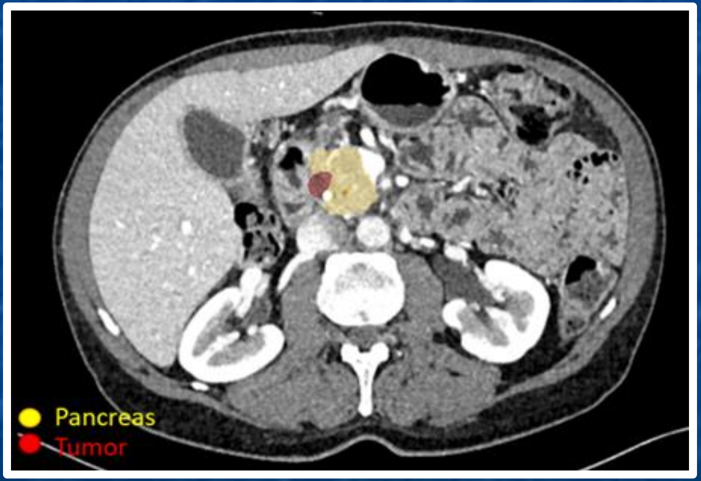
Utility of CT Radiomics Features in Differentiation of Pancreatic Ductal Adenocarcinoma From Normal Pancreatic Tissue.

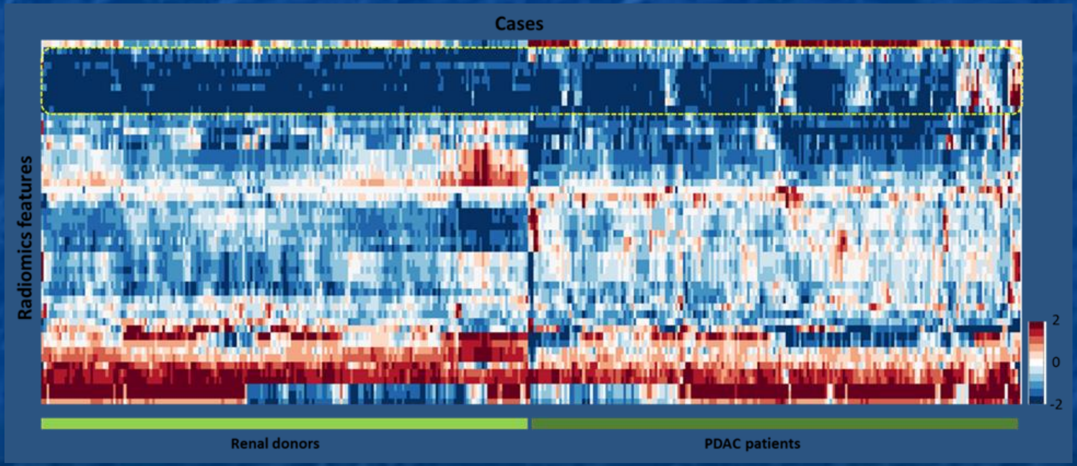
Chu LC, Park S, Kawamoto S, Fouladi DF, Shayesteh S, Zinreich ES, Graves JS, Horton KM, Hruban RH, Yuille AL, Kinzler KW, Vogelstein B, Fishman EK.

AJR Am J Roentgenol. 2019 Aug;213(2):349-357.

Detection of PDAC

- Extracted 478 radiomics features from CTs of whole 3D pancreas volume to differentiate 190 PDAC vs. 190 normal controls





Chu LC et al. AJR

Detection of PDAC

- 40 radiomics features were selected for random forest classifier
- Validation dataset (n = 125)
  - 60 PDAC + 65 normal controls
- Overall accuracy: 99.2% (124/125)
- Sensitivity: 100% (60/60)
- Specificity: 98.5% (64/65)

Radiomics features can achieve high accuracy in detection of PDAC

“Radiomics converts imaging data into high-dimensional features that can be used to characterize spatial heterogeneity inherent in disease processes. The features of radiomics can be classified into signal intensity, shape, and texture. Signal intensity (first-order) features are derived from histograms of individual voxel signal intensities, providing measures of central tendency and shape of the distribution. Shape features are extracted from the three-dimensional surface of the region of interest. Texture features are calculated in three dimensions, considering the correlation of signal intensities of adjacent voxels. In addition, feature extraction may be performed after applying a secondary filter, such as a wavelet or Gaussian filter.”

