AHOD 2131 RT Guidelines including sample cases

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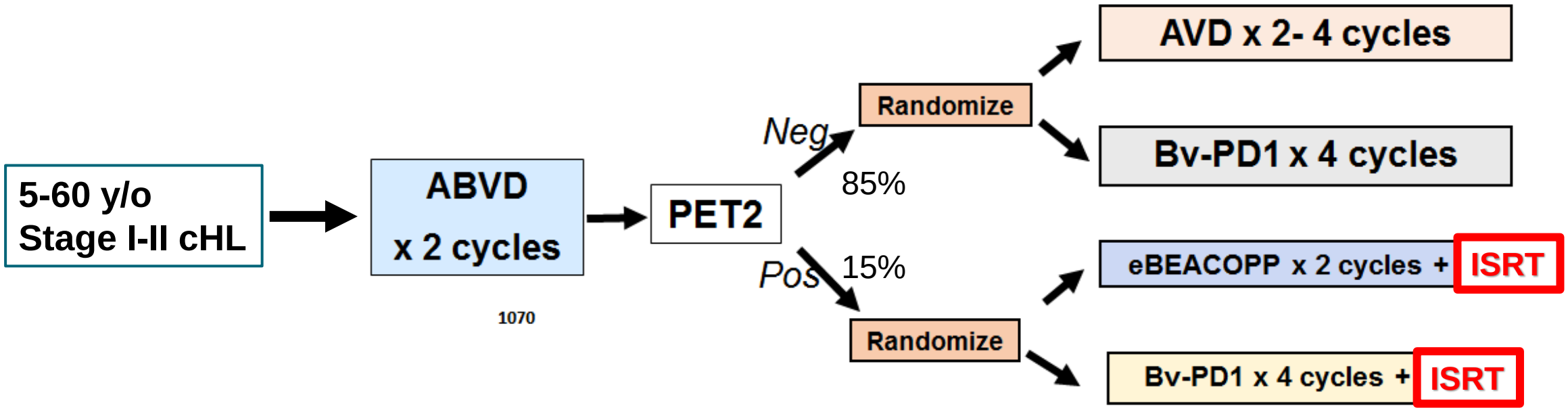
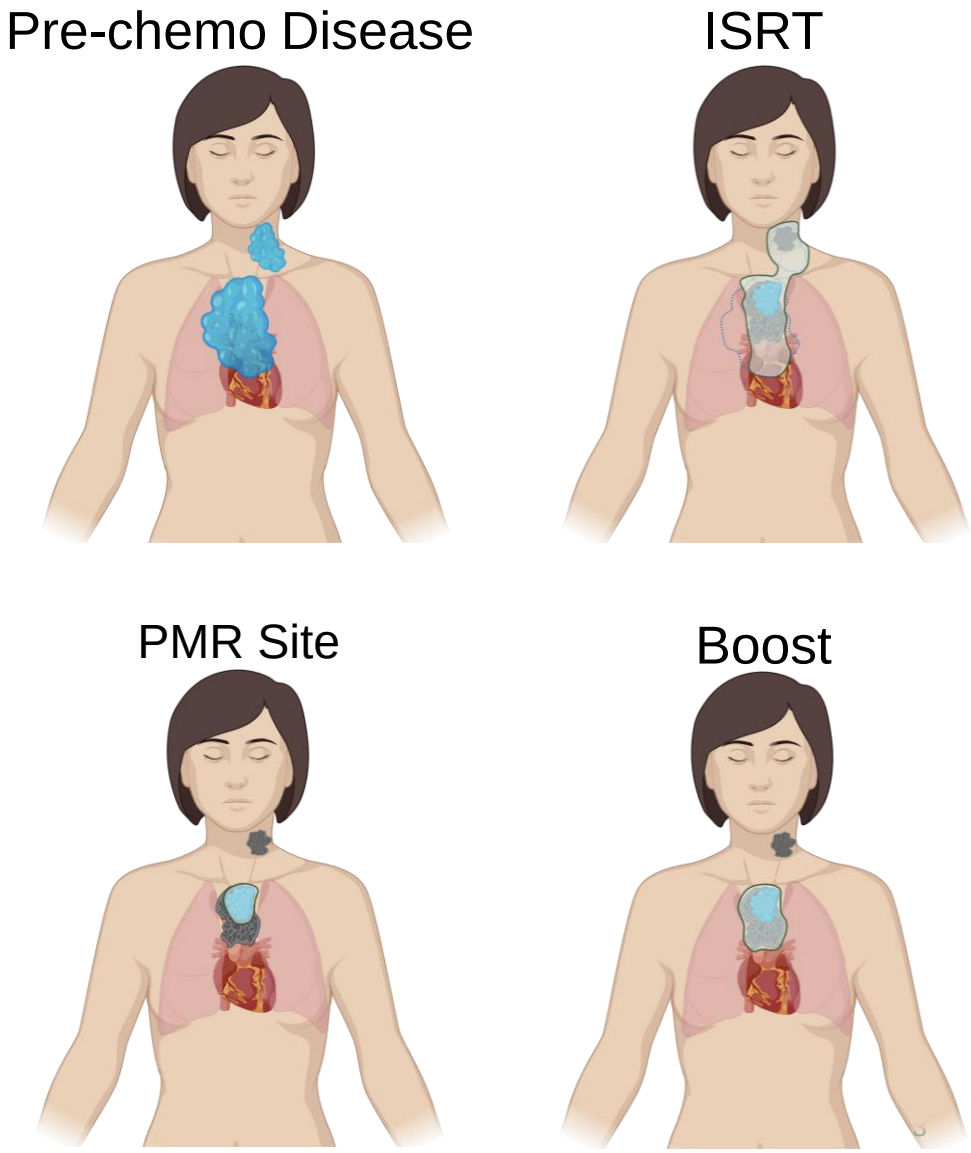
AHOD2131 Radiation Approach: Patient Selection



