Liver MRL

Laura Dawson
Clinical Motivation

- Primary liver cancer increasing cause of cancer death
  - Top increasing cause of cancer death in Canada/US
  - Third cause of global cancer death
    - ~ 700,000 deaths/year
- Need for improved therapies
  - Tends to have local/regional spread to liver and liver vasculature
  - 5 year survival improving
    - e.g. 8% → 22% over 30 years in Ontario
- Increasing role of local therapies in colorectal cancer and other liver and ‘oligo’ metastases
Clinical Motivation

- Growing role of RT
  - RT role not well established (despite its effectiveness)
  - Need for comparative studies, registries, with clinically relevant endpoints: PROs, QOL, survival, PFS, time off systemic therapy
  - Fine balance btwn. local control and toxicity
    - many dose limiting OARs with potential for grade 3-5 toxicity
  - Improved imaging and IGRT improves outcomes

<table>
<thead>
<tr>
<th>Tumor</th>
<th>Local control</th>
<th>Toxicity</th>
<th>OAR limiting</th>
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<tbody>
<tr>
<td>HCC</td>
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<td>↑↑↑↑</td>
<td>Liver, luminal GI</td>
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<td>Cholangio</td>
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<td>Biliary, liver, luminal GI</td>
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<td>CRC liver mets</td>
<td>↓↓</td>
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<td>Luminal GI</td>
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<tr>
<td>Non-CRC liver mets</td>
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<td>Luminal GI</td>
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Clinical Motivation for MR

• Challenging to effectively treat liver cancer pts with RT
• Tumors challenging to see and contour
  • Tumors often missed if no or inappropriate use of IV contrast
  • Multi-phasic CT and MR standard of care
  • Challenging to identify extent of vascular invasion
• High contouring variability
• Motion (breathing motion, luminal GI filling, gas, peristalsis)
• Need for better IGRT surrogates (fiducials, CBCT)
Opportunities MR

• Liver cancers more obvious on MR
• Can see tumor on non-contrast T1W, T2W and DWI MR
  • Uncommon to see tumor with non-contrast CT
• Opportunity to improve therapeutic ratio/ outcomes
  • Reduce PTV and reduce toxicity
  • Improve local control (better target identification and IGRT)
  • Better understand changes during RT
    • Biomarkers for response (DWI)
    • Mechanisms of normal tissue injury
• 1.5 Tesla better than 3 Tesla MR for liver cancer imaging
2018 MRL Liver Brainstorm Activities

- 34 attendees registered for onsite brainstorm session
- Survey: 11 interested sites with variable experience in liver RT
- Preliminary MR imaging and contouring discussions
  - Multiple MR sequences and multi-phasic MR for simulation
  - GTV often seen on unenhanced T1W and T2W MR images
  - Liver imaging on MRL: Excellent image quality
- Consensus on strong need for technical advances
  - Motion management/ tracking and trailing solutions
- Start of discussion regarding clinical protocols and trials
HCC: Multi-Phasic Imaging

- HCC characteristics (hepatic arterial > portal venous):
  - Hypervascular on arterial phase (AP)
  - Washout on portal venous phase (PVP) and delayed phase (DP, 3 minutes post injection)

Diagnostic criteria for HCC in high-risk patients
Breath hold, multiphase imaging - HCC

Arterial | Portal venous | Delayed (3 min)

Courtesy of Hyun-Jung Jang, UHN, Toronto
HCC: MR Imaging → improved GTV identification and characterization

- Multi-phasic CE T1WI
  - Hypervascular, washout
- T1WI
  - Hypo > iso or hyper
  - In- and opposed-phase: fat
- T2WI
  - Hyper > iso or hypo
- Diffusion WI
- Liver-specific contrast
  - Gd-EOB-DTPA
Peritumoral Enhancement in Metastasis

• Multi-phasic MR images
• Hypovascular metastasis

• Metastasis from Colon cancer

Yu JS. AJR 2006
Peritumoral Enhancement in Metastasis

- Multi-phasic MR images
- Hypervascular metastasis

- Hypervascular metastasis such as NET or RCC
- Both AP and PVP are needed.

Yu JS. AJR 2006
MR Immobilization

- **Position (goal: comfort)**
  - Arms down

- **Motion management:**
  - Lorazepam
  - Abdominal compression (Diacor, Qfix, Civco, etc.)
  - Breath hold (volunteer)

- **Luminal GI prep**
  - Empty stomach (NPO 2 hours prior)
  - Low flatulence diet
Liver Motion Management

• Cine imaging/ monitoring during RT delivery available
  – Goal: Move towards use of in mid-position, reduced symmetrical PTV workflow

• Short term needs:
  – 4DMR
  – Gating
  – Ability to adapt to drifts/baseline shifts
    • e.g. adaption to position during treatment

• Long term:
  – 4DMR, trailing, tracking
NKI’S LIVER RT WORKFLOW FOR THE MR-LINAC

PRE-TREATMENT IMAGING
4D-CT + 4D-MRI

TREATMENT PLANNING

DAILY IMAGING
4D-MRI

IMAGE REGISTRATION & PLAN ADAPTATION

TREATMENT DELIVERY
2018 Liver Brainstorm Summary

- Technical needs
  - Motion management
  - 4D MR and mid position determination
  - Shorter time on unit
- MRL liver workflow preparation
  - Mid-position workflow
- Serial MR studies, target changes during RT/ contour reproducibility
- MR imaging and contouring education / consensus
- Clinical treatment ‘protocol’ development
  - Doses/ fractionations/ dose constraints (3 and 5 fraction SBRT)
  - Common endpoints
    - 1 month patient reported outcomes
    - 3 month liver function, toxicity
    - 6, 12 month, 3 year and 5 year outcomes
- Clinical questions / trials
  - Liver metastases registry (in parallel with oligo-met brainstorm group)
  - HCC with poor liver function: Treatable with acceptable toxicity?
  - HCC early stage: Can SBRT cure?
  - HCC late stage: Does facilitated target identification and targeting led to reduce toxicity and improved local control/survival?
  - Diffusion MR as biomarker
Liver MRL Proposals (in development)

Clinical
1. Run-in to optimize workflow
2. Obtain serial MR imaging during RT
   • Define ideal and unsuitable tumors (number of tumor, size limitations, vascular invasion?)
   • Characterize GTV changes during RT
3. Clinical trials

Technical:
1. Adapt to position to start
   • Region of interest – liver near tumor
   • ‘virtually shift’
2. Adapt to shape
   ▪ Contour propagation based on DIR (MR to MR) – starting contours “almost there”
3. Exploit geometric differences to improve therapeutic index

Research/Technical advances
1. Biomarker imaging
   • Diffusion weighted MR
2. Motion management
   • 4D MR
   • Tracking/trailing
3. IV contrast
Clinical Trials

- Registry
- Patient population?
- Endpoints?
  - Research
  - Clinical
- Other