

MR Linac and Adaptive RT in Lymphoma

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**4th ILROG Educational Conference:
Radiotherapy in Modern Management of Haematological Malignancies**

MR Linac

Ideal for targets that are:

- Difficult to delineate on CBCT
- Mobile and/or affected by respiratory motion
- With potential to progress or respond during therapy course
- In close proximity to OARs

Image Guided

- Use MRI imaging to guide daily setup, gate treatment, but do not change treatment plan



Gastric MALT lymphoma (8)
Duodenal lymphoma (4)

Adaptive

- Adjust the target/OAR contours while the patient is on the table
- Generate a new re-optimized plan based on that day's anatomy



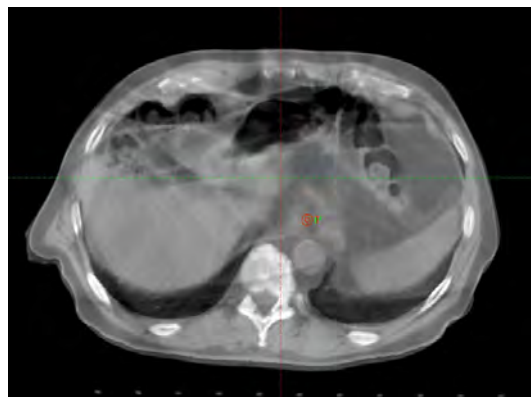
Mesenteric lymphoma (3)
Duodenal lymphoma (1)

Gastric MALT Lymphoma: CT-Guided

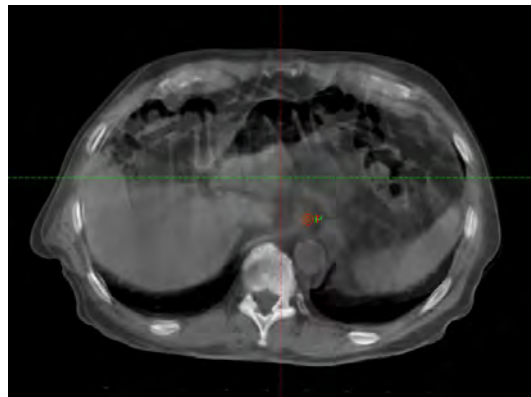
- NPO 4 hours prior to sim/treatment, oral contrast immediately prior to sim, antiemetics 1 hour before treatment
- Motion management: 4D or DIBH
- Technique: 3D CRT or IMRT
- CTV = stomach
- ITV = 1.5 cm margin on CTV
- PTV = 0.5 cm margin on ITV
- Dose: 20-24 Gy in 2 Gy per fraction
- Image guidance: daily kV, CBCT

Gastric MALT Lymphoma: CT-Guided

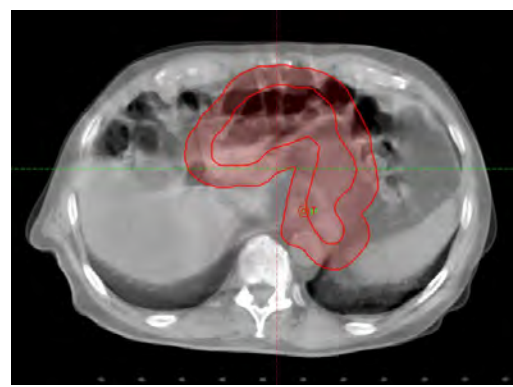
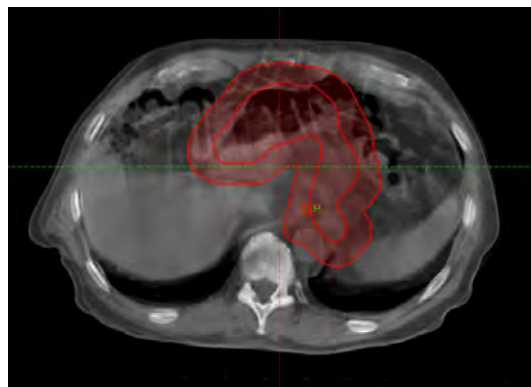
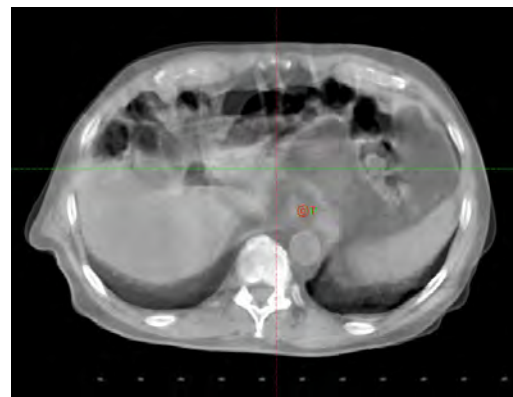
CBCT Week 1



Week 2



Week 3



Gastric MALT Lymphoma: MR-Guided

Premedication Tx:

- Simethicone 1 tablet 4 times daily (before sim and restart 1 week prior to treatment)
- NPO 4 hours prior to sim and treatment → **NPO overnight, first case in am**
- Zofran 8mg 30 minutes pre treatment

Motion Management:

- LIBH

Target delineation:

- CTV = stomach
- ITV= 0.5 cm margin on CTV
- PTV= 0.5 cm margin on ITV

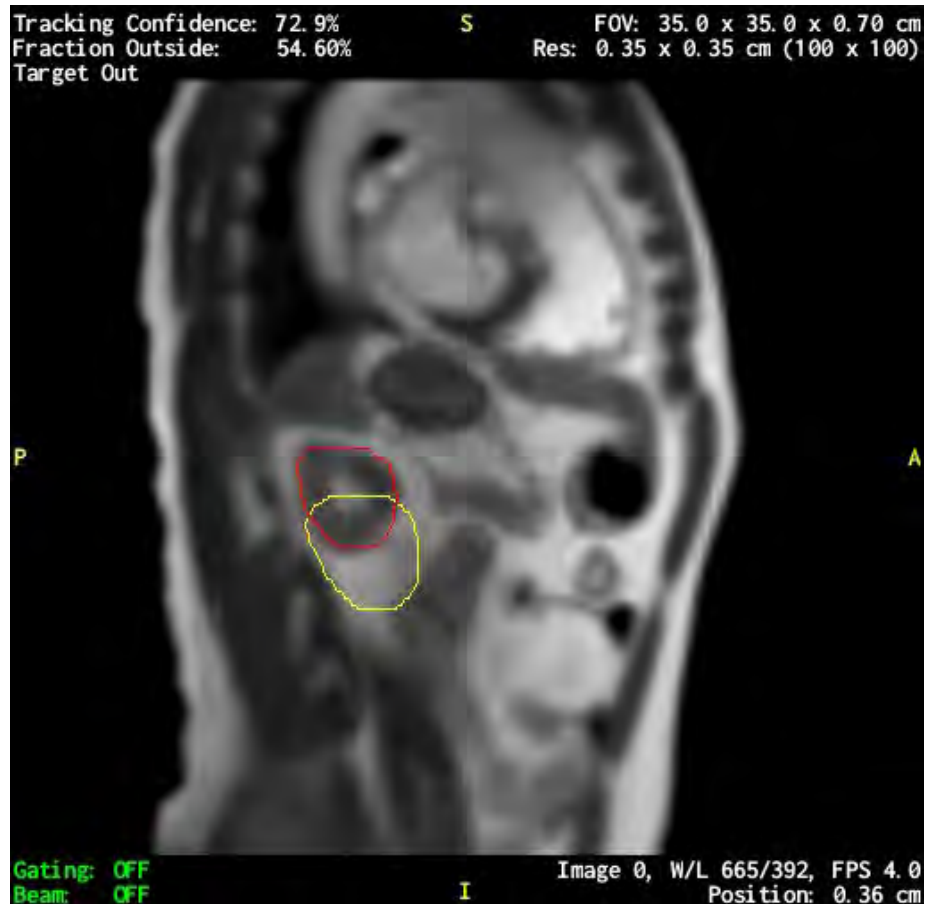
Technique:

