GI13
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Alliance of Pancreatic Consortia (APaCC): Pre-diagnostic and early stage PDAC imaging repository project

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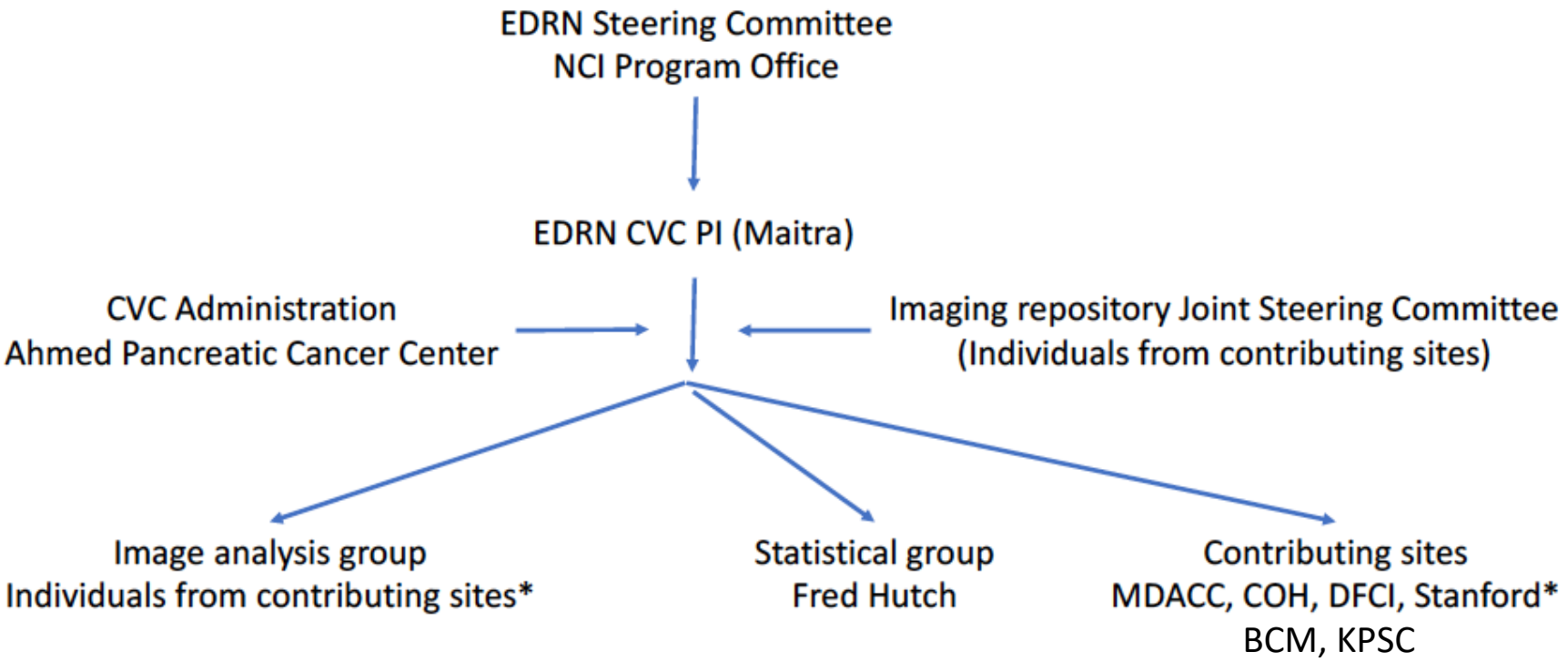
Specific aims

1. Establish a multi-institutional imaging repository for pre-diagnostic and early pancreatic cancer cases with clinical annotation
2. Validate quantitative imaging tools for early detection of pancreatic cancer

Aim 1:
EDRN prediagnostic and early stage PDAC imaging repository



*The initial participants are included in this proposal. The imaging repository is expected to grow and include more contributing sites and imaging researchers over time.

