Interactive Exhibit On Imaging Updates For Staging And Response Assessment In Pancreatic Cancer

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Introduction

- Pancreatic ductal adenocarcinoma (PDAC) is deadly cancer with **lowest 5-year-survival**
- Prognosis remains poor with 1-year survival rate of 20% and 5-year survival rate of 7.2%, as majority (50%) of the patients present with metastatic disease.
- **Surgical resection** offers the only cure for PDAC in a **minority of patients (15-20%)** as tumor has invaded into crucial adjacent structures.
- Imaging has assumed a crucial role in helping to stratify patients to **stage-appropriate therapies** and successful patient management.

**Learning objectives of this exhibit are to-**

1. Review the recent surgical and other **therapeutic advances** in PDAC
2. Describe imaging implications of local **tumor staging and structured reporting**
3. Discuss role of **imaging biomarkers** in assessment of treatment response
**Vascular Involvement:**

Vessels closely related to pancreas are of critical importance for resectability and include –

- **Venous**- Portal vein (PV), Superior mesenteric vein (SMV), Inferior vena cava (IVC)
- **Arterial**- Superior mesenteric artery (SMA), Hepatic artery (CHA), celiac axis (CA) and aorta

**Adjacent Structure Involvement:**

PDAC can directly invade *adjacent structures* (e.g. stomach, duodenum, adrenal gland and colon); However, if tumor extension can be *adequately and safely resected*, the tumor is considered as *borderline resectable*.

**Peri-neural Invasion:**

In head and uncinate process tumor, perineural invasion is seen, indicating *poor prognosis*.

However, this is a histopathological diagnosis and imaging cannot reliably detect this.

**Nodal Involvement:**

PDAC can also spread to *locoregional nodes* and commonly metastasizes (50% at presentation) to liver, peritoneum and lungs.
Surgical Treatment of PDAC

- In patients with resectable PDAC, surgical resection is considered the gold standard.
- **Tumor Location** determines the route of local spread of disease and type of resection
  - *Whipple’s procedure:* For pancreatic head PDAC’s resection of pancreatic head and duodenum with pancreatico-jejunostomy, hepatico-jejunostomy and gastro-jejunostomy is a standard procedure
  - *Distal pancreatectomy:* For Tumors in the body and tail region
- Survival benefits from surgery (15% -27% after complete resection) have led to the development of *novel venous and arterial reconstruction techniques.*
- These novel techniques have extended the surgical resection to patients with *limited degree* of vascular invasion, with *equivalent survival benefits*
Different types of venous reconstruction techniques can be used after excision of involved mesenteric/portal vein to preserve the portal blood flow.

(a) Resection with interposition IJV graft

(b) Primary anastomosis for short-segment resection

(c) Patch placement, for minimal venous involvement
Common Hepatic artery (CHA) flow must be preserved to avoid postoperative hepatic ischemia. Several surgical resection/reconstruction techniques can be used to achieve this objective in cases with limited arterial involvement.

Types of hepatic artery reconstruction. For a surgical reconstruction procedure to be possible, tumor must not involve the proximal one 1cm of the CHA as it originates from the CA. If tumor involvement is minimal (a), then a primary anastomosis of the existing CHA ends can be done. However, if the involved CHA segment is longer (b), then a vascular graft is needed.
**Appleby procedure** – This procedure allows en bloc resection of the proximal hepatic, celiac and splenic arteries in combination with a distal pancreatectomy. The *gastro-duodenal artery (GDA) must be preserved*, because perfusion of the liver is by retrograde flow through this vessel to the common hepatic artery.
Chemo-Radiation Therapy

- PDAC can be treated with different approaches depending on stage at presentation -
  - **Palliative chemotherapy**; traditionally including 5-FU and Gemcitabine-based regimens is used for metastatic PDAC.
  - **Adjuvant chemoradiation** (CT+RT) is indicated to decrease the risk of locoregional and metastatic recurrence, in patients with positive margins following surgery.
  - **Neo-adjuvant therapy** is indicated in patients with locally advanced/borderline disease at presentation.