- IMRT

Image guidance:

- Daily MR

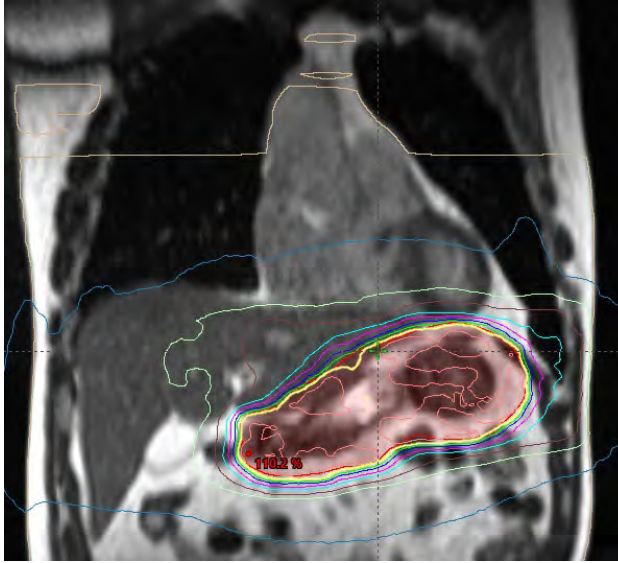
Real-Time Intraabdominal Lymphoma Tracking Considerations



- Difficult to track on mobile structures (i.e. stomach, duodenum, mesenteric masses)
- Typically use kidney to capture breath hold motion
- Recent software upgrade allows tracking on multiple planes
- 3 mm tracking boundary

Gastric MALT Lymphoma: MR-Guided

Plan



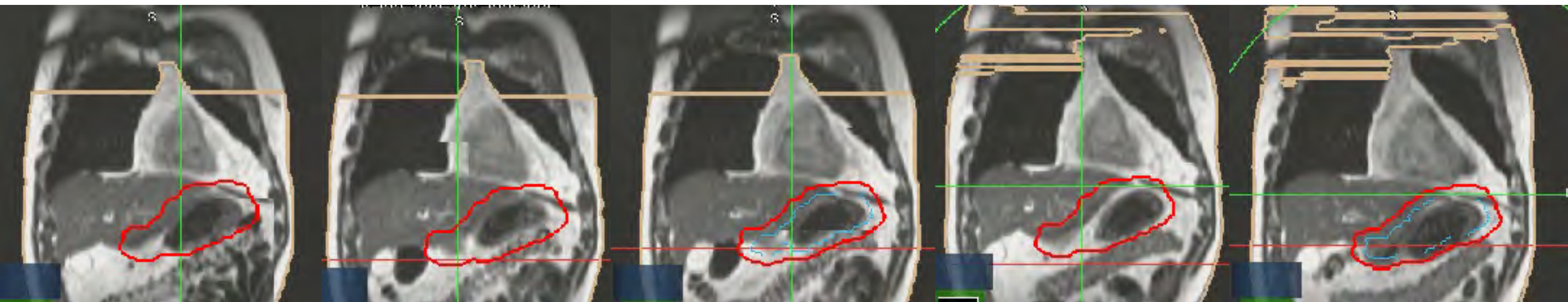
Day 1

Day 3

Day 6

Day 8

Day 10

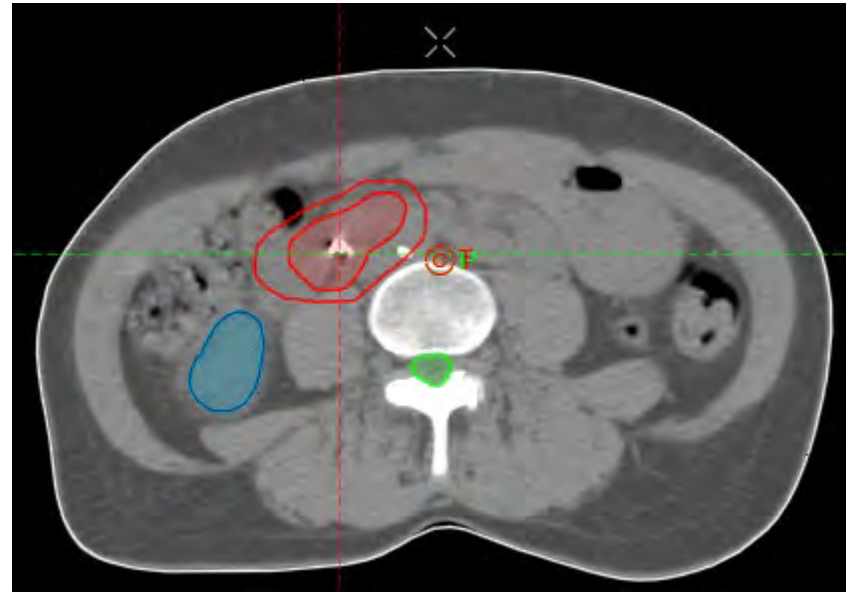


Duodenal Lymphoma: CT-Guided

- Gastroenterologist to place clips outlining the disease extent
- NPO 4 hours prior to sim/treatment
- Technique: 3D CRT or IMRT
- Motion management: 4D
- CTV= **2-3 cm beyond clips** within the intestinal lumen circumferentially, entire part of the duodenum longitudinally
- ITV = **1.5 cm** margin on CTV
- PTV = **0.5 cm** margin on ITV
- Dose: 24 Gy
- Image guidance: daily kV, CBCT

Duodenal Lymphoma: CT-Guided

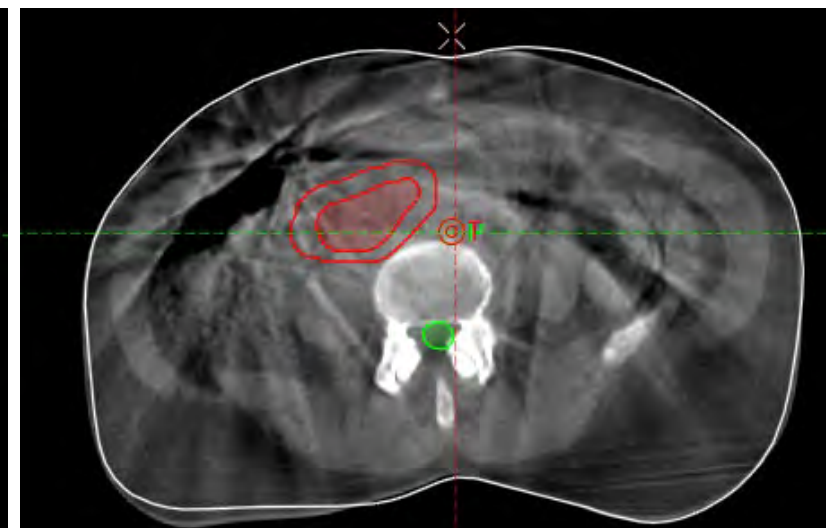
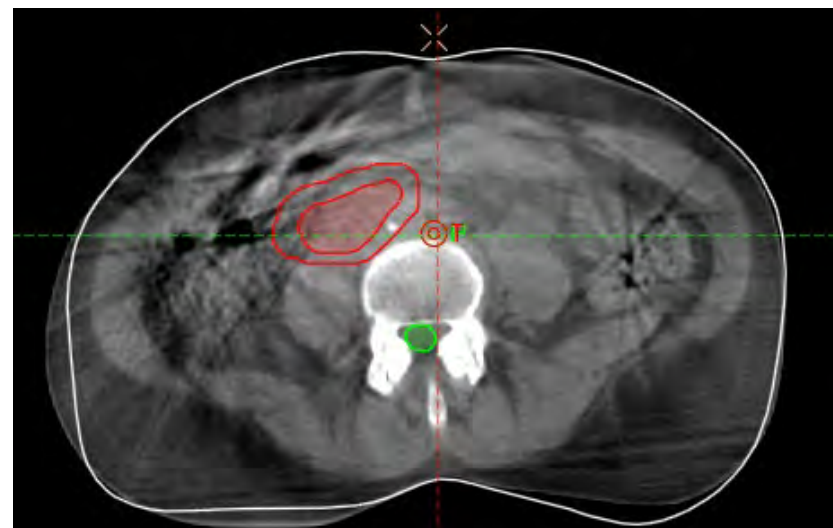
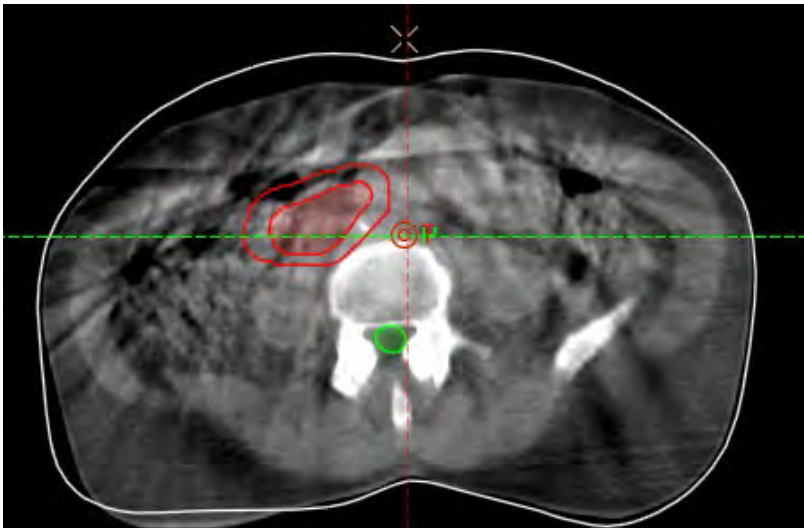
Plan