Estimated sample size for pre-diagnostic cohort and controls

Institution	Pre-diagnostic cases	Control 1	Control 2
MD Anderson	100	100	50
COH	40-80	40-60	20-40
BCM	200-300	100	100
Stanford	250	250	150
DFCI	350	1000	1000
UPMC	300	100	100
KPSC	50-100	100	100
Total	1300-1600	~1600	~1500

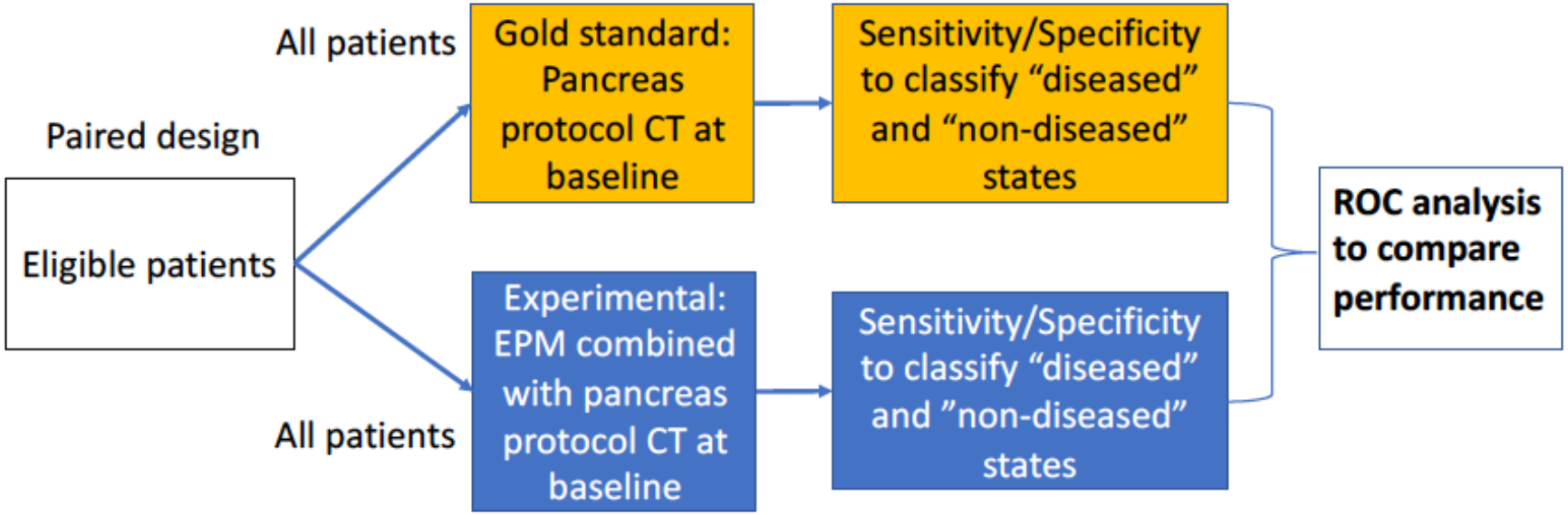
Control 1: Patients with a single CT or MRI scan with no cancer diagnosis who have the following info: age at time of scan, gender, race (roughly categorized), IV contrast (yes/no), and year of scan.
Control 2: Patients with serial CT or MRI scans with no cancer diagnosis who have the same info as Group 1.

Estimated sample sizes for early stage cohort and controls

Institution	Early stage cases	Control 1	Control 2	Control 3	Control 4
MD Anderson	200	100	1000	Dozens	Dozens
COH	100	Dozens	Hundreds	Dozens	Dozens
BCM	150	1000	500	1000	100
Stanford	135	135	135	135	135
DFCI	~200	1000	1000	500	500
UPMC	400	200	500	50	50
KPSC	50-100	50	50	50	50
Total	1200-1300	2000-2500	2000-3000	1500-2000	700-900

Control 1: Patients with no pancreatic lesions
Control 2: Patients with benign pancreatic cysts (mucinous and non-mucinous)
Control 3: Patients with acute pancreatitis and no PDAC
Control 4: Patients with chronic pancreatitis and no PDAC

