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MD Anderson Cancer Center
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Quantitative imaging response metrics for hepatobiliary and pancreatic cancers

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AI for Predicting Response
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Overview: Imaging-based responses for Pancreatic and Hepatobiliary

- Clinical challenges
- Radiographic metrics of response
- Towards AI

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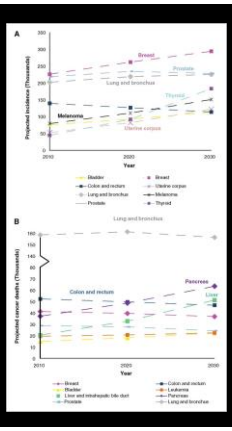


Increasing burden of pancreas and liver cancers

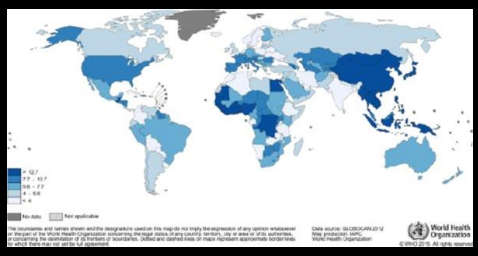
Rahib et al, Cancer Res 2014

Heterogeneity (variability) of cancer: a multi-faceted term

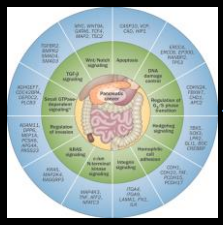
- Within the patient:
  - Intratumoral heterogeneity
- Among patients:
  - Molecular heterogeneity
  - Clinical heterogeneity
- Epidemiological heterogeneity
  - Individual country
  - Worldwide

These different sources of variability must be factored into the design and interpretation of response metrics

Epidemiological heterogeneity of HCC



Multi-scale heterogeneity of PDAC



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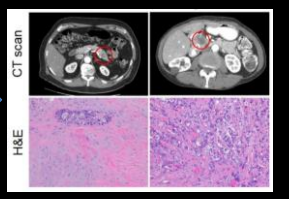
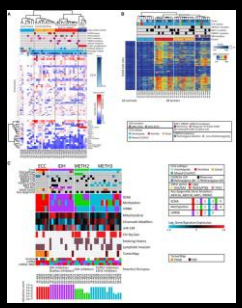


Molecular Cellular Microenvironment Patient

Molecular heterogeneity in cholangiocarcinoma



Kwong et al, Cell Rep, 2017

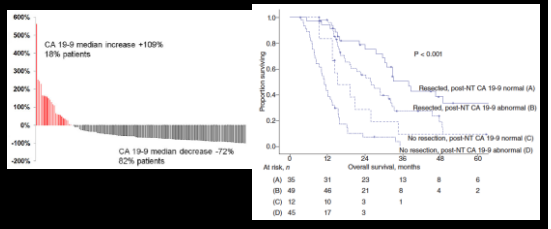
Overview: Imaging-based responses for Pancreatic and Hepatobiliary

- Clinical challenges
- **Radiographic metrics of response**
- Towards AI

Pancreatic cancer responses

- CA19-9 only FDA approved biomarker for PDAC
- CEA also has been associated with response
- RECIST not predictive of survival in PDAC (Katz et al 2012)
- Perfusion, morphological changes, diffusion weighted imaging, and body composition changes associate with response

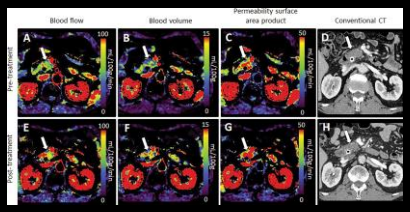
Changes in CA19-9 as a marker of response to neoadjuvant therapy



Tzeng et al, HPB 2014

*CA19-9 is the only FDA approved biomarker of PDAC

Perfusion CT for pancreatic cancer

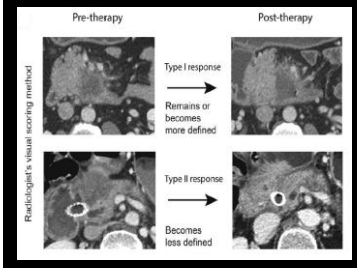


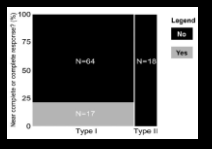
Parameter and Response Group	Before CRT	After CRT	*P* Value
Blood flow (mL/100 g/min)			
Responders ($n = 8$)	44 (39–64)	54 (42–73)	.04
Nonresponders ($n = 10$)	33 (16–52)	43 (28–53)	.06
Blood volume (mL/100 g)			
Responders	4.3 (3.7–6.9)	6.8 (4.7–9.6)	.01
Nonresponders	2.8 (1.8–6.8)	4.8 (2.6–7.4)	.06
PSP (mL/100 g/min)			
Responders	26 (19–32)	32 (26–43)	.05
Nonresponders	20 (10–35)	28 (19–38)	.10

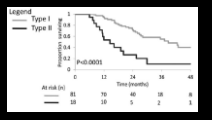
- 18 pts with pre- & post-tx CTs
- Categorized by path response
- Pre and post blood flow differed in responders/non-responders