CBCT Week 1

CBCT Week 2

CBCT Week 3



Duodenal Lymphoma: MR-Guided Online Adaptive

Premedication Tx:

- Continue Simethicone 1 tablet 4 times daily (pre-sim and restart 1 week prior to treatment)
- Zofran 8mg 30 minutes pre sim and pre treatment
- NPO 4 hours prior to treatment

Motion Management:

- LIBH

Target delineation:

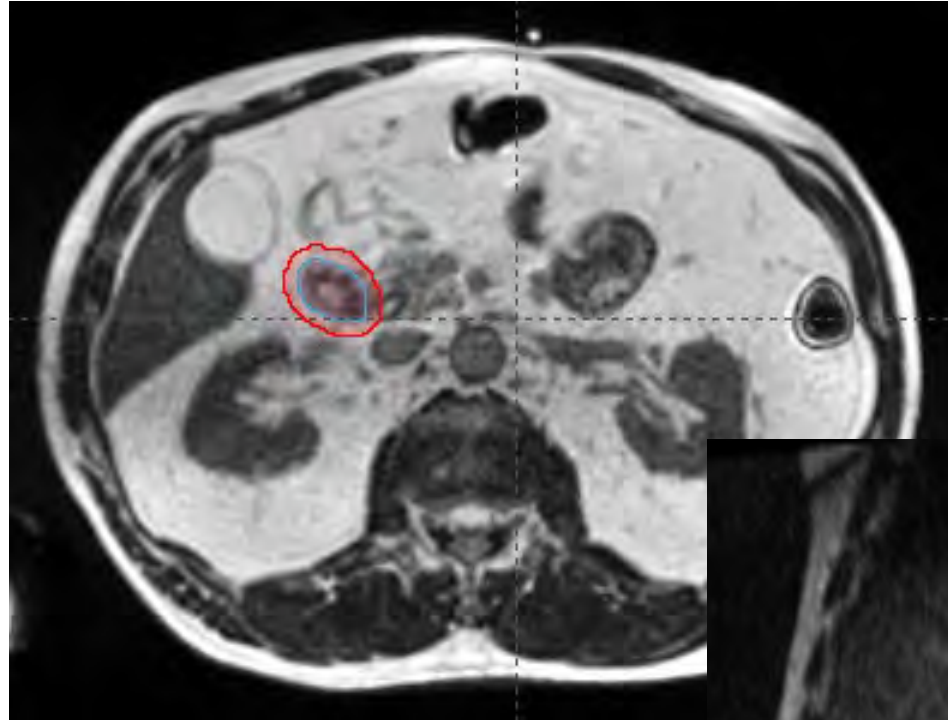
- CTV= entire part of duodenum
- ITV= **no ITV expansion**
- PTV= **0.5 cm** margin on CTV

Technique:

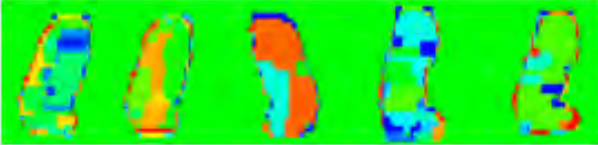
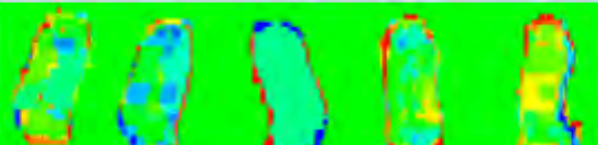
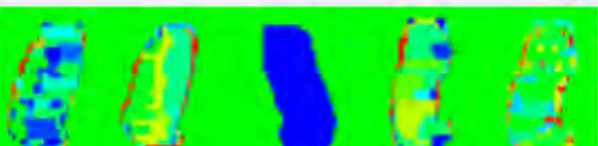
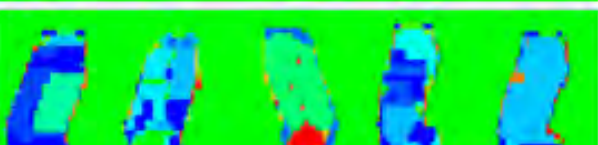

- IMRT
- Daily MR adaptive planning

Duodenal Lymphoma: MR-Guided Online Adaptive

- Stage IE follicular lymphoma involving 2nd portion of duodenum
- Plan: Adaptive MR-Guided ISRT 20 Gy in 5 fractions



Duodenal Lymphoma: MR-Guided Online Adaptive

| | Difference Between Original and Adapted Plan | PTV Coverage (V100%) | |
|-------|--|----------------------|-----------------------|
| | | Predicted | Treated |
| Day 1 |  | 97.38% | 97.38% |
| Day 2 |  | 97.97% | 97.97% |
| Day 3 |  | 88.92% | 97.53% (re-optimized) |
| Day 4 |  | 91.37% | 98.09% (re-optimized) |
| Day 5 |  | 92.88% | 97.47% (re-optimized) |

