Liver MRL

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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

Tumor	Local control	Toxicity	OAR limiting
HCC	~	↑↑↑	Liver, luminal GI
Cholangio	↓	↑	Biliary, liver, luminal GI
CRC liver mets	↓↓	~	Luminal GI
Non-CRC liver mets	~	~	Luminal GI

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

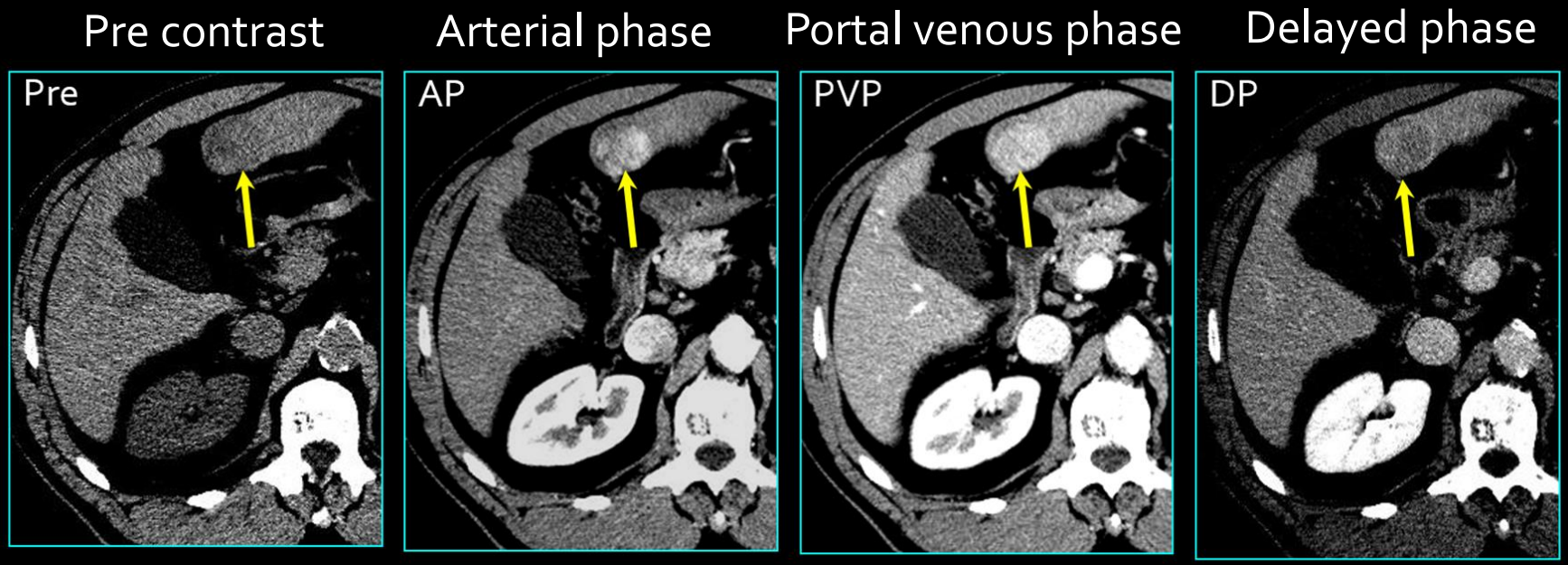
- Liver cancers more obvious on MR
- Can see tumor on non-contrast T1W, T2W and DWI MR
  - Uncommon to see tumor with non-contrast CT
- Opportunity to improve therapeutic ratio/ outcomes
  - Reduce PTV and reduce toxicity
  - Improve local control (better target identification and IGRT)
  - Better understand 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
AASLD practice guidelines, *Hepatology 2011;53:1020*

