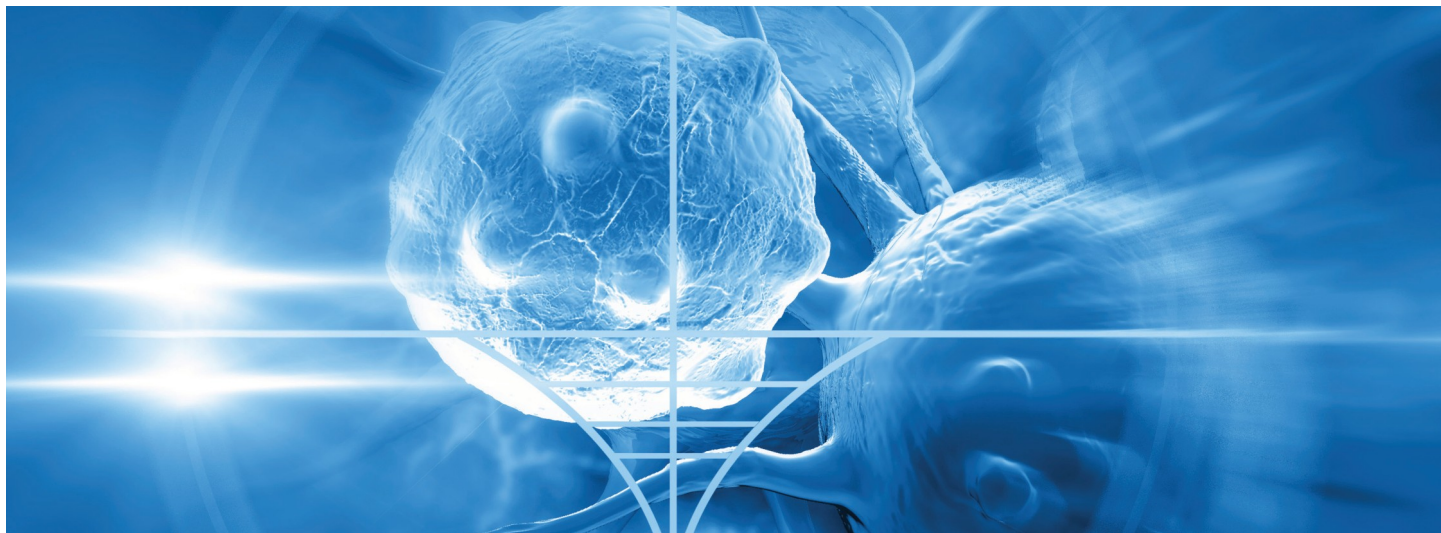


Immunotherapy and Imaging of Metastatic Pancreatic Adenocarcinoma

By Nisha Sainani, M.D., Board-Certified Radiologist · Updated for 2026 by Intrinsic Imaging



Pancreatic adenocarcinoma remains one of the most lethal cancers, with a five-year relative survival of 13% and a rising share of U.S. cancer deaths. After a decade in which checkpoint immunotherapy largely failed in this disease, the therapeutic landscape is finally changing: a new first-line chemotherapy regimen has been approved, and in 2026 an oral RAS inhibitor doubled overall survival in a Phase 3 trial of previously treated patients. These advances raise the stakes for imaging. Contrast-enhanced CT, MRI and FDG-PET/CT must deliver staging and response data that are standardized, reproducible and interpretable under the right criteria, including iRECIST when immunotherapy is involved.

Metastatic Pancreatic Adenocarcinoma

An estimated 67,530 Americans will be diagnosed with pancreatic cancer in 2026, and 52,740 will die of it.¹ It is now the third leading cause of cancer death in the United States,² and its five-year relative survival is only 13%.¹ Complete surgical resection remains the only curative treatment, yet most tumors are locally advanced or metastatic at diagnosis, and the large majority of patients require systemic therapy.

That therapy is evolving. In 2024, FDA approved NALIRIFOX (liposomal irinotecan, oxaliplatin, leucovorin and fluorouracil) for first-line treatment of metastatic disease after the Phase 3 NAPOLI-3 trial improved median overall survival from 9.2 to 11.1 months compared with nab-paclitaxel and gemcitabine.³ Immune checkpoint inhibitors, by contrast, have benefited only the small subset of tumors with high microsatellite instability, fewer than 1% of cases.⁴ The most striking advance has come from targeting RAS, which is mutated in the great majority of these tumors. In the Phase 3 RASolute 302 trial, 500 previously treated patients received the oral RAS(ON) inhibitor daraxon-rasib or chemotherapy. Median overall survival was 13.2 versus

6.6 months (hazard ratio 0.40), and the objective response rate was 33.2% versus 11.8%.⁵ Trials combining targeted agents, chemotherapy and immunotherapy are now multiplying, and each depends on precise imaging.

Medical Imaging

Imaging is fundamental to diagnosis, staging and the assessment of treatment response. The principal modalities are contrast-enhanced CT, contrast-enhanced MRI and FDG-PET/CT.