- **Neo-adjuvant CT+RT with FOLFIRINOX** enhances the resection rate in patients with locally advanced cancers and borderline cancers.
- More recently adopted **more aggressive FOLFIRINOX** (5-fluorouracil, leucovorin, irinotecan and oxaliplatin) regimen has been reported to result in a higher median overall survival (11.1 months) compared to older gemcitabine-based regimens (6.8 months) in the palliative situation.
Multiphasic pancreatic protocol CT with imaging acquisition in the pancreatic phase and portal venous phase allows optimal local staging.

Modern contrast-enhanced MRI has been demonstrated to be equivalent to MDCT in detection and staging of PDAC.

MRI provides superior contrast resolution and lesion conspicuity and may be better than CT at detecting small cancers. A limitation of MRI however is the susceptibility to significant degradation by respiratory motion artifact.

Dynamic contrast enhanced phases for a pancreatic protocol (CT/MRI) includes

- **Pancreatic phase** (45-50 sec after intravenous contrast injection)
- **Portal venous phase** (60-70 sec after intravenous contrast injection)
- **Delayed phase** is used whenever required for characterization of focal liver lesions
• Pancreatic phase image (a) shows a hypoenhancing mass in the head region. Detection of the lesion is facilitated by the peak enhancement of pancreatic parenchyma.

• The pancreatic parenchymal phase image (b) from a different patient is showing good opacification of celiac artery facilitating the evaluation of tumor-vessel relationship.

• The portal venous phase image (c) shows a metastatic lesion in segment 7 of the liver with a background of enhancing liver parenchyma. This phase also delineates the relation of tumor with venous structures (SMV, PV, SV).
Standard Terminology: Vascular Involvement:

- **National Comprehensive Cancer Network (NCCN) guidelines** recommend standard terminology for vascular involvement, as vascular involvement has huge impact on resectability.

- **≤180° tumor contact** of the vessel circumference is described as “abutment” and is not considered a sensitive sign of vessel invasion.

- **>180° tumor contact** of the vessel circumference, an imaging sign of vascular invasion with a sensitivity of 84% and specificity of 98%, is referred to as “encasement”.

- **Additional findings suggestive of vessel invasion** are tumor causing deformity, narrowing and irregularity of vessels, direct invasion into a vessel, and thrombosis.
Standard Terminology: Vascular Involvement

Arterial tumor contact

≤ 180° tumor contact without deformity

>180° tumor contact without deformity

Tumor contact with deformity (arrow)

Venous tumor contact

≤ 180° tumor contact without deformity

>180° tumor contact without deformity

Tumor contact with deformity

Tear drop deformity (arrows)

Dashed line represents 180° circumference.
**Standard Terminology: Vascular Involvement**

- **Tumor abutting SMV (red arrow)**
- **Tumor abutment with both SMA and SMV**
- **>180° contact with CA (encasement)**
- **Occlusion of SMV with intraluminal thrombus**
- **Tumor contact with SMV with “tear drop” deformity**
- **Occlusion of portal venous confluence with collaterals**
## Local Staging