-10.32%

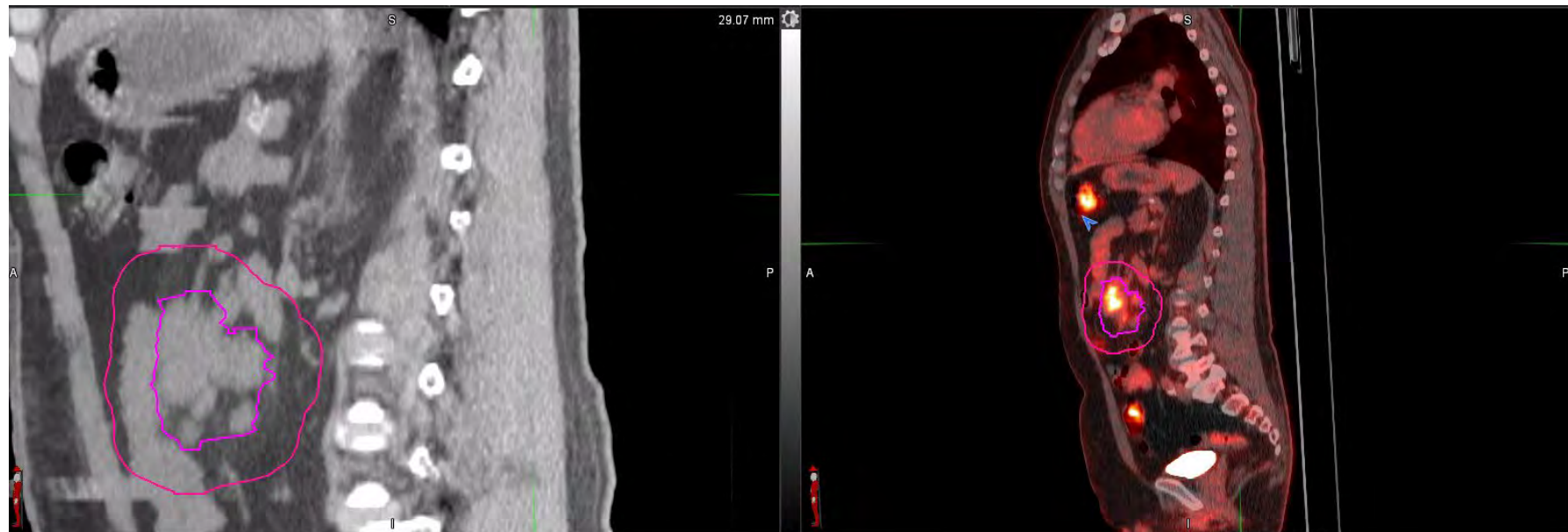
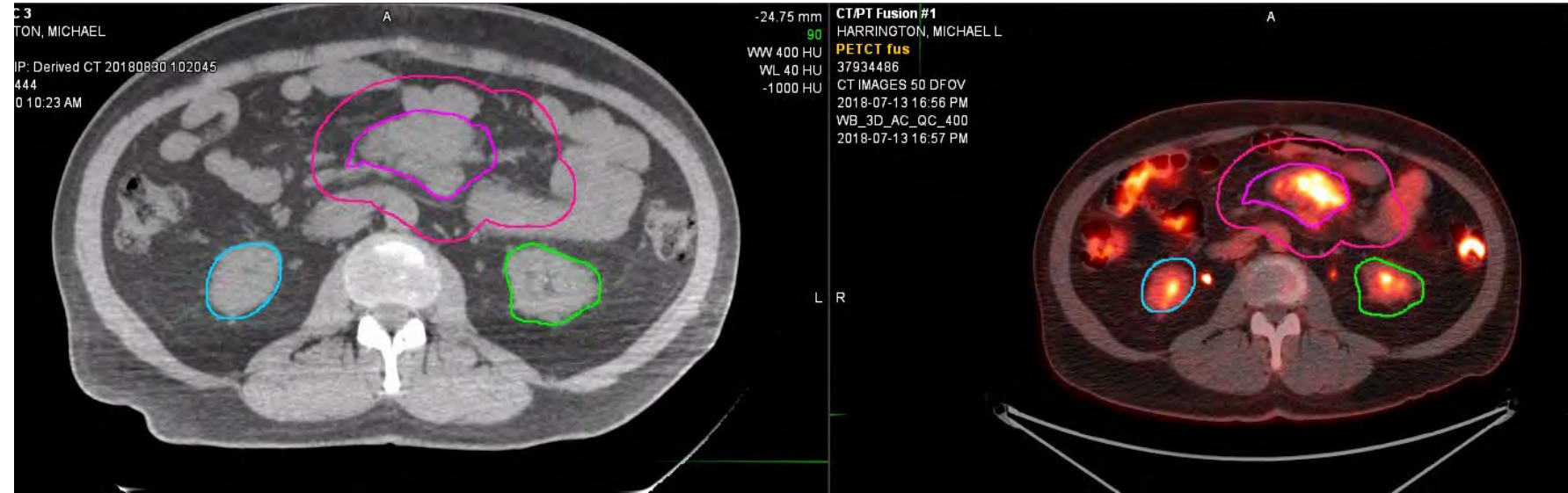
+10.29%

Mesenteric Lymphoma: CT-Guided

- NPO 4 hours prior to sim/treatment
- Technique: 3D CRT or IMRT
- Motion management: 4D
- PET-CT fusion to determine CTV
- CTV → ITV → PTV expansion: 2.5 - 3 cm
- Dose: 24 to 30 Gy depending on histology
- Image guidance: daily kV, CBCT

Mesenteric Lymphoma: CT-Guided

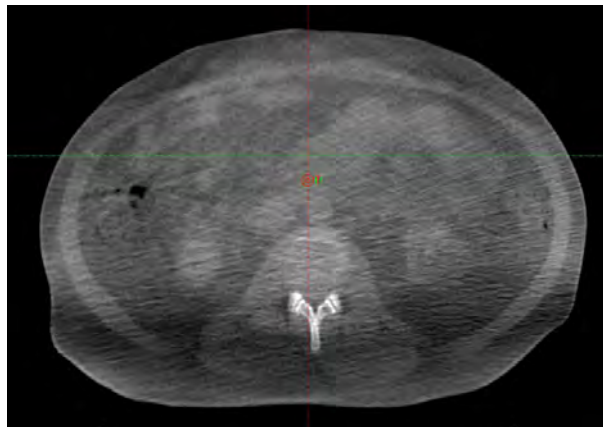
- Stage I mesenteric FL
- PTV= CTV+2.5 cm
- 24 Gy in 12 fractions