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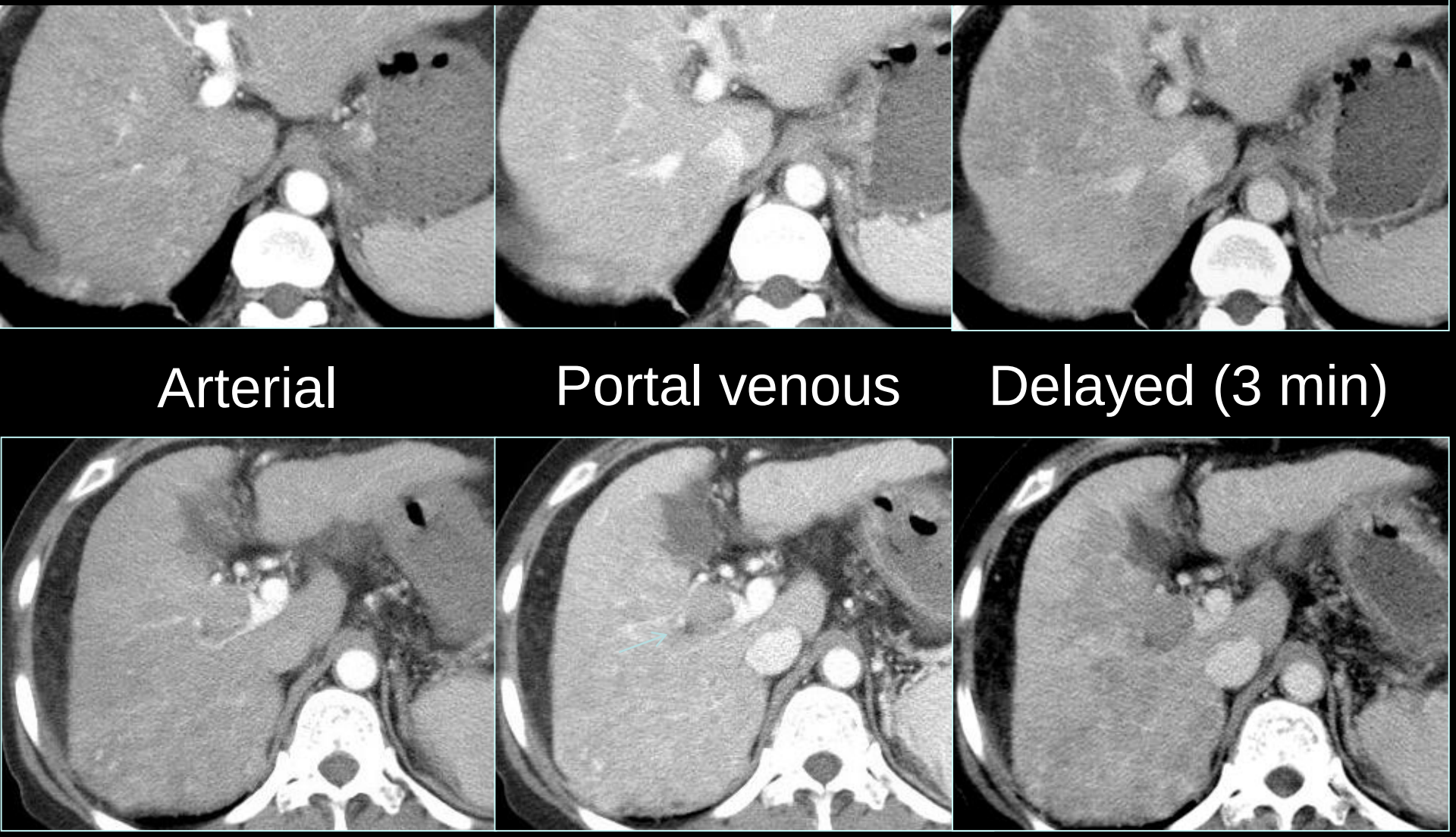
Breath hold, multiphasic imaging - HCC



Arterial | Portal venous | Delayed (3 min)