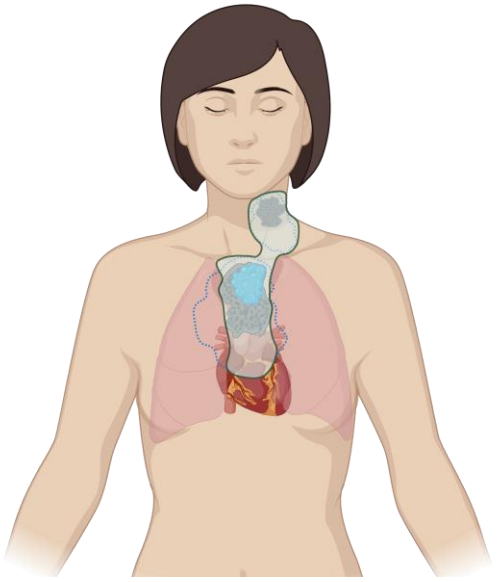
- RT is used for **SERs** only
  - RT is used for SERs due to their higher relapse risk
  - Anticipated to comprise ~15% of the total cohort
    - For comparison, on AHOD0031: ~75% received RT

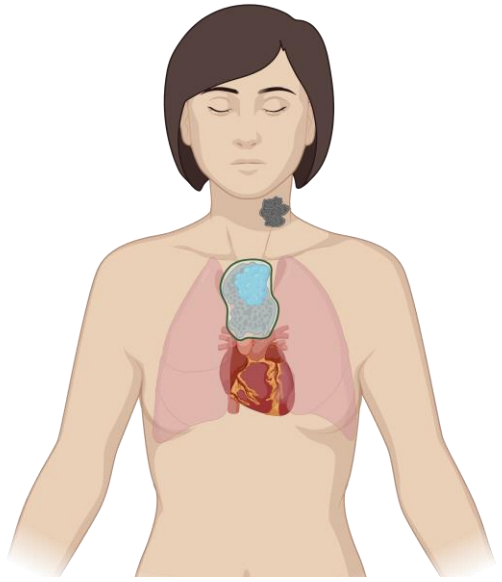
AHOD2131 Radiation Approach: Target Volume

- Involved site RT +/- PET-directed boost
  - **ISRT**: LNs/tissues originally involved with HL, accounting for anatomic changes following chemotherapy
    - Volumes are individualized & typically smaller than historic IFRT fields
  - **PET-directed boost**: tissue in PMR at completion of systemic therapy
    - Deauville 4-5, even if LYRIC IR



AHOD2131 Radiation Approach: Dose





SER → CMR	**30 Gy**	
SER → CMR • <16 y/o • Any age, OAR constraints would be exceeded with 30 Gy ISRT	**21 Gy**	**9 Gy (SER)**
SER → PMR	**30 Gy**	**6-10 Gy (PMR)**