Pancreatic ductal adenocarcinoma staging: a narrative review of radiologic techniques and advances

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International Journal of Surgery (2024) 110:6052–6063

Example of Pancreas Segmentation

JHMI case #0652 ($\mathrm{DSC} = 90.74\%$), axial view, slice #279

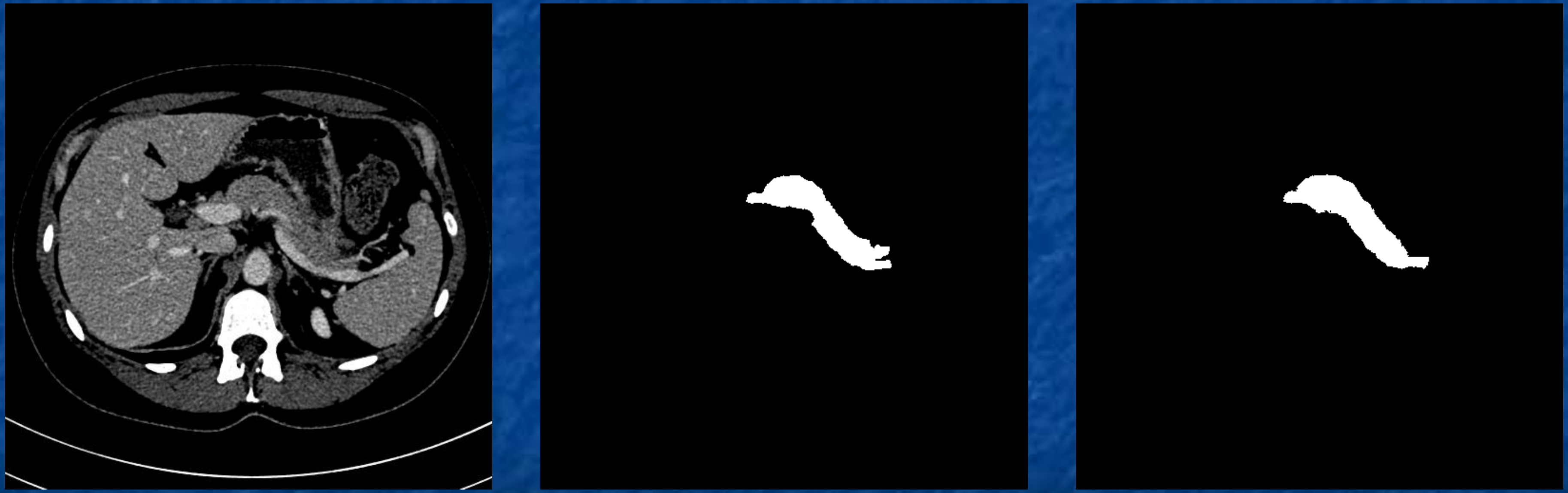
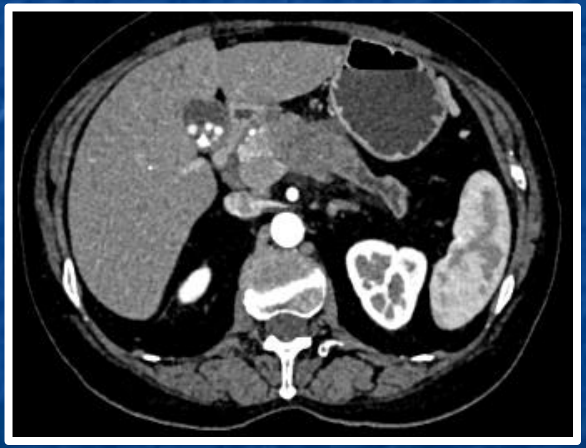


