Overview: Imaging-based responses for Pancreatic and Hepatobiliary

• Clinical challenges
• Radiographic metrics of response
• Towards AI

Disclosures

• Sponsored research agreement with Philips Healthcare
• Royalties from Taylor and Francis LLC for book
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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

Molecular heterogeneity in cholangiocarcinoma

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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

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

Tzeng et al, HPB 2014
**Perfusion CT for pancreatic cancer**

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

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**CT-based morphological responses of pancreatic cancer**

Amer et al., Cancer 2018

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**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

Response criteria for hepatobiliary

Koay and Crane, HBSN 2017
HCC radiographic responses

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

HCC radiographic response to Y90

72 year old male with HCC
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, EAVI, mRECEST predicted CPN

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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

Garbage in (biased data) → Perfect model → Garbage out (biased answer)

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 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

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

Bridge, Rosenthal et al, 2018
combined approach for HCC

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• NCI: “Objective indications of medical state observed from outside the patient — which can be measured accurately and reproducibly”

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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