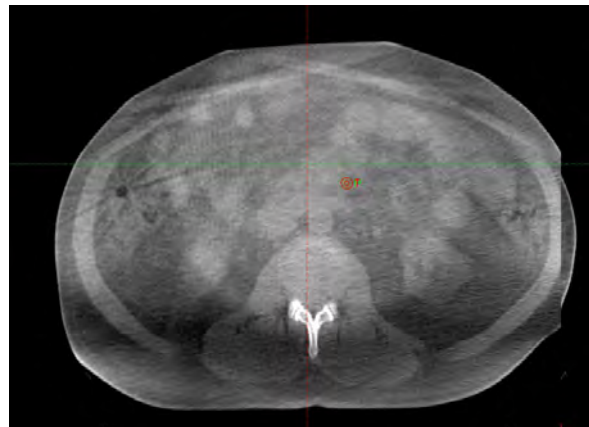
Mesenteric Lymphoma: CT-Guided

CBCT

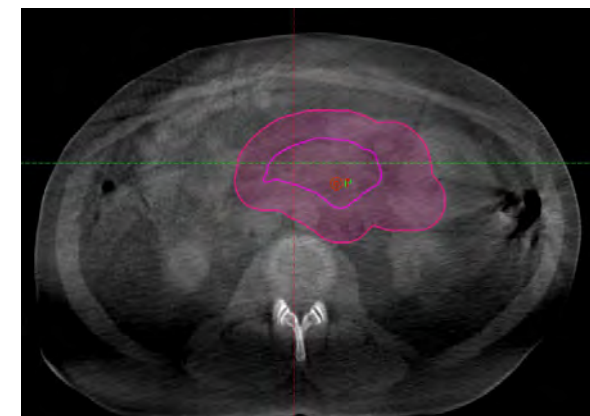
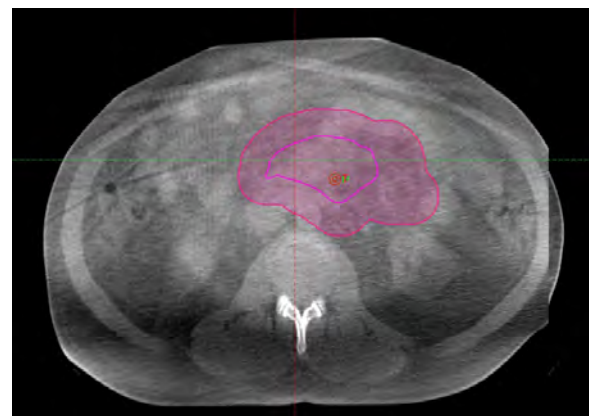
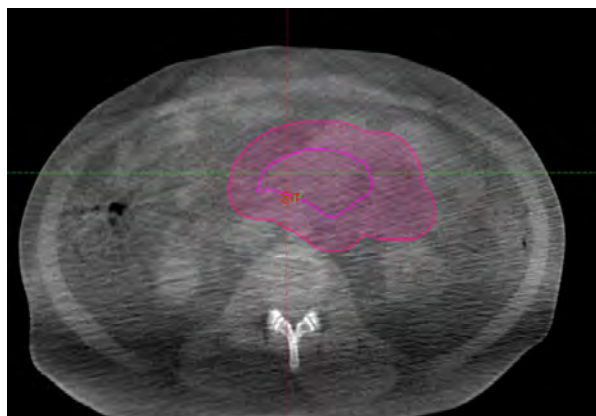
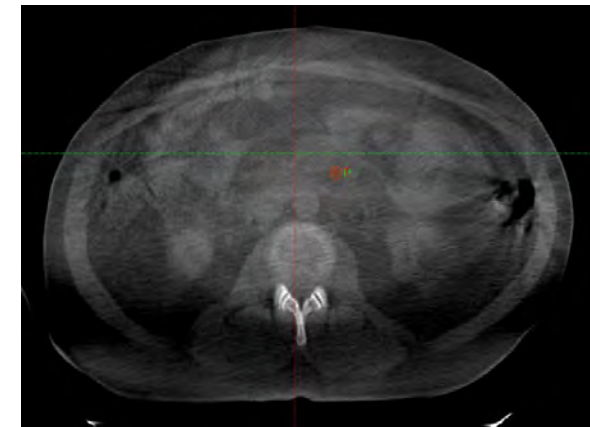
Week 1



Week 2



Week 3



Mesenteric Lymphoma: MR-Guided Online Adaptive RT

- Limited-Stage NLPHL of the mesentery
- Plan: Adaptive MR-Guided ISRT 25 Gy in 5 fractions



Mesenteric Lymphoma

MR-Guided Online Adaptive RT

- Premedication Tx:

NPO 3 hours

Zofran 8 mg 30 min prior to treatment

- Motion Management:

LIBH

- Target delineation:

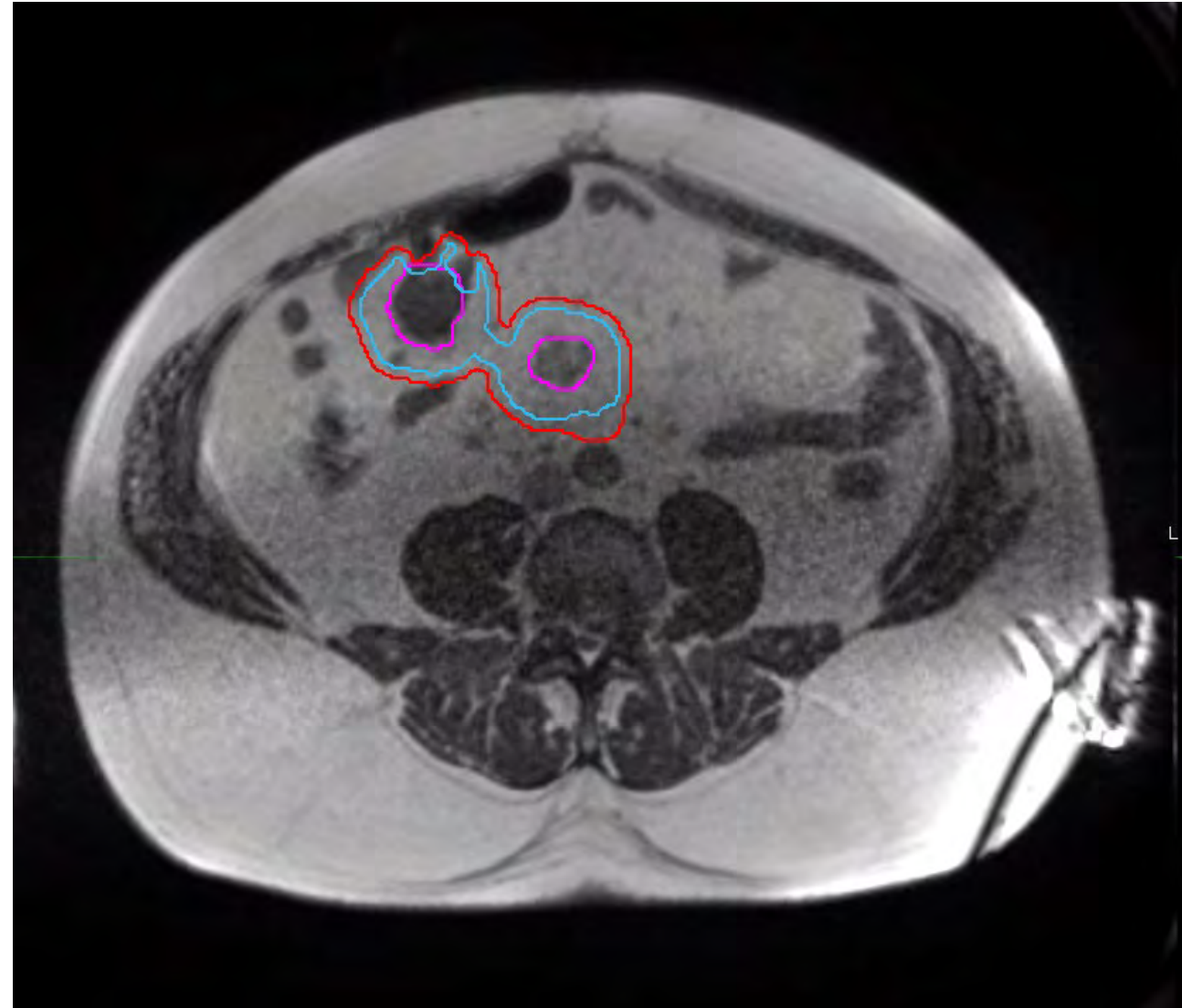
CTV= GTV + 1 cm, small bowel subtracted

PTV= 0.5 cm margin on CTV

- Technique:

IMRT

Daily MR adaptive planning

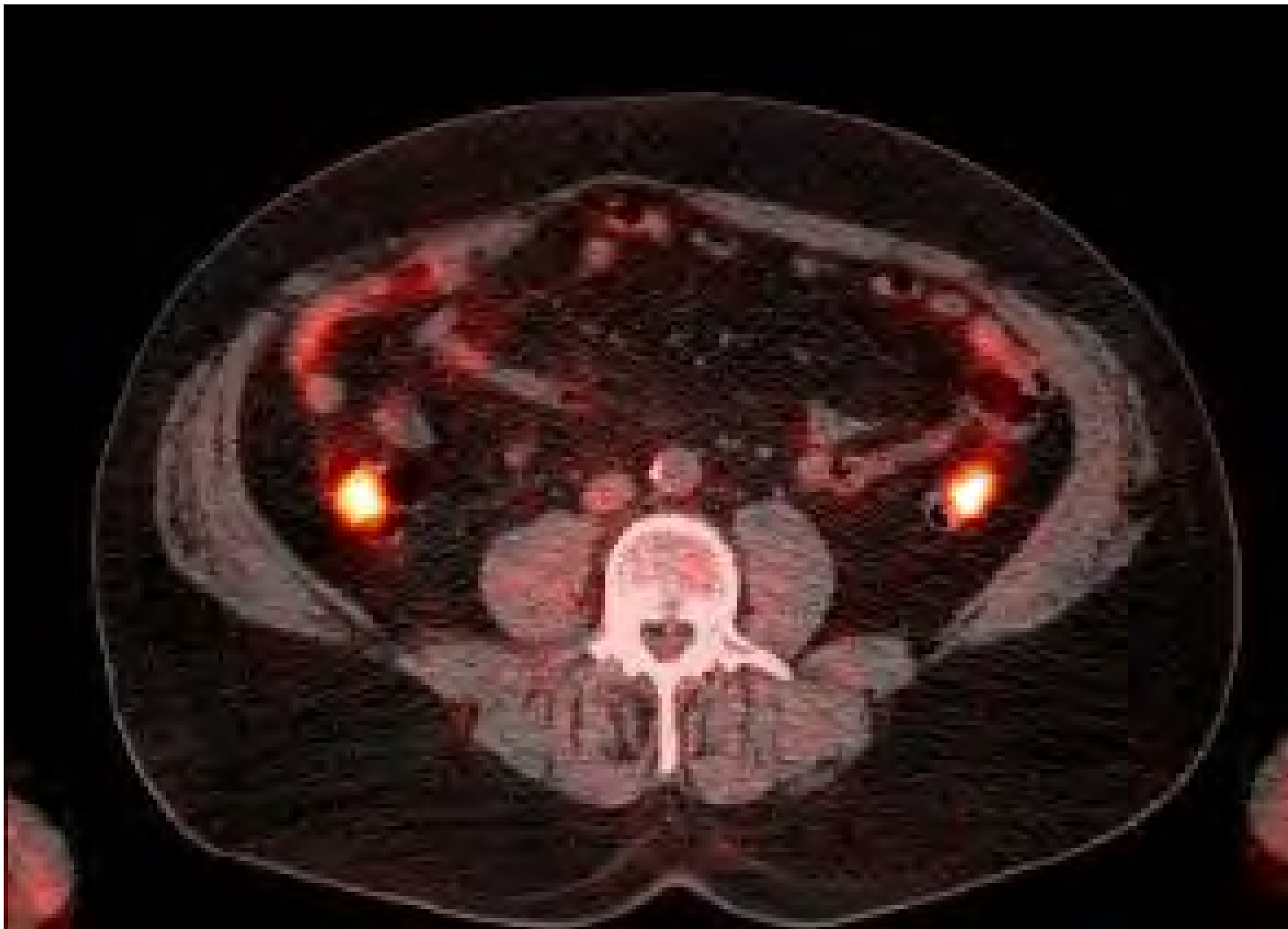


Mesenteric Lymphoma

MR-Guided Online Adaptive RT



| | PTV_Opt | PTV Coverage (V100%) | |
|-------|-----------|----------------------|--------------|
| | | Predicted | Re-optimized |
| Day 1 | 249.39 cc | 82.25% | 95.07% |
| Day 2 | 253.28 cc | 91.70% | 95.6% |
| Day 3 | 247.36 cc | 90.40% | 96.24% |
| Day 4 | 245.79 cc | 93.99% | 95.63% |
| Day 5 | 236.27 cc | 91.39% | 96.00% |



NED 18 months post-treatment

Trade-Offs

Pros

- Better target visualization, narrower target expansion, OAR-sparing
- Adaptive planning to account for tumor regression (or progression)
- Hypofractionation
- Potential for informing target expansions for CT-guided RT
- Potential for MR-derived biomarkers
- Potential for adapting final dose based on response

Cons

- Cost/labor intensive
- Dosimetric benefit unlikely to translate to clinically meaningful differences
- Limited by pts with claustrophobia, large body habitus, metals, pacemaker, artifacts from surgical clips near target, long wait time (4-6 weeks)

**ADAPTIVE BRIDGING RT
ON ETHOS FOR R/R LBCL**

Adaptive Bridging Radiation Therapy

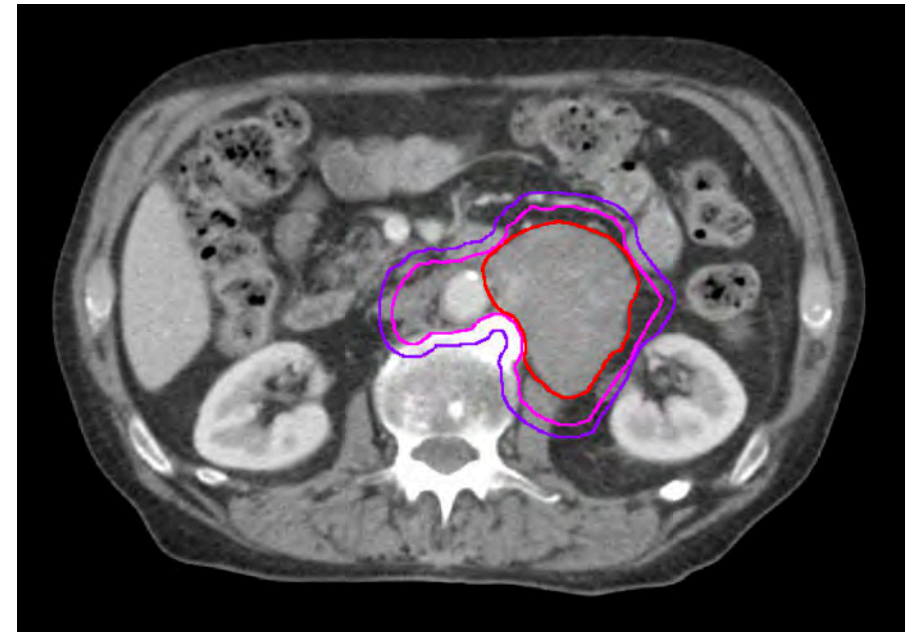
Chirayu G. Patel, MD, MPH
Department of Radiation Oncology

September 2023

Background

- Low-dose, hypofractionated palliative radiation therapy is locally effective for high grade B cell lymphomas¹
- Significant tumor shrinkage on CBCT is not uncommon during the course of treatment
- As CAR T significantly improves survival, there will be more concerns regarding late effects of RT

Can we use adaptive radiation to facilitate and personalize bridging radiation therapy?

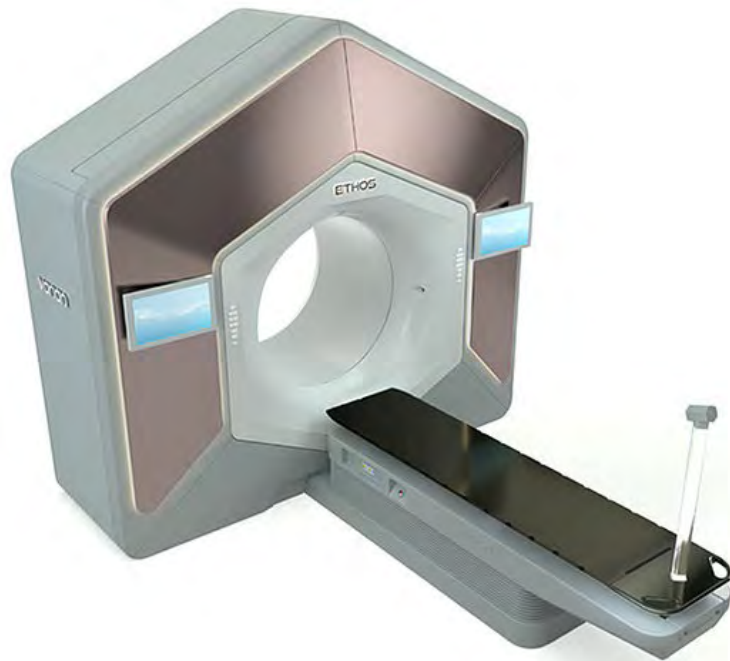


¹Wright CM, Dreyfuss AD, Baron JA, Maxwell R, Mendes A, Barsky AR, Doucette A, Svoboda J, Chong EA, Jones JA, Maity A, Plataras JP, Paydar I. Radiation Therapy for Relapsed or Refractory Diffuse Large B-Cell Lymphoma: What Is the Right Regimen for Palliation? *Adv Radiat Oncol.* 2022 Jul 3;7(6):101016.