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<thead>
<tr>
<th>Local Stage</th>
<th>Arterial extent</th>
<th>Venous extent</th>
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<tbody>
<tr>
<td><strong>Resectable</strong></td>
<td>• No distant metastases&lt;br&gt;• Clear fat planes around the celiac axis (CA),&lt;br&gt;common hepatic artery (CHA), and SMA. (Figure 10)&lt;br&gt;• In case of pancreatic tail lesions the involvement of splenic artery is considered resectable</td>
<td>• No radiographic evidence of superior mesenteric vein (SMV) or portal vein (PV) distortion&lt;br&gt;• ≤180° contact without vein contour irregularity&lt;br&gt;• In case of pancreatic tail lesions the involvement of splenic vein is considered resectable</td>
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<td><strong>Borderline</strong></td>
<td><strong>Pancreatic head /uncinate process:</strong>&lt;br&gt;• Solid tumor contact with CHA without extension to CA or CHA bifurcation&lt;br&gt;• Solid tumor contact with the SMA of ≤180°&lt;br&gt;• Note accessory/replaced right hepatic artery &amp; replaced CHA with relation to tumor&lt;br&gt;<strong>Pancreatic body/tail:</strong>&lt;br&gt;• Solid tumor contact with the CA of ≤180°&lt;br&gt;• <strong>Solid tumor contact with the CA of &gt;180° without involvement of aorta &amp; GDA</strong>*</td>
<td>• Solid tumor contact with the SMV or PV of &gt;180°, contact of ≤180° with contour irregularity or thrombosis but with &quot;suitable vessel&quot; proximal and distal to involvement&lt;br&gt;• Solid tumor contact with IVC&lt;br&gt;• Limited involvement of stomach, duodenum, adrenal gland, kidney and transverse colon (If excisable)</td>
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<td><strong>Unresectable</strong></td>
<td>• Distant metastasis (including non-regional nodes)&lt;br&gt;<strong>Head/uncinate process:</strong>&lt;br&gt;• Solid tumor contact with SMA &gt;180°&lt;br&gt;• Solid tumor contact with the CA &gt;180°&lt;br&gt;• Solid tumor contact with the first jejunal SMA branch&lt;br&gt;<strong>Body and tail</strong>&lt;br&gt;• Solid tumor contact of &gt;180° with SMA/ CA*&lt;br&gt;• Solid tumor contact with the CA/aorta</td>
<td><strong>Head/uncinate process</strong>&lt;br&gt;• Unreconstructible SMV/PV due to tumor involvement or occlusion (tumor or bland thrombus)&lt;br&gt;• Contact with most proximal draining jejunal branch into SMV&lt;br&gt;<strong>Body and tail</strong>&lt;br&gt;• Unreconstructible SMV/PV due to tumor involvement or occlusion</td>
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*disagreement between members.
Resectable Cancer

Figure a: Axial contrast enhanced pancreatic phase image shows a small hypoenhancing mass lesion confined to the pancreatic head with intact fat planes around the SMA and SMV.

Figure b: Coronal image shows a dilated main pancreatic duct with cut-off at the lesion.

Another example of PDAC in the head region

Figure c: Axial contrast enhanced CT image in portal venous shows a pancreatic head mass; abutting the portal venous confluence (<180° contact) without contour deformity.
Figure a-Axial contrast enhanced portal venous phase image (a) shows an ill-defined hypoenhancing mass lesion in the pancreatic head/uncinate process with encasement and deformity of SMV. Fat planes around the SMA are preserved. Figures b, c- Axial MIP and coronal reformatted image (c) show that branches of SMV are not involved.
Unresectable Cancer

Figure a, b- Axial contrast enhanced pancreatic parenchymal phase images show an ill-defined hypoenhancing mass lesion in the uncinate process/neck region with >180\(^\circ\) encasement of SMA.

Figure c-Axial contrast enhanced pancreatic parenchymal phase image from a different patient showing encasement of the CA with large area of contact with the aorta.
Summary: Borderline Resectable Cancer

Borderline resectable cancer includes limited degree of vascular invasion where blood flow can be restored after resection of involved segments (more details in local staging slide).

**Arterial involvement**
- Contact with SMA <180
- Contact with Celiac A not extending to aorta

**Venous involvement**
- Single lumen on both ends after resection of involved segment

*Short segment involvement (< 3cm) of PV/SMV can be safely excised if there is reconstructable anatomy after resection; i.e. single lumen at both resected ends.*
Imaging: Nodal and Distant Metastasis

• Nodal size of greater than one cm in the short axis is the threshold for identifying metastatic nodes.

• EUS-guided FNA has a high specificity in the evaluation of suspicious lymph nodes, and acts as a useful problem solver.

• CT, MR, and PET/CT play complementary roles in the evaluation of metastatic disease. MR imaging has a greater sensitivity than CT (85% vs 69%) for metastases.

• Contrast-enhanced PET/CT, unenhanced PET/CT, and PET alone have been reported to have sensitivities of 82%, 46%, and 46%, respectively for liver metastases.