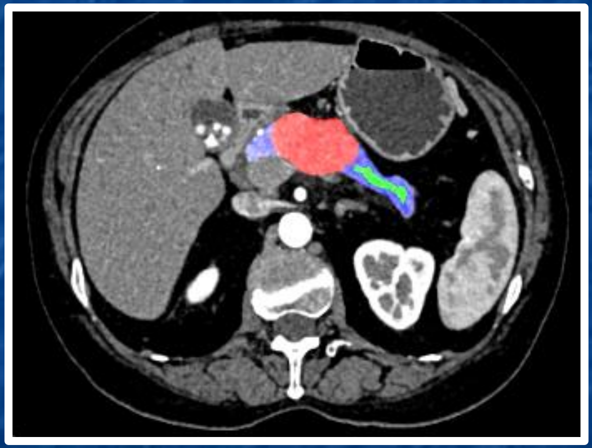
Image | Annotation | Prediction

Task: Recognizing Tumor

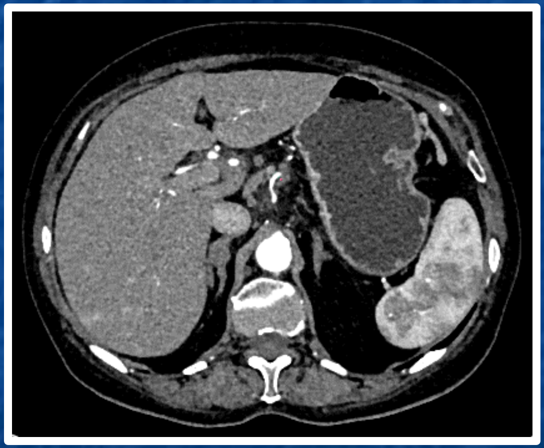
- We have developed a number of deep learning algorithms that can recognize pancreatic ductal adenocarcinoma based on abnormal shape and/or texture