AHOD2131 Radiation Approach: Dose

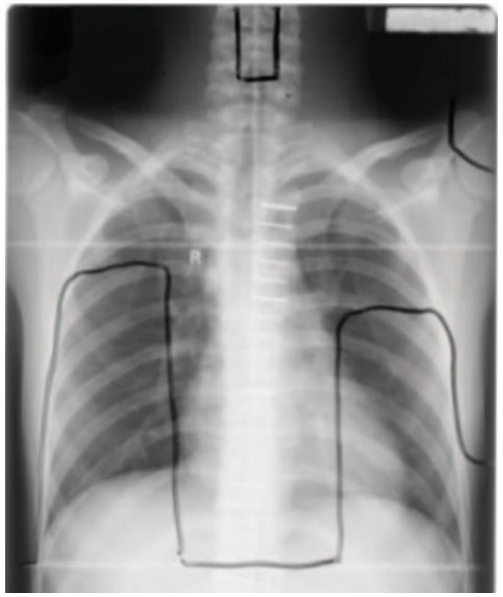
- **Why 30 Gy instead of 21 Gy?**
  - 21 Gy may be insufficient
    - AHOD0031: 90% of relapses occurred within the RT field [1]
    - AHOD0431: 80% of relapses in patients with SER/PR occurred within the RT field [2]
    - In-field relapses are less common after 30-36 Gy
    - GHSG HD11: PFS is *not* non-inferior after 20 Gy vs. 30 Gy following ABVD x 4 [3]
  - 30-36 Gy is used on pediatric & adult trials after an incomplete metabolic response
    - S1826, AHOD1331
  - AHOD2131 is using RT for SERs, who have less chemoresponsive disease
- **However, 21 Gy ISRT + 9 Gy boost** to SER sites is an option for patients with CMR on EST-PET who are
  - <16 years old
  - Any age, if normal tissue constraints cannot be achieved with 30 Gy ISRT

1. Dharmarajan, IJROBP 2015
2. Parekh, Blood 2022
3. Eich, JCO 2010

AHOD2131 Radiation Approach: Technique

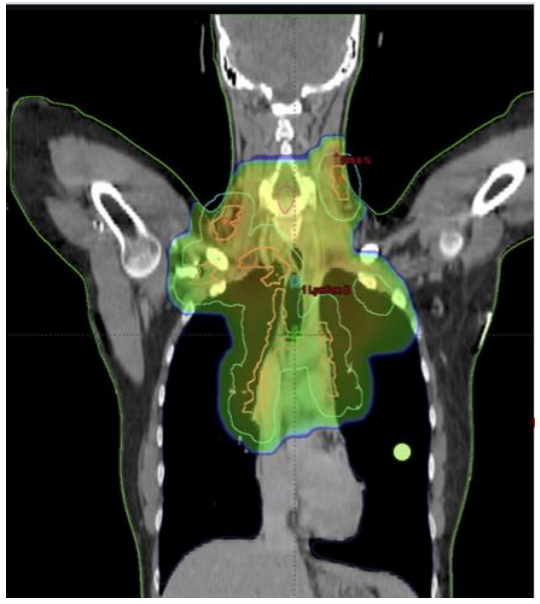
- Advanced RT techniques are allowed (IMRT, VMAT, proton therapy)
  - Highly conformal
  - Minimize dose to normal tissues compared to historic 2D and 3D techniques
- Motion assessment/reduction is encouraged (ex DIBH)

