Ablative Radiation Therapy
For Inoperable Cholangiocarcinoma

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Facts about radiation treatment

• High doses (2x the standard) are able to ‘ablate’ solid tumors
  – 15-25 treatments is best to protect surrounding organs if they are close
• Equivalent dose – 100 Gy (new) vs 50 Gy (old)
Facts about Cholangiocarcinoma treatment

• Operable tumors – resection can be curative
  – If not cured, patients live a lot longer
• For inoperable tumors
  – Chemotherapy alone is the standard
  – Gemcitabine and cisplatin
• The role of radiation is not established, but emerging
Challenges in Cholangiocarcinoma

- Proximity of duodenum, stomach colon
- Sparing (often diseased) liver
- Organ motion
  - Respiratory motion
  - Day to day differences
Solutions/Innovations

• **Gating:** Inspiration Breath Hold
  – Varian RPM
  – Feedback-guided Breath Hold

• **Image guidance:** Diagnostic quality CT
  – CT on rails

*The treatment is complex - very few centers have the ability to do this well for all tumors*
Feedback Guided Gated Breath-hold (FGBH)

- Patient to voluntarily holds their breath within the gate (visual feedback helps this process)
- Turn the beam on when the patient is holding their breath in the gate.
- CBCT or CT-on-rails can be done during FGBHs
Radiation treatment plan and illustration of the Simultaneous Integrated Boost/Protection (SIB/SIP) technique

5mm expansion of organs at risk to form planning risk volume (PRV)

Stomach
Max 60Gy

Simultaneous integrated boost (SIB) of 100 Gy

PTV 75 Gy
CT on rails vs Sim CT
CT guidance - Monitoring Stomach Position
Hfx XRT PancCa

67.5 Gy
- 15 fx -
45Gy
Outline- Ablative Liver XRT

- SBRT for small mets
- Why patients die of liver tumors
- Intrahepatic Cholangiocarcinoma results
Steriotactic XRT for Liver Metastasis
SBRT for liver mets: OS benefit?

Local control according to maximal tumor diameter.

Overall survival for according to primary site.

Rusthoven K E et al. JCO 2009;27:1572-1578
Treatment options for small liver mets

- Surgical resection
- RFA - not near vessels or bile ducts
- SBRT - third option
  - Poorly located tumors
  - More likely OS benefit
- Y-90 embolization
Vascular or biliary tumor extension = mortality

HV / IVC confluence

PV and biliary Bifurcation
51 y/o WF IHCa S/P 6 mo Chemo
6 Wks Later - Simulation CT – RT HV Occlusion
2 Mo Later – S/P Avastin with Response
60Gy / 15fx Respiratory Gating + CT image guidance

60Gy/15 fx

75Gy/15 fx
4 months after XRT
MDACC Results 2002-2014, n=79
Inoperable IHCa/ Definitive XRT

- Worse prognosis than operable tumors
  - Larger
  - Node+
  - Metastatic

- RT doses range 35-100 Gy

- 50 (63%) concurrent CTX
  - Capecitabine most common
Dose Response for Intrahepatic CholangioCa
MDACC, 2002-2014

MVA: Dose only sign factor for LC (p=0.004) and OS (p=0.006)

Tao and Crane, JCO, 2015
Effect of radiation dose - BED of >80.5 Gy or less

A. Local Control (%)

- BED>80.5 Gy
- BED<=80.5 Gy

Time of Follow-Up (months)

B. Overall Survival (%)

- BED>80.5 Gy
- BED<=80.5 Gy

Tao and Crane JCO, 2015

<table>
<thead>
<tr>
<th>Radiation Dose</th>
<th>BED</th>
<th>Local Control</th>
<th>Overall Survival</th>
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<tbody>
<tr>
<td>75 Gy in 25 fx</td>
<td>95.5</td>
<td>75%</td>
<td>95.5 BED</td>
</tr>
<tr>
<td>67.5 Gy in 15 fx</td>
<td>97.9</td>
<td>75%</td>
<td>97.9 BED</td>
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local control overall survival
Intrahepatic CCa
(XRT - compared to Surgery)

Unresectable tumors

Resected tumors

MDACC High vs low Dose
Inoperable IHCa

SEER Results, Resected Tumors
Intrahepatic CCa
(XRT - compared to Chemo)

Unresectable tumors

MDACC High vs low Dose
Inoperable IHCa

ABC 2: Advanced / met tumors

Causes of Death – IHCCa
(inadequate XRT dose / tumor control)

- Biliary, 44
- PV occlusion, 19
- HV/IVC occlusion, 8
- Parenchymal liver failure/combination, 16
- Metastatic disease, 11

89% of deaths were related to complications related to liver tumors

Tao and Crane, submitted, 2015
NRG GI001—Phase III Trial

Unresectable Cholangioca

- liver confined
- no cirrhosis or CPC A
- up to 2 satellite lesions
- 12 cm or less

Stratify:

- Largest tumor > 6 cm
  -- satellite y/n

Gem/Cis x 4

Re-staging AND Randomization after cycle 3 Radiation Planning during cycle 4

67.5 Gy / 15 fx

Gem/Cis x 4

Ted Hong, PI
Unresectable 14 cm IHC - Before XRT
Liquefaction
3 months post therapy
Same SIB Technique with Protons

100Gy/25x

75Gy/25fx
Liquefaction
IHCA (segments 2&3) near stomach: 67.5Gy/15fx - IMRT
9 months later...
Satellitosis – segments 4a & 4b
Here’s what we did: 60Gy in 15fx IMRT

Challenges: stomach and liver dose
Laparoscopic/open Alloderm Placement

Yoon, et al, PRO, 9/2013
Sometimes the bowel is too close
Colon, duodenum, stomach are dose limiting

 Courtesy Tom Aloia
AlloDerm® Envelope

Courtesy Tom Aloia
Open AlloDerm® Spacer Placement

Courtesy Tom Aloia
Unresectable Intrahepatic Cholangio near Stomach
IMRT after Alloderm Placement

100Gy/25x

75Gy/25fx
IMRT after Alloderm Placement

100Gy/25x

75Gy/25fx
IMRT after Alloderm Placement

100Gy/25x

75Gy/25fx
Pre vs post XRT scan
IMRT vs Protons

- IMRT- better bowel sparing
  - sharper edge (penumbra)
- Protons / Charged particles– better liver sparing
  - don’t exit, but high dose volume larger
6cm Isolated Unresectable IHCCa
Max dose greater with Proton than IMRT

IMRT
50GGE /10 fx

Proton
70CGE / 10 fx
25Gy /15fx
Summary
Ablative XRT for Liver Tumors

- Tumor control is dose related
  - Protons / IMRT complementary options
  - Choice based on protecting organs
- Major survival benefit (years)
- Inoperable patients: Curative treatment option
  - Comparable to surgery
Take home point
Large Liver Tumors

• Equivalent dose (BED) of 100 Gy is needed to control tumors
  – Liver, bile duct, and bowel are dose limiting
  – Possible with 15-25 treatments
  – Not possible with 5 treatments
    • Liver damage
    • Bile duct stricture
    • Bowel – bleeding