Image



Deep Network Prediction

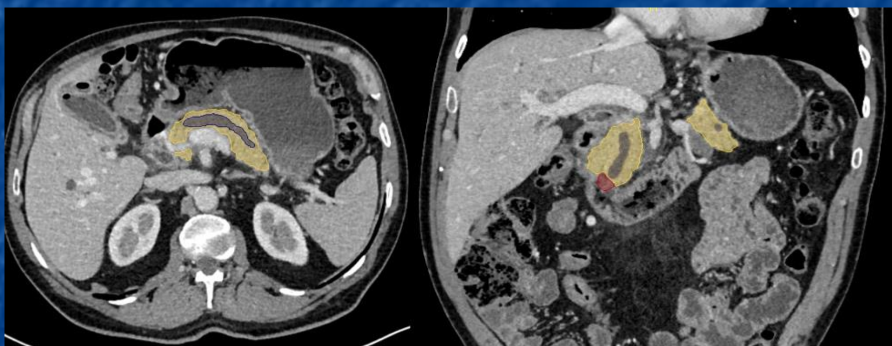


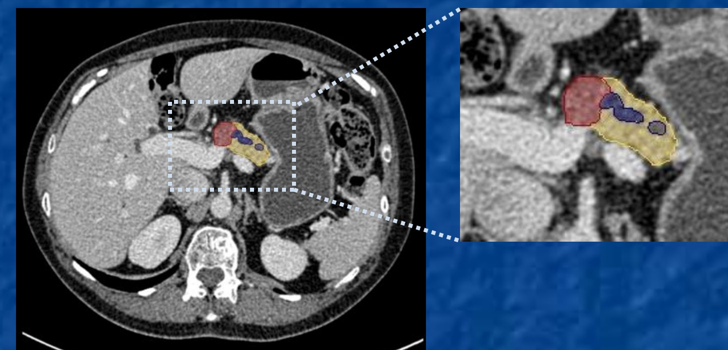
Deep Network Prediction

Tumor Prediction   Pancreas   Pancreatic Duct

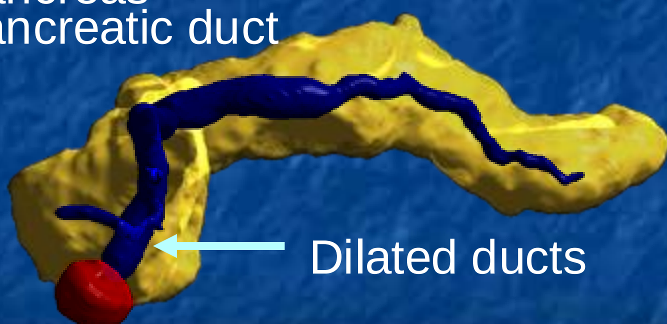
Liu F et al. arXiv:1804.10684. Zhu Z et al. arXiv:1807.02941.

PDAC Detection with Dilated Ducts





Tumor
Pancreas
Pancreatic duct



“Development of the algorithms using deep learning to automatically detect the pancreas and PDAC on CT scans is dependent on the quality of data input and therefore, it is vital to have high-quality annotated data to maximize their performance and clinical utility. The accuracy of manual segmenting the pancreas on CT images is one factor that can affect performance and reproducibility. Segmentation of the pancreas and other abdominal organs for supervised learning in particular via the manual approach is tedious, time consuming, and requires experienced radiologists. Furthermore, it is operator dependent with inter-observer and intra-observer variability being recognized as issues for manual segmentation.”

Deep neural network-based segmentation of normal and abnormal pancreas on abdominal CT: evaluation of global and local accuracies.

Kawamoto S, Zhu Z, Chu LC, Javed AA, Kinny-Köster B, Wolfgang CL, Hruban RH, Kinzler KW, Fouladi DF, Blanco A, Shayesteh S, Fishman EK.

Abdom Radiol (NY). 2024 Feb;49(2):501-511

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Pancreatology xxx (xxxx) xxx

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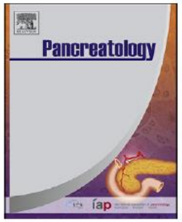


Performance of explainable artificial intelligence in guiding the management of patients with a pancreatic cyst

Juan M. Lavista Ferres [a, 1], Felipe Oviedo [a, 1], Caleb Robinson [a], Linda Chu [b], Satomi Kawamoto [b], Elham Afghani [d], Jin He [e], Alison P. Klein [d, f, h], Mike Goggins [h], Christopher L. Wolfgang [c], Ammar A. Javed [c], Rahul Dodhia [a], Nick Papadopolous [f, g], Ken Kinzler [f, g], Ralph H. Hruban [h], William B. Weeks [a], Elliot K. Fishman [b, 2], Anne Marie Lennon [b, d, e, f, g, *, 2]

[a] AI for Good Lab, Microsoft Corporation, 4330 150th Ave NE, Redmond, WA, 98052, USA
[b] Department of Radiology, Johns Hopkins University, 1800 Orleans Street, Baltimore, MD, 21287, USA
[c] Department of Surgery, New York University School of Medicine, NYU, New York, NY, 10016, USA
[d] Department of Medicine, Johns Hopkins University, 1800 Orleans Street, Baltimore, MD, 21287, USA
[e] Department of Surgery, Johns Hopkins University, 1800 Orleans Street, Baltimore, MD, 21287, USA
[f] Sidney Kimmel Comprehensive Cancer Center, Department of Oncology, Johns Hopkins University, 1800 Orleans Street, Baltimore, MD, 21287, USA
[g] Ludwig Center and Howard Hughes Medical Institute at the Sidney Kimmel Cancer Center, Johns Hopkins University, 1800 Orleans Street, Baltimore, MD, 21287, USA
[h] The Sol Goldman Pancreatic Cancer Research Center, Department of Pathology, Johns Hopkins University, 1800 Orleans Street, Baltimore, MD, 21287, USA

Explainable Boosting Machines

EBM is an interpretable model developed at Microsoft Research[*]. It uses modern machine learning techniques like bagging, gradient boosting, and automatic interaction detection to breathe new life into traditional GAMs (Generalized Additive Models).