Courtesy of Hyun-Jung Jang, UHN, Toronto

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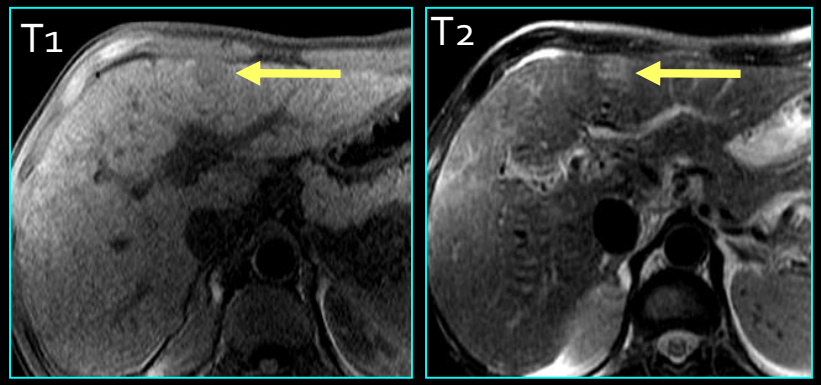
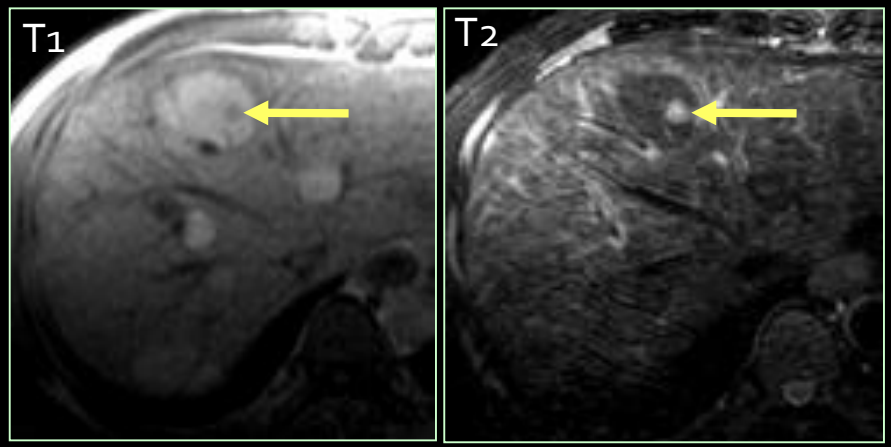
HCC: MR Imaging → improved GTV identification and characterization