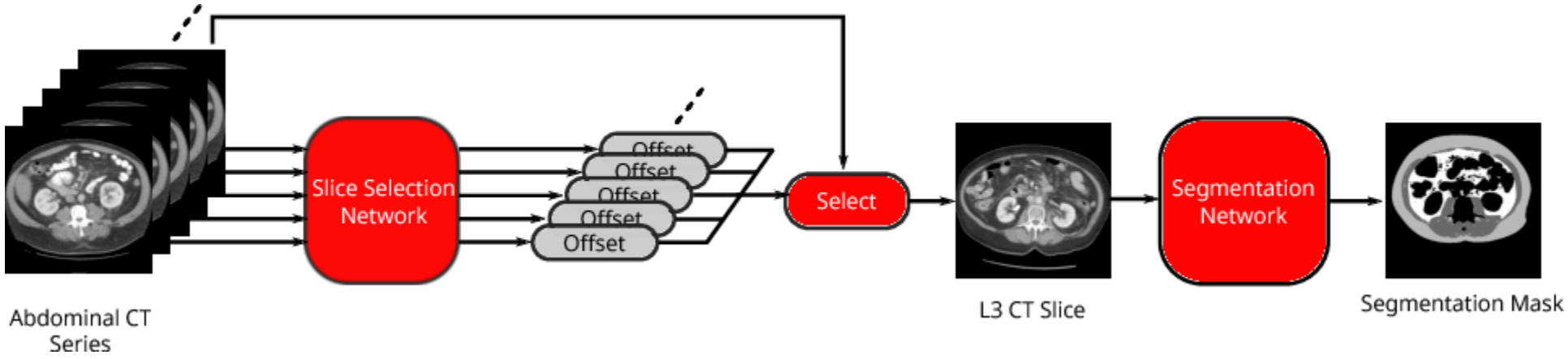
Aim 2:
Primary pancreas lesion evaluation

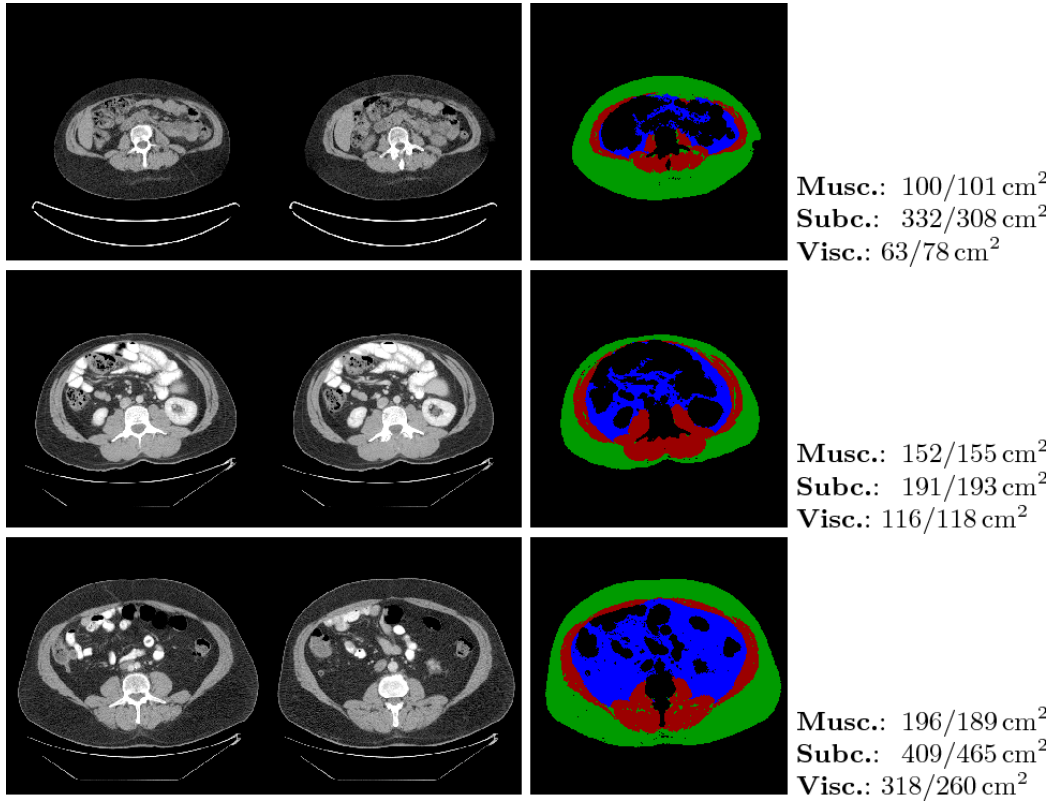


*Patient-based and lesion-based sensitivity/specificity
"Diseased" = pathologically confirmed PDAC
"Non-diseased" = no PDAC