GAMs are simply a class of statistical Models in which the usual Linear relationship between the Response and Predictors are replaced by several Nonlinear smooth functions to model and capture the Non linearities in the data.

Classification Performance (AUROC)					
Model	heart-disease (303, 13)	breast-cancer (569, 30)	telecom-churn (7043, 19)	adult-income (32561, 14)	credit-fraud (284807, 30)
EBM	**0.916**	**0.995**	**0.851**	**0.928**	0.975
LightGBM	0.864	0.992	0.835	**0.928**	0.685
Logistic Regression	0.895	**0.995**	0.804	0.907	0.979
Random Forest	0.89	0.992	0.824	0.903	0.95
XGBoost	0.87	**0.995**	0.85	0.922	**0.981**

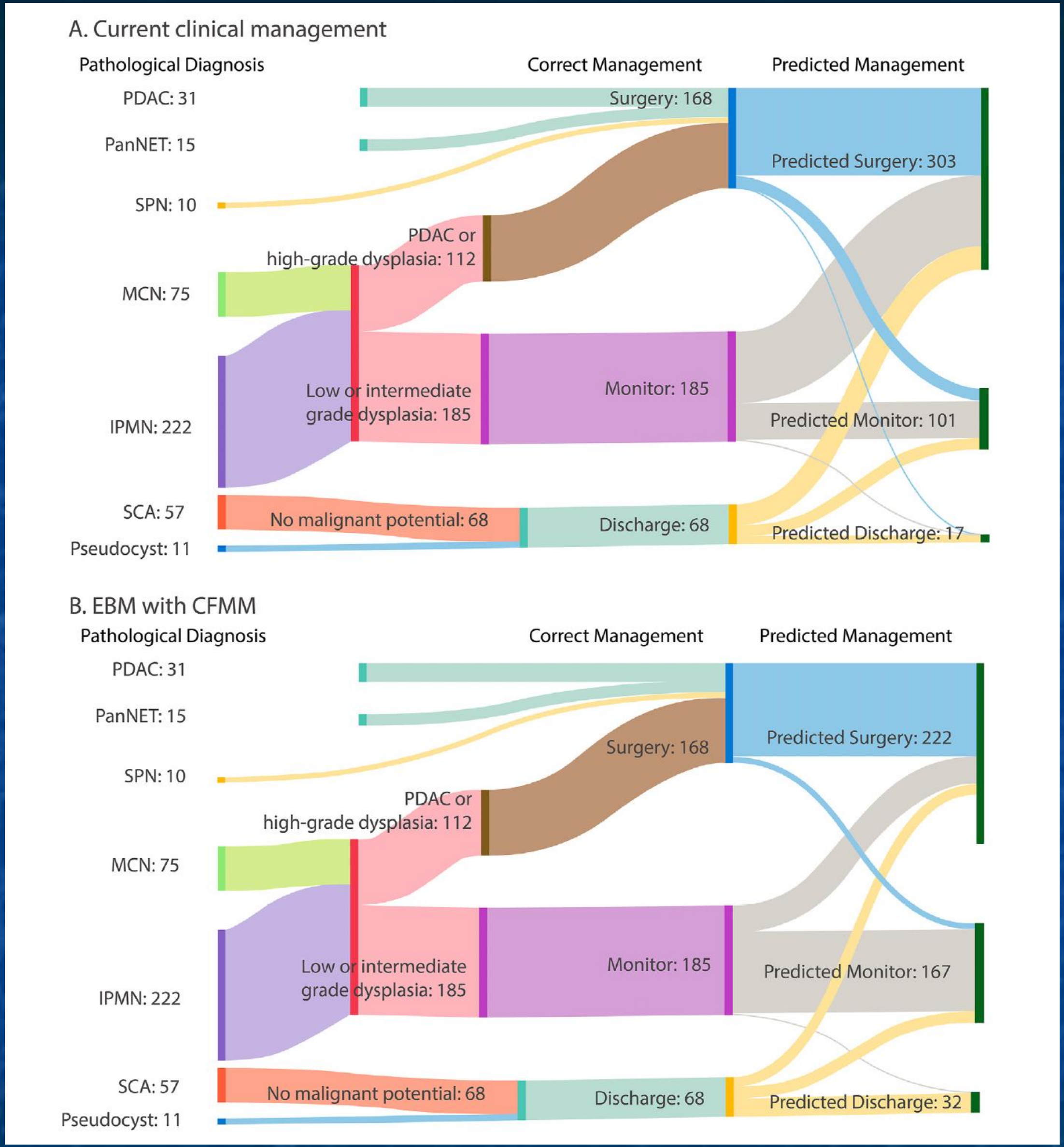
Figure 3: Classification performance for models across datasets (rows, columns).