- 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



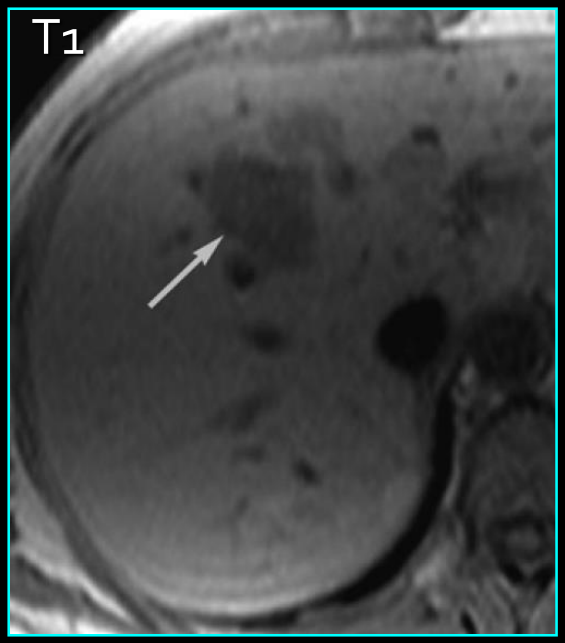
MD HCC

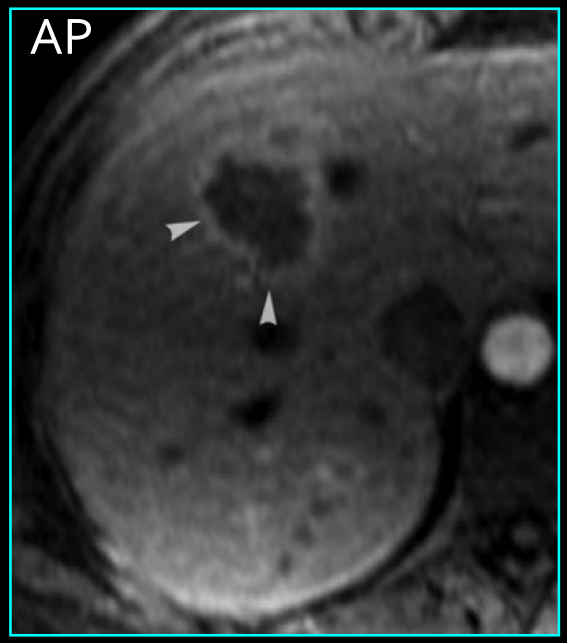


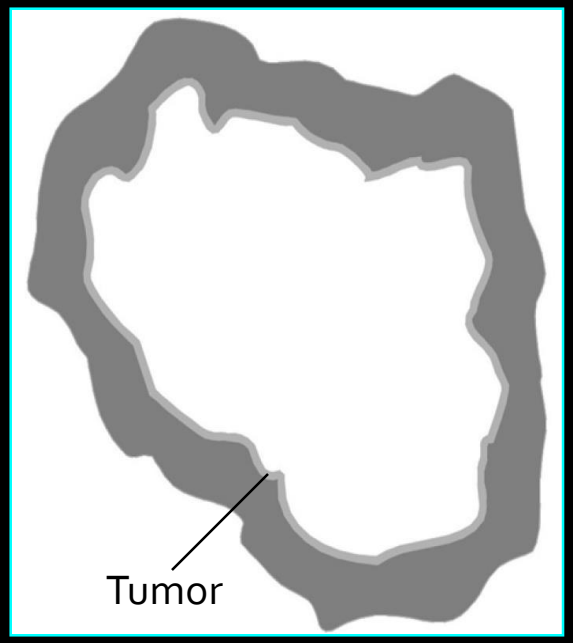
HCC in dysplastic nodule

Peritumoral Enhancement in Metastasis

- Multi-phasic MR images
- Hypovascular metastasis





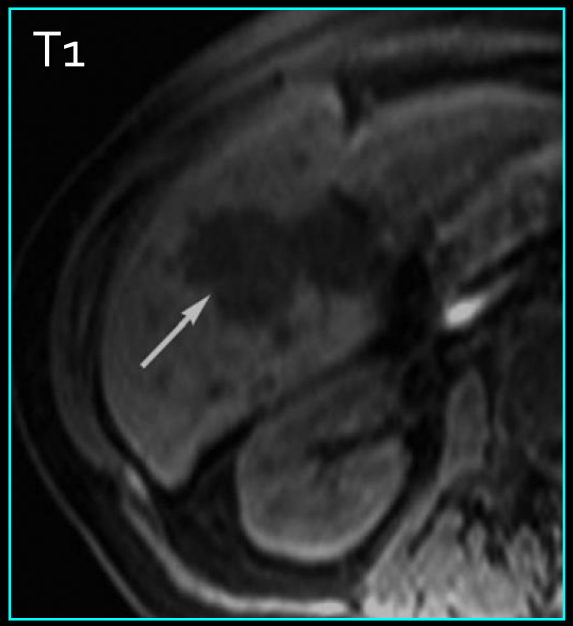


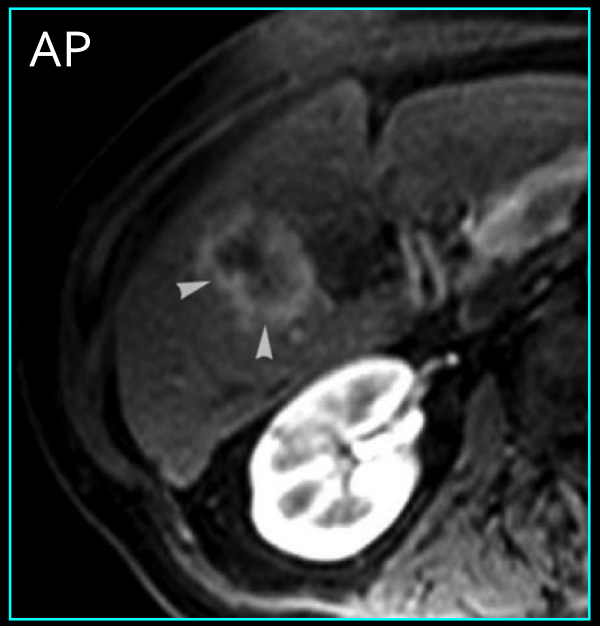
- Metastasis from Colon cancer

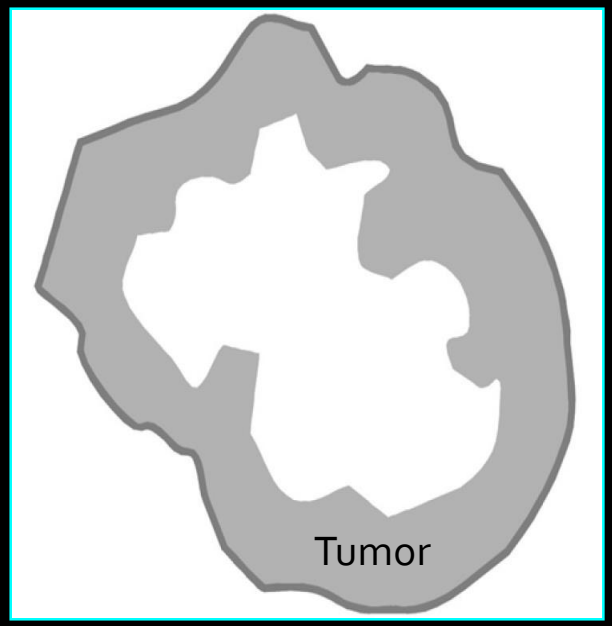
Yu JS. AJR 2006