Axial contrast enhanced pancreatic parenchymal phase images (a) shows a hypodense focal lesion in the left hepatic lobe with PET image (b) shows high FDG avidity, suggestive of metastasis.
Response Assessment: Post-Chemoradiation

• Following CT±RT, MDCT is performed for determination of therapeutic response.

• **Following palliative CT±RT for metastatic disease:** RECIST 1.0 or 1.1 criteria can be used to monitor therapeutic response.

• Following neoadjuvant CT±RT: Morphological methods such as RECIST are often unreliable for assessing local tumor response to due to complex changes in tumor microvasculature and development of intratumoral fibrosis.

• **Imaging Response Criteria post Neo-adjuvant CT±RT:** Partial regression of tumor-vessel contact has been suggested as a sign of suitability for surgical exploration, irrespective of degree of decrease in tumor size or residual vascular involvement.
Response Assessment: Post-Chemoradiation

Figure a- Axial pancreatic phase image shows solid tumor contact with SMA.
Figure b- Post chemo-radiation axial image shows that solid tumor contact has been replaced by hazy stranding around the SMA.

The criteria of resectability after chemo-radiation remains the same but with a minor change, as **solid tumor contact may be replaced with increased hazy density /stranding of the fat surrounding the peri-pancreatic vessels**.
Response Assessment: Diffusion Weighted Imaging & PET-CT

- **Diffusion Weighted Imaging** has been tested in patients undergoing neoadjuvant therapy for pancreatic tumors.

- Preliminary studies suggest that *pretreatment ADC values differ significantly between responders and non-responders* (161 × 10⁻³ compared to 125 × 10⁻³ mm²/s) and can help in prediction of treatment response.

- These studies need further validation.

- **PET-CT** may play a role in monitoring response to chemo- and radiation therapy in patients with Unresectable PDAC.

- A significant reduction in FDG uptake may precede volumetric reduction at CT or MRI.

- Therefore, earlier depiction of tumor response to therapy at FDG PET could influence the continuation or withdrawal of treatment.
Pancreatic surgery carries a high risk for significant morbidity including pancreatic fistula, postoperative abscesses, portal vein or superior mesenteric vein thrombosis, postoperative hemorrhage, pseudoaneurysm formation, hepatic ischemia or infarction, delayed gastric emptying, and pancreatic and bile duct strictures. Imaging plays an important role in detecting post-surgical complication and detection of local and distant recurrence.

Post-surgical imaging. Axial CECT image (a) shows fat stranding around the celiac artery without any nodular soft tissue suggestive of postoperative changes. Axial CECT image (b) from a different patient shows nodular soft tissue surrounding the celiac artery, suggesting local recurrence.
Question 1 - What is local stage based on the extent of venous involvement?

Answer - Unresectable tumor; as the mass involves the jejunal branches of SMV (c&d; arrows)
Involvement of pylorus, duodenum (a), splenic pedicle (b), adrenal (c) and proximal jejunum (d) do not contraindicate resection.

Answer- None

Involvement of pylorus, duodenum (a), splenic pedicle (b), adrenal (c) and proximal jejunum (d) do not contraindicate resection.
Question 3- Identify the vascular variant and local stage of the pancreatic head mass?

Answer- CHA shows early branching (a, b). Left hepatic artery (LHA) is encased (a, c; red arrows), while right hepatic artery (RHA) is spared (d). LHA can be resected with RHA supplying the liver, hence tumor is borderline resectable.
Question 4- Identify the vascular variant and local stage of the pancreatic head mass?

Answer- Replaced common hepatic artery (a, b) arising from SMA; The tumor does not involve the proximal segment and bifurcation (yellow arrows)- Artery is reconstructable hence tumor is borderline resectable.
Question 5 - What is the local stage based on the extent of arterial involvement?

Answer - Unresectable tumor: tumor encases CA with abutment of aorta (b&d; arrows)
Conclusion

- Imaging plays a critical role in pre-operative staging and response assessment in PDAC.

- Advances in pancreatic cancer therapy have led to increased role of imaging and modifications in resectability criteria.

- Knowledge about the resectability criteria and imaging descriptors; and adopting structured reporting format are important for radiologists to enhance patient care.

Thank you for your kind attention!