- Null hypothesis: 0.75/0.85 for sensitivity/specificity
- With 120 cases, the power to reject the null hypothesis for sensitivity is 83%/>99% if the true sensitivity of the experimental procedure is 85%/90%.
- With 800 controls, the power to reject the null hypothesis for specificity is >99% if the true specificity of the experimental procedure is 90%.

Aim 2: Body compartment measurements



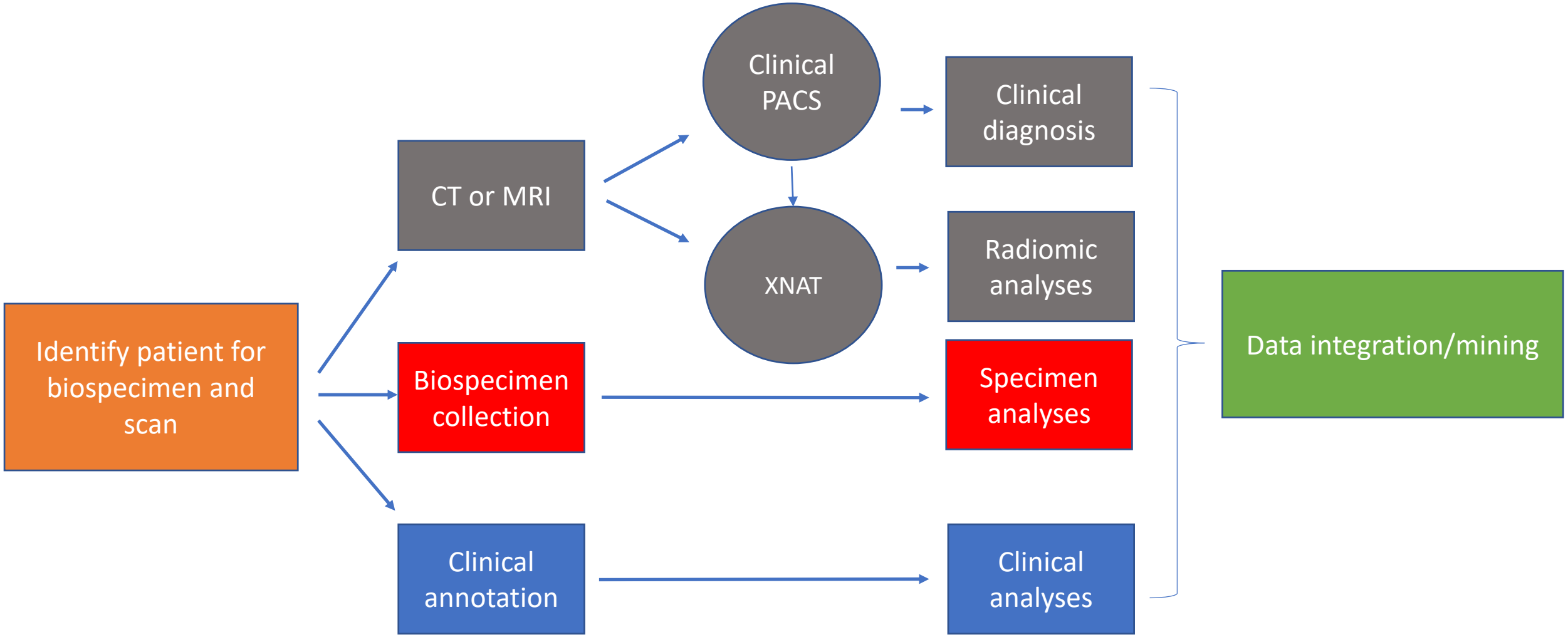


Two step process:

1. DenseNet to select CT slice
2. U-Net for segmentation

Bridge, Rosenthal et al, 2018

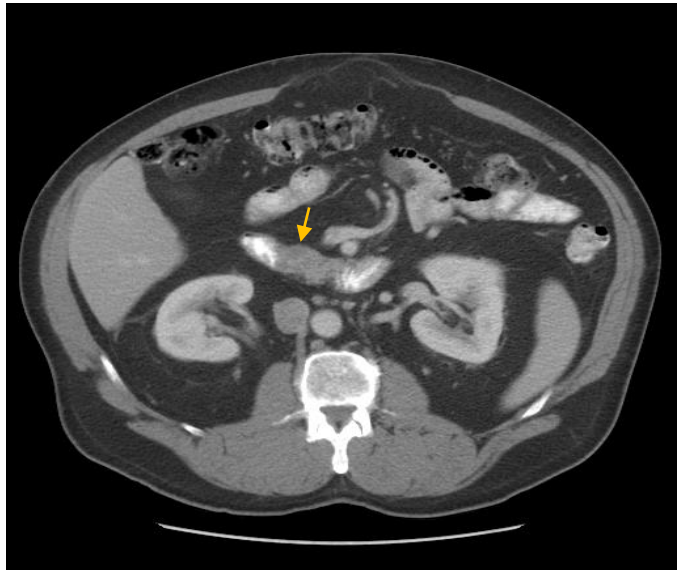
Informatics workflow

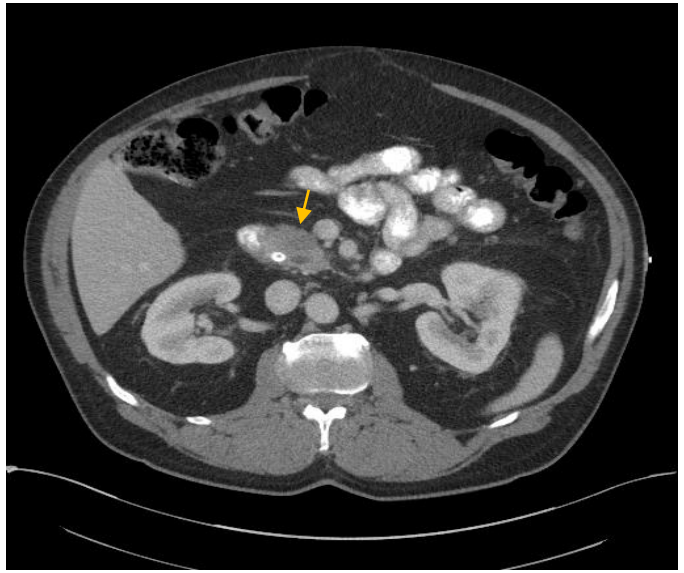


Pre-diagnostic scan

Diagnostic scan

High Delta

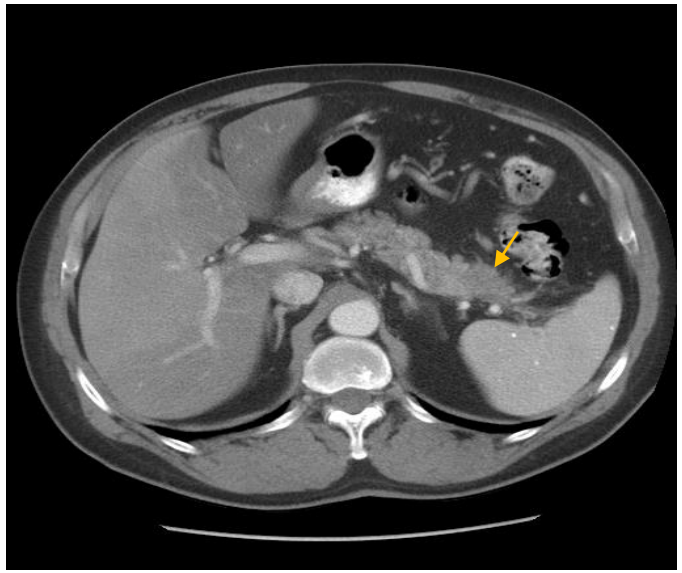


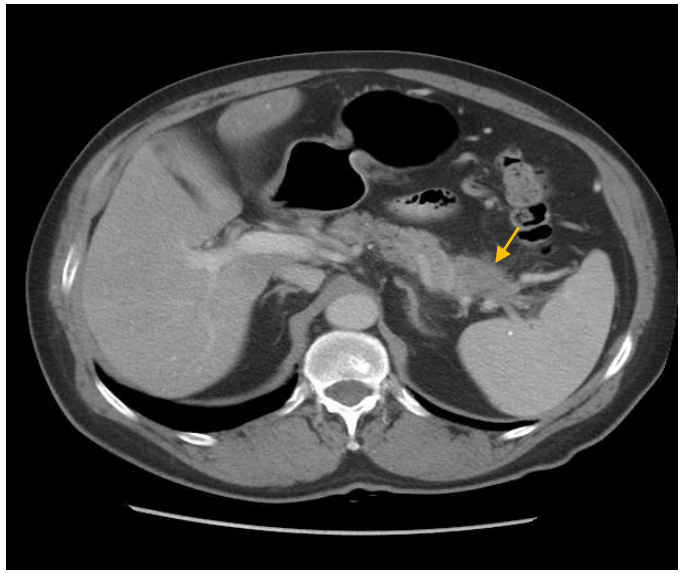


Longest diameter increase: 15.2% per month

Time between shown scans is 13.8 months

Low Delta





Longest diameter increase: 0.4% per month

Time between shown scans is 7.2 months

Modeling tumor growth for early detection: Gompertz function

The following form of Gompertz function was fit to tumor growth kinetics data:

$$X(t) = Ke^{\ln(\frac{X_0}{k})e^{-\alpha t}}$$

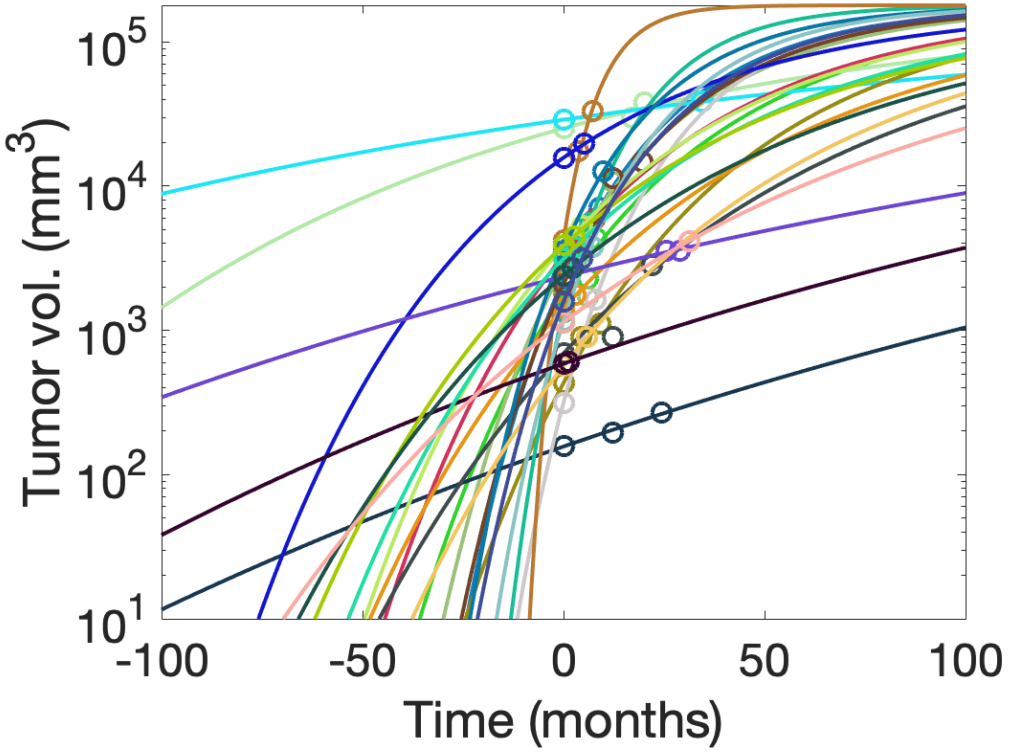
where, $X(t)$ is tumor size at time t, K is the tumor size as $t \to \propto$, α is the tumor growth rate constant, and X_0 is the size of the tumor at first observation.

The first derivative of the above function gives the tumor growth rate X':

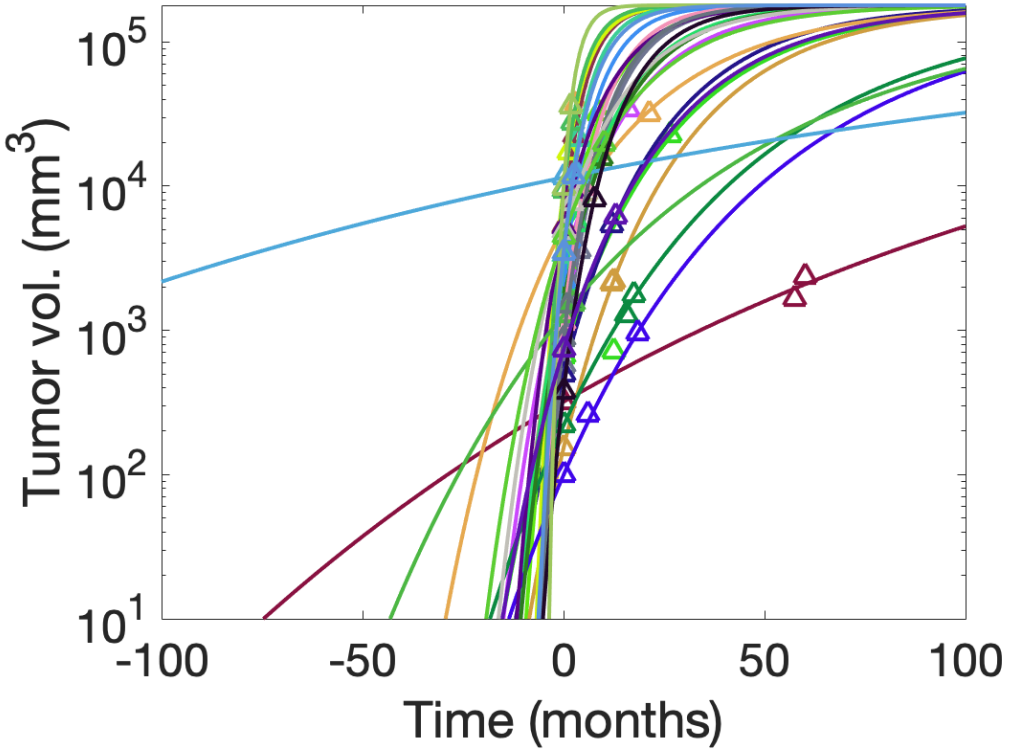
$$X'(t) = \alpha \log\left(\frac{K}{X(t)}\right) X(t)$$

Gompertz function fitting for low and high delta PDAC during pre-diagnostic period