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

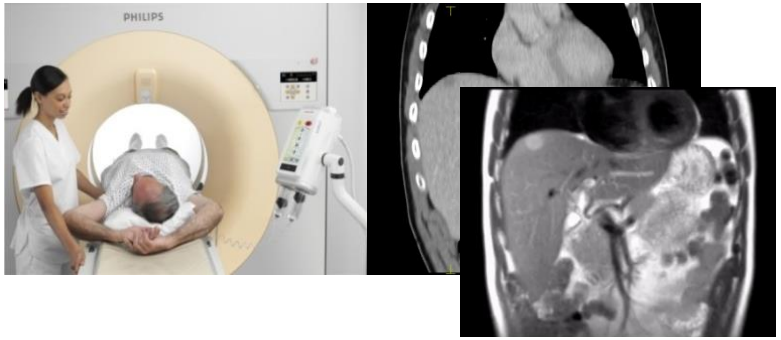
Liver Motion Management

- 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

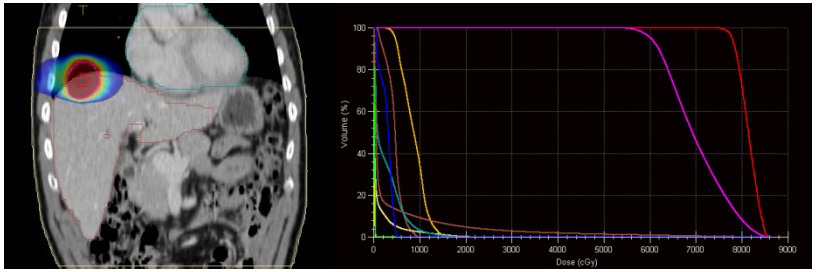
NKI'S LIVER RT WORKFLOW FOR THE MR-LINAC

PRE-TREATMENT IMAGING

4D-CT + 4D-MRI



TREATMENT PLANNING



DAILY IMAGING

4D-MRI

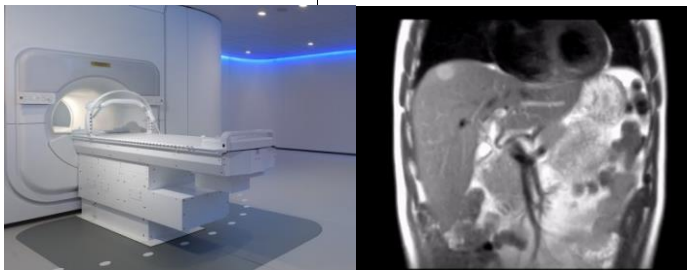
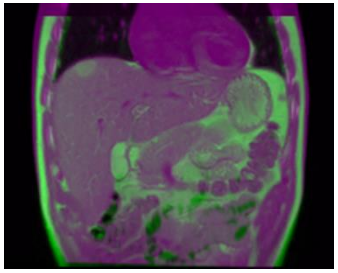


IMAGE REGISTRATION & PLAN ADAPTATION



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