Background

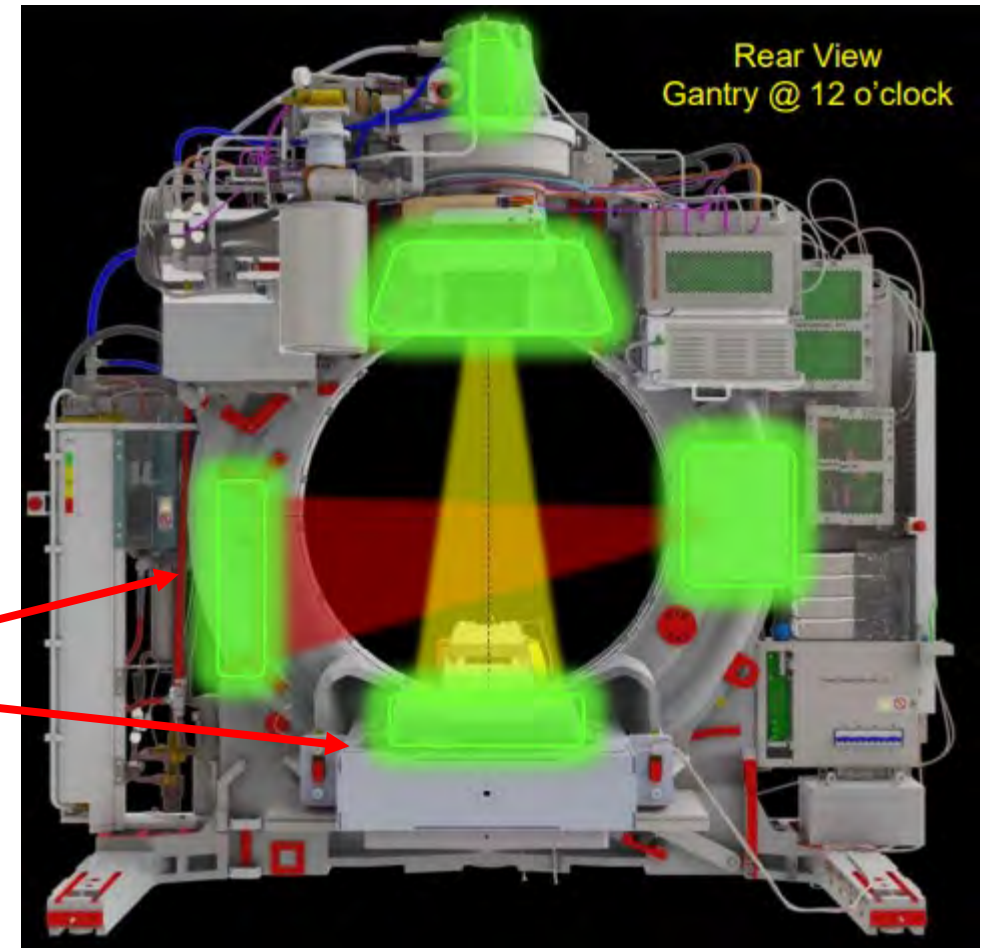
CT-based adaptive radiation - Ethos

- Produces and focuses a high-energy beam of x-rays
 - 6 MV (6,000 kV) compared to 140 kV x-rays for imaging
- kV imaging x-ray tube and detector provide high-quality cone-beam CT images



Imaging
detectors

MV x-ray
accelerator



kV x-ray
tube



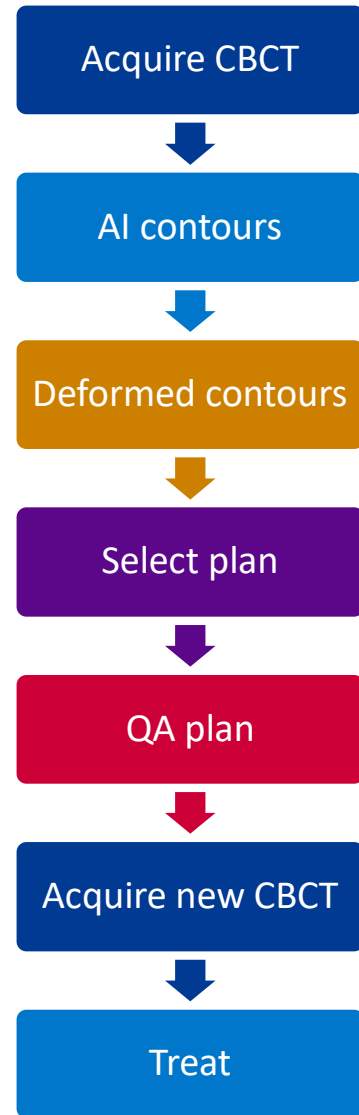
Background

Ethos cone-beam CT quality and workflow

CT scan



Ethos CBCT scan for the same patient



5-5-5 Adaptive Bridging Radiation Therapy (ABRT) for Rel/Ref B-cell Lymphoma Prior to CAR T-cell Therapy

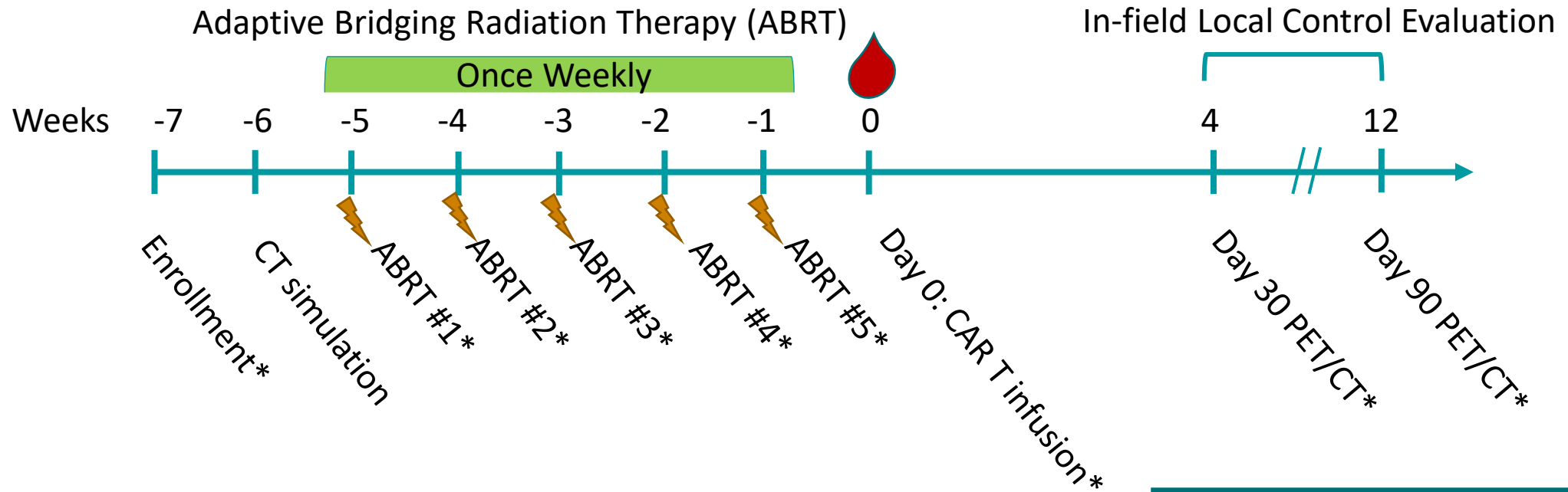
Specific Aims for Pilot Study (n=10)