Computed Tomography

Multiphase, pancreas-protocol CT is the modality of choice for diagnosis, staging and response monitoring. It shows the primary tumor and its relationship to the adjacent vessels while surveying local and distant spread. Pancreatic carcinoma typically appears as a hypoattenuating mass, although approximately 10% of tumors are isoattenuating to normal parenchyma. In those cases, indirect signs such as abrupt cutoff of a dilated pancreatic duct, upstream parenchymal atrophy and biliary dilatation point to the lesion. CT also classifies tumors as resectable, borderline or unresectable by defining the extent

and degree of vascular involvement. The consensus reporting template of the Society of Abdominal Radiology and the American Pancreatic Association standardizes these descriptions, a valuable discipline in multicenter trials.⁶

MRI

Gadolinium-enhanced MRI resolves equivocal CT findings and characterizes liver lesions suspicious for metastasis. Diffusion-weighted imaging helps detect small tumors and metastases, and MRI with gadoxetic acid has been reported to detect pancreatic liver metastases with a sensitivity of 85%, compared with 69% for CT.⁷

FDG-PET/CT

FDG-PET/CT distinguishes metabolically active tumor from benign tissue. High-quality CT remains superior for judging local resectability, but PET can reveal metastases missed by CT and distinguish post-treatment fibrosis or necrosis from viable tumor, making it more sensitive than CT for assessing response after chemotherapy or radiation. Standardized uptake values carry independent prognostic weight: tumors with distant metastases show higher uptake and shorter survival.⁸

Response Criteria for Immunotherapy

Response to cytotoxic and targeted therapy is measured with RECIST 1.1, under which tumor growth or a new lesion constitutes progression.⁹ Immunotherapy can behave differently. Tumors may enlarge transiently, or new lesions may appear, before durable shrinkage, a pattern known as pseudoprogression. A meta-analysis of checkpoint inhibitor trials placed its overall incidence at 6%, and below 10% across tumor and drug types.¹⁰ Uncommon as it is, misclassifying it as progression can end an effective treatment prematurely.

The RECIST Working Group addressed this in 2017 with iRECIST, which introduced "unconfirmed" progression (iUPD) that must

be confirmed on a subsequent scan, generally four to eight weeks later, before it becomes confirmed progression (iCPD). iRECIST is intended to complement RECIST 1.1, which remains the basis of primary efficacy endpoints in most trials.¹¹ It has largely replaced earlier immune-related criteria such as irRC and irRECIST.

Guidance for Sponsors

Imaging a pancreatic cancer trial

- **Standardize the protocol.** Specify multiphase pancreas-protocol CT, with MRI for equivocal liver findings, in the imaging charter.¹²
- **Use structured reporting.** Apply the SAR-APA template for resectability and vascular involvement.⁶
- **Choose the right criteria.** Use RECIST 1.1 for primary endpoints and iRECIST when immunotherapy is involved.^{9,11}
- **Plan for confirmation.** Build confirmatory scans into the schedule so that unconfirmed progression can be resolved.¹¹
- **Read centrally.** Independent, blinded central review reduces variability in multicenter trials.¹²

Summary

For the first time in many years, pancreatic cancer trials are producing meaningful survival gains. Combination regimens that pair chemotherapy, RAS inhibition and immunotherapy will demand imaging assessment that keeps pace with the biology of response. Standardized acquisition, structured reporting, the right response criteria and expert central review are now essential to executing these trials successfully.

About the Author

Dr. Nisha Sainani, a board-certified radiologist, wrote the original edition of this issue at Intrinsic Imaging. She completed her residency in diagnostic radiology in India and subspecialized in abdominal imaging and intervention at Harvard Medical School's Massachusetts General Hospital and Brigham and Women's Hospital in Boston, where she has held an academic appointment. She has published widely in the *American Journal of Roentgenology*, *Radiology* and *RadioGraphics*, has contributed chapters to radiology textbooks, and is a member of the Society of Gastrointestinal Radiologists, the American Roentgen Ray Society and the Radiological Society of North America.

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About Intrinsic Imaging, LLC

Headquartered in Bolton, Massachusetts, Intrinsic Imaging is an imaging CRO and core lab supporting Phase I–IV drug trials, medical device studies and AI/CAD validation studies. The company has completed three FDA Bioresearch Monitoring Program inspections, each with zero Form FDA 483 observations, and holds five BSI certifications: ISO 9001, ISO 13485, ISO 22301, ISO/IEC 27001 and ISO/IEC 27018. Its network of more than 1,000 board-certified, fellowship-trained physicians has supported trials at more than 4,000 sites in 64 countries.



Contact

Intrinsic Imaging, LLC
 580 Main Street, Suite 210
 Bolton, MA 01740
 Tel: +1 978-616-4650
Contact@IntrinsicImaging.com
www.IntrinsicImaging.com