Historic 2D



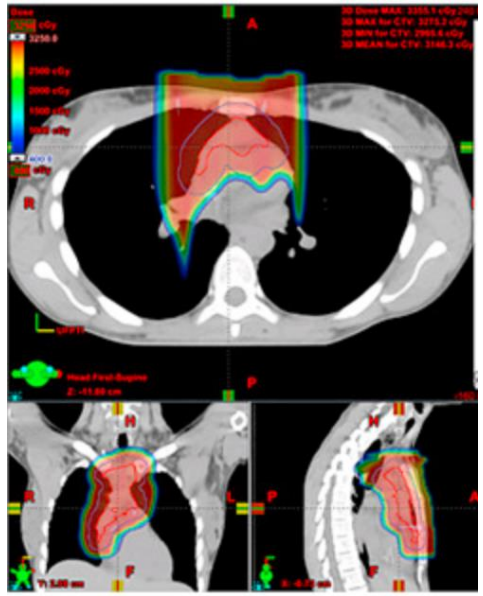
Cutter et al. JNCI 2015

IMRT with DIBH



Specht et al. IJROBP 2014

Protons

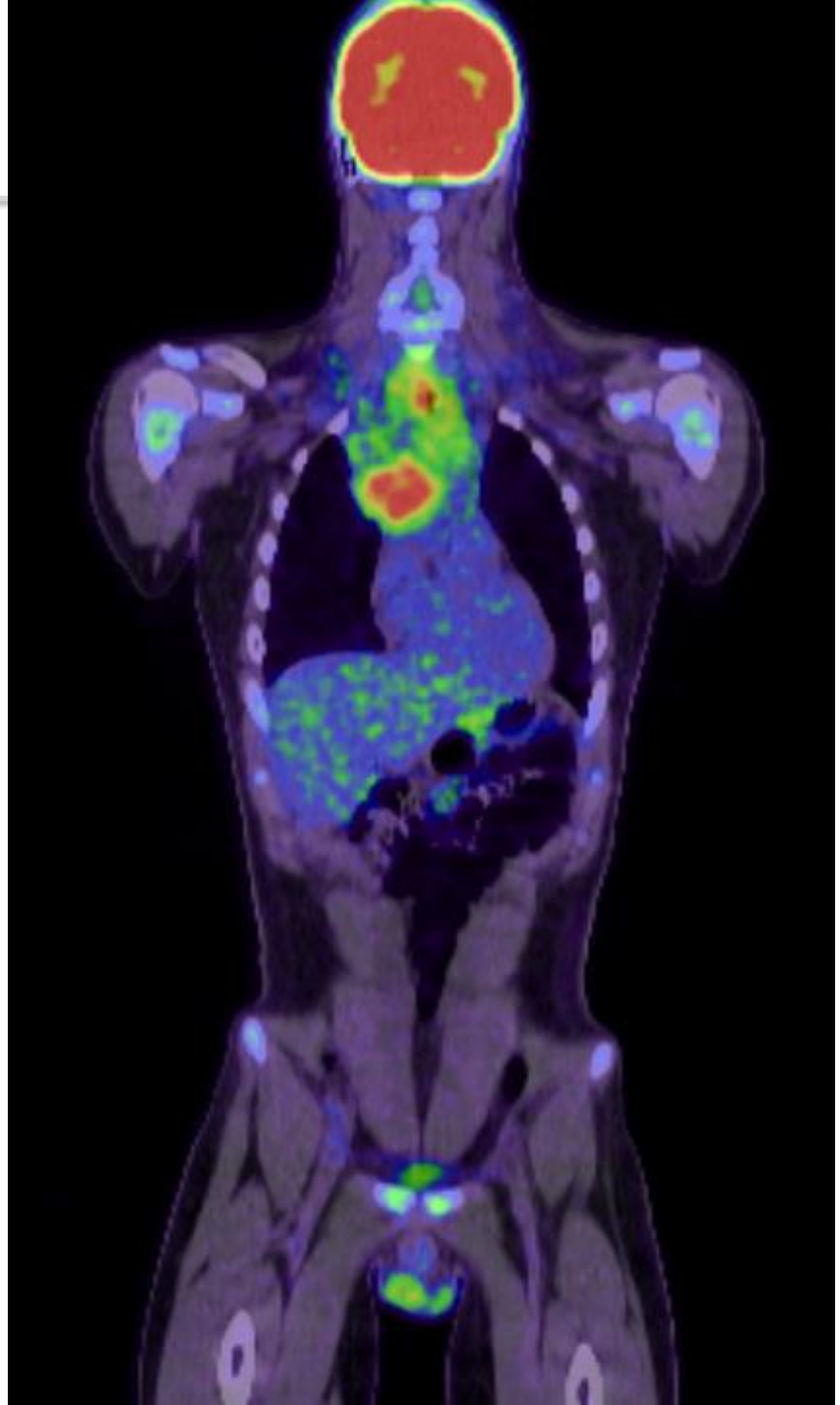


Hoppe et al. IJROBP 2014

AHOD2131 Case #1