1. To assess the feasibility of once weekly, CBCT-guided adaptive RT
2. To determine the safety and toxicity profile of once weekly adaptive RT
3. To evaluate the in-field local control at 30 and 90 days post-CAR T cell therapy
4. *Exploratory: To evaluate the effect on the immune system via cytokine profiling*



Schema

Note: Patients may be referred as soon as 3-4 weeks prior to CAR T and receive fewer fractions



*Surveys administered:
CTCAE/PRO_CTCAE
FACT-Lym
FACIT-COST

Immunologic correlatives
-CRP/ferritin/cytokines



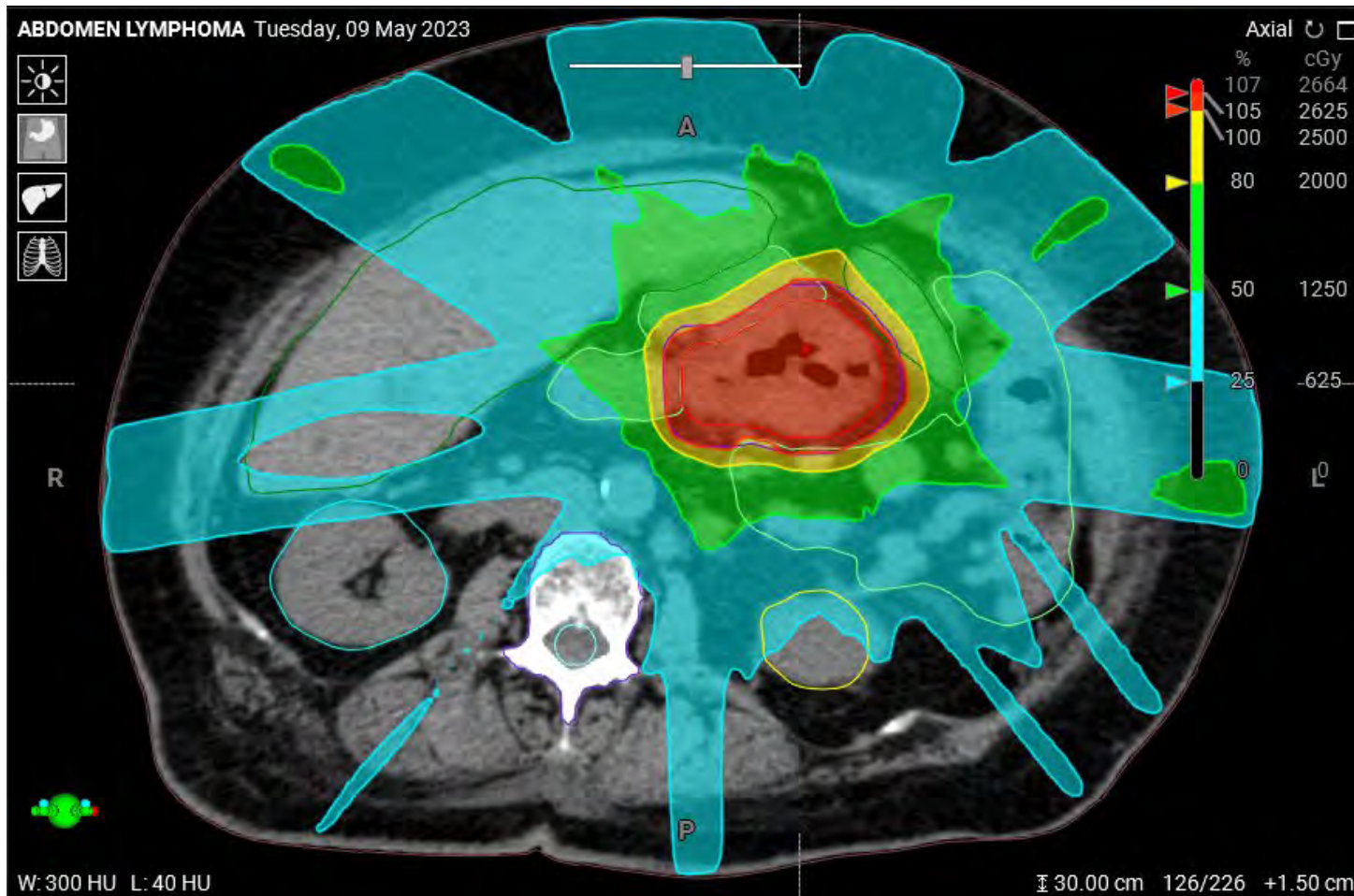
To irradiate or not

Can we go beyond improving target conformality?

- Treatment can be withheld if:
 - $\geq 10\%$ shrinkage in any dimension on Ethos CBCT compared to the previous fraction or
 - $\geq 30\%$ shrinkage compared to first fraction
- For targets measuring ≥ 5 cm, if there is $\geq 20\%$ growth in any dimension on Ethos CBCT between fractions:
 - Transition to conventional daily radiation plan to deliver up to 30 Gy in 10 fractions



Lymphoma Patient Planned with Ethos



Goals

1 Most Important | 4 goals

| | | | |
|-------------------------------------|-------|----------------------|----------|
| <input checked="" type="checkbox"/> | GTV | V2500 cGy ≥ 99.0 % | 100.0 % |
| <input checked="" type="checkbox"/> | PTV | V2400 cGy ≥ 99.0 % | 99.7 % |
| <input checked="" type="checkbox"/> | PTV | V2650 cGy ≤ 0.03 cm3 | 0.00 cm3 |
| <input checked="" type="checkbox"/> | Bowel | D0.03 cm3 ≤ 2625 cGy | 2600 cGy |

2 Very Important | 7 goals

| | | | |
|-------------------------------------|------------|------------------------|------------|
| <input checked="" type="checkbox"/> | Liver | V2000 cGy ≤ 20.00 cm3 | 21.28 cm3 |
| <input checked="" type="checkbox"/> | Liver | D0.03 cm3 ≤ 2625 cGy | 2591 cGy |
| <input checked="" type="checkbox"/> | Bowel | V2000 cGy ≤ 100.00 cm3 | 133.91 cm3 |
| <input checked="" type="checkbox"/> | Kidney_L | V800 cGy ≤ 10.00 cm3 | 2.35 cm3 |
| <input checked="" type="checkbox"/> | Kidney_R | V800 cGy ≤ 10.00 cm3 | 0.06 cm3 |
| <input checked="" type="checkbox"/> | SpinalCord | D0.03 cm3 ≤ 1000 cGy | 802 cGy |
| <input checked="" type="checkbox"/> | PTV | V2500 cGy ≥ 95.0 % | 96.0 % |



Acknowledgement

Varian – funding for ABRT trial



MGH Ethos adaptive treatment overview (~20 mins)

1. Review CBCT for artifacts and appropriate anatomy (RTT/CMD/QMP)
 - Movement causes artifacts, can't visualize anatomy and impact dose calculation
2. Review and edit AI-generated contours (RTT/CMD/QMP)
3. Review and edit deformed contours (RTT/CMD/QMP)
 - Physician is called to review contours, both target and normal structures
4. Review scheduled vs adapted plan and decide which to use (MD/CMD/QMP)
 - If adapted, physician signs plan and then can leave
5. Perform physics QA if using adapted plan (QMP)
 - Mobius secondary dose calculation, compare MU and isodoses with scheduled plan
 - Review synthetic CT generated from CBCT for accuracy
6. Repeat CBCT to check anatomy and alignment prior to treatment (RTT/CMD/QMP)
 - Changes in bowel gas or bladder filling → may need to shift to align