Hamdy et al. Radiology 2019

CT-based morphological responses of pancreatic cancer

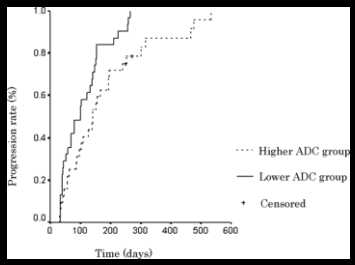






Amer et al., Cancer 2018

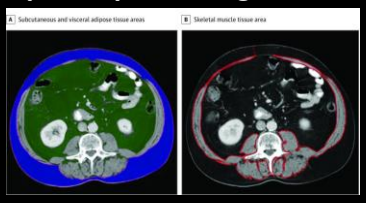
DWI for pancreatic cancer



- 63 patients with advanced PDAC
- Treated with gemcitabine
- Progression assessed at 3 and 6 months
- Lower ADC had shorter time to progression

Niwa et al, BJR 2008

Anthropomorphic changes in PDAC



- Sarcopenia and sarcopenic obesity previously shown to associate with poor outcomes
- 193 patients at 4 institutions, BRPC or LAPC
- All received neoadjuvant therapy
- Evaluated resection rates and changes in body composition

Sandini et al, JAMA Surg 2018

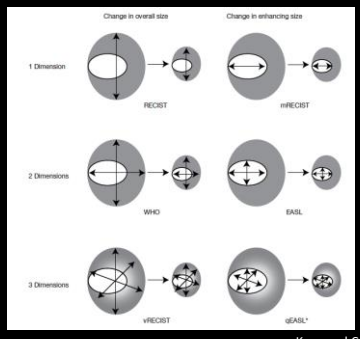
Diagnostic Performance of Variables Independently Associated With Resection at Multivariate Analysis and Accuracy of Calculated Cutoff Points

Predictor	AUC	Optimal Cutoff Point	Sensitivity, %	Specificity, %	Adjusted OR (95% CI)	*P* Value
Δ TAMA	0.711	+4 cm^2/m^2	63.2	75.9	3.7 (1.5-9.6)	.006
Tumor size post-NT	0.697	30 mm	70.4	64.2	4.7 (2.4-37.1)	<.001

Abbreviations: AUC, area under the curve using receiver operating characteristic curve method; NT, neoadjuvant treatment; OR, odds ratio; TAMA, total abdominal muscle area.

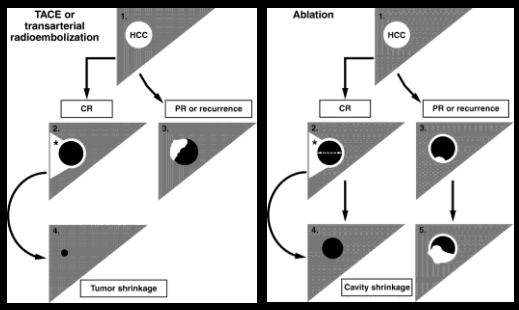
Sandini et al, JAMA Surg 2018

Response criteria for hepatobiliary



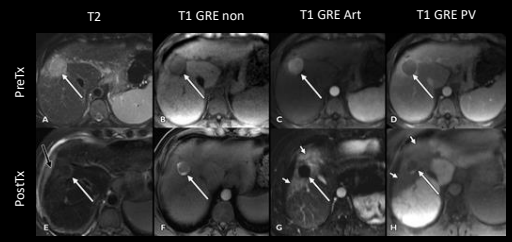
Koay and Crane, HBSN 2017

HCC radiographic responses



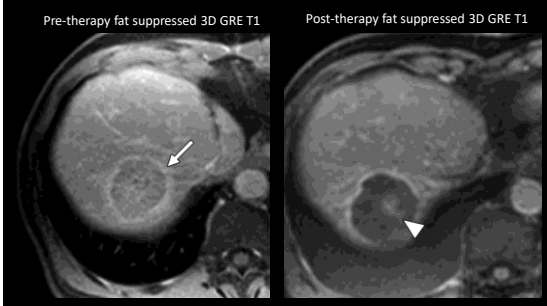
Yaghmai et al, AJR 2013

56 year old with HCC, s/p TACE, SBRT



Yaghmai et al, AJR 2013

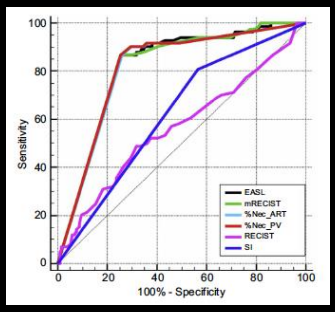
HCC radiographic response to Y90



72 year old male with HCC

Yaghmai et al, AJR 2013

HCC response metrics



- 61 patients, 97 HCC lesions
- TACE + Ablation or Y90
- All underwent transplant
- Measured complete path necrosis (CPN)
- Evaluated different response metrics
- Subtraction, EASL, mRECIST predicted CPN