$$y = a_0 + a_1 \cdot f_1(x_1) + \ldots + a_k \cdot f_k(x_k)$$

AI for Good Lab

Current

EBM



Performance of explainable artificial intelligence in guiding the management of patients with a pancreatic cyst.
Lavista Ferres JM, Oviedo F, Robinson C, Chu L, Kawamoto S, Afghani E, He J, Klein AP, Goggins M, Wolfgang CL, Javed AA, Dodhia R, Papadopolous N, Kinzler K, Hruban RH, Weeks WB, Fishman EK, Lennon AM.
Pancreatology. 2024 Sep 2:S1424-3903(24)00730-0. doi: 10.1016/j.pan.2024.09.001. Epub ahead of print. PMID: 39261223.

Microsoft

Results

Having genetic data improves =
- 7pts more accuracy in discharge
- 9pts more accuracy in monitoring
- 16pts more accuracy in surgery

Our EBM with biopsy improves versus clinical standard of care
- 5pts more accuracy in discharge
- 20pts more accuracy in monitoring
- 24pts more accuracy in surgery

If our model generalizes it could have
- Send 11 patients that needed surgery to surgery (7.5% improvement)
- Discharge correctly an additional 18 patients (138% improvement)
- Send correctly to monitor an additional 76 patients (122% improvement)
- Avoid 92 unnecessary surgeries (59% reduction)
- Reduce in 2 the number of discharge patients that require monitoring (from 3 to 1)

"The results are even more striking when compared with clinical care. In this test cohort of patients, all of whom underwent surgical resection, use of the EBM with CFMM model decreases the number of unnecessary surgeries by 59 % (n=92), increases the number of correct surgeries by 7.5 % (n=11), better identifies patients who truly require monitoring by 122 % (n=76), and increases the number of patients correctly classified as being safe to discharge by 138 % (n=18) compared to clinical care. Overall, in this cohort of patients the use of the EBM with CFMM could have changed the management of at least 25 % of patients."

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”What the introduction of AI algorithms might do, providing that data management and safety regulations are in place, is reduce the cost and time needed to diagnose the disease. This will enable health practitioners to spend more time developing efficient and holistic treatment protocols, and will make state-of-art diagnostics more affordable. Furthermore, AI can be a training tool that provides immediate specialist feedback to generalists so that, in time, they may perform at an expert level.”

The future of early cancer detection

Rebecca C. Fitzgerald et al.

Nature Medicine| VOL 28 | APRIL 2022 | 666–677

“Pancreatic cancer is a complicated disease with molecular heterogeneity. Integrating multiomics data, such as genomes, transcriptomics, proteomics, and metabolomics, can offer a complete picture of the disease pathology. Future research should concentrate on building artificial intelligence algorithms capable of assessing and combining these disparate datasets in order to uncover strong molecular signatures, biomarkers, and therapeutic targets for pancreatic cancer.”

From Machine Learning to Patient Outcomes: A Comprehensive Review of AI in Pancreatic Cancer.

Tripathi S, et al.

Diagnostics (Basel). 2024 Jan 12;14(2):174. doi: 10.3390/diagnostics14020174. PMID: 38248051;

Future of Pancreatic Imaging and Staging

- Improved scanning protocols
- Post processing techniques like Cinematic Rendering for better staging (3D mapping)
- Use of AI for image interpretation and tumor detection
- Use of radiomics for earlier detection as well as defining nodal involvement and in predicting resectability (staging)