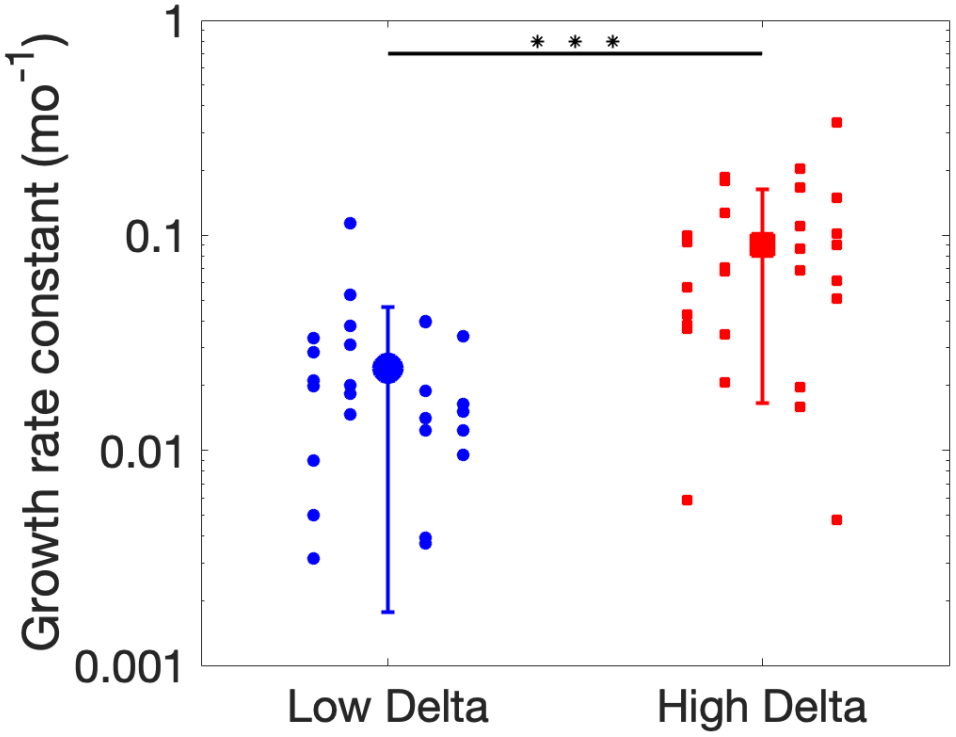
Low delta



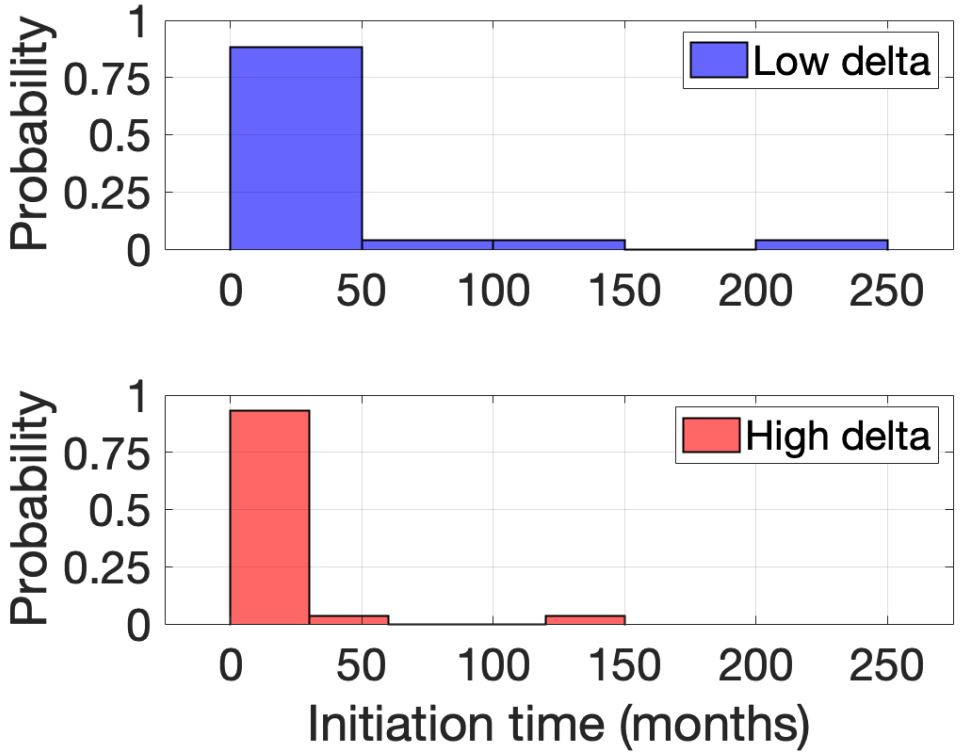
High delta



Differences in growth rates and predictions of time to detection



Probability distributions of backward predictions of time to growth from a single cell to a 1 cm^3 tumor



Ongoing work

- Biology of early detection of PDAC
  - Correlation of the growth rate parameter with changes in body compartments
  - Validation of the associations of the growth rates with high/low delta in multi-institutional repository
- Imaging repository for pre-diagnostic and early stage PDAC
  - Image transfer from participating sites to MDACC is occurring
  - Working with JPL to establish DMSA
  - Image analyses ongoing
  - Adding KPSC to the group

Summary

- EDRN PDAC imaging repository aims to serve immediate and long-term goals for collaborative research
- Initial applications will focus on changes in body compartments and on changes in the pancreas in the pre-diagnostic period
- Data transfer, image analyses, and addition of new sites are ongoing

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5 minute Q&A

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