Gordic et al, J Hepatol 2017

Overview: Imaging-based responses for Pancreatic and Hepatobiliary

- Clinical challenges
- Radiographic metrics of response
- **Towards AI**

Just like biomarker cohorts, imaging cohorts need to ensure good representation

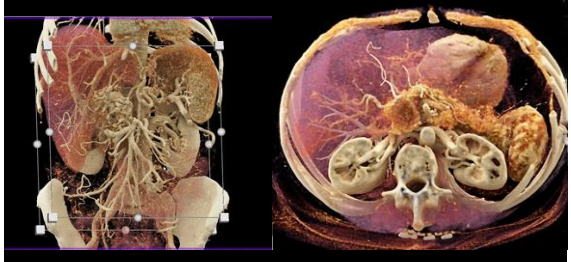
Considerations with machine learning and potential path forward

- Considerations: gender, ethnicity, risk factors, imaging modalities, manufacturer, reconstruction algorithms
- Path forward: ensure entire spectrum is well represented

Potential applications of AI

- Radiographic:
  - Direct visualization of a tumor mass and its morphology
  - Anthropomorphic measurements
- Combined:
  - Clinical and radiographic approaches

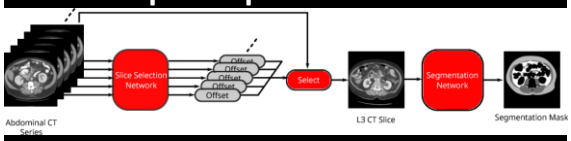
AI for pancreatic imaging

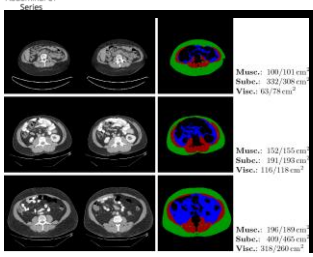


1000 healthy and 1100 pancreatic cancer cases
Deep learning to improve detection of pancreatic cancer

Elliot Fishman et al, JHMI Felix Project

Anthropomorphic measurements

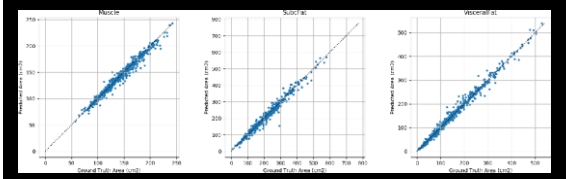




Two step process:
1. DenseNet to select CT slice
2. U-Net for segmentation

Bridge, Rosenthal et al, 2018

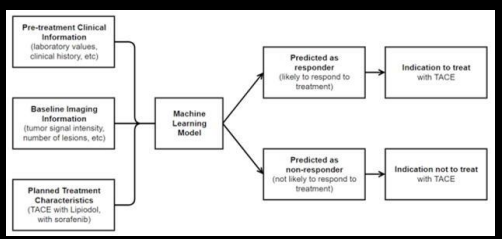
Anthropomorphic measurements using convolutional neural networks



- Dice scores 0.95-0.98
- Correlation coeff 0.99

Bridge, Rosenthal et al, 2018

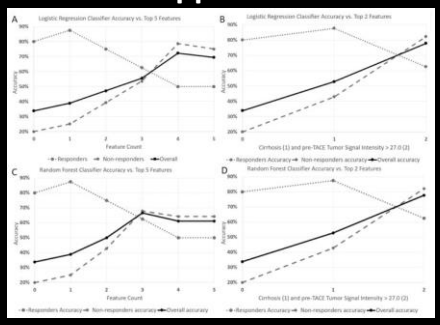
Combined approach for HCC



- 36 patients treated with TACE
- Considered clinical, imaging, and treatment details
- Logistic regression and random forest models used to predict responders and non-responders

Abajian et al, J Vasc Interv Radiol 2019

Combined approach for HCC



Abajian et al, J Vasc Interv Radiol 2019

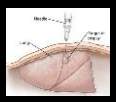
bi·o·mark·er
ˈbīōˌmärkər/

- NCI: "Objective indications of medical state observed from outside the patient – which can be measured accurately and reproducibly"

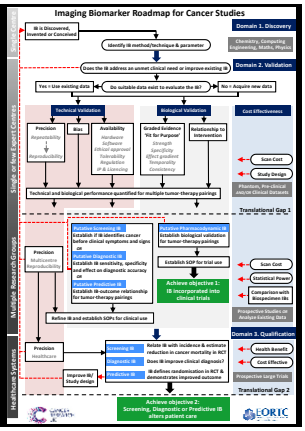




Proteins, exosomes, ctDNA, cfDNA, miRNA, noncoding RNA, metabolites, CTCs, microbiome, immune profiling…



Imaging biomarker: Does it address an unmet need?



Future Directions

- Consortia for early detection of PDAC and liver cancers
- Integration of multiparametric signals
- Novel imaging modalities

Summary: Prognostic imaging biomarkers exist, AI may improve implementation

- Quantitative and semantic imaging features have been identified for pancreatic and hepatobiliary cancers
- Implementation of AI so far has been limited but appears promising
- Development of AI approaches needs to consider sources of bias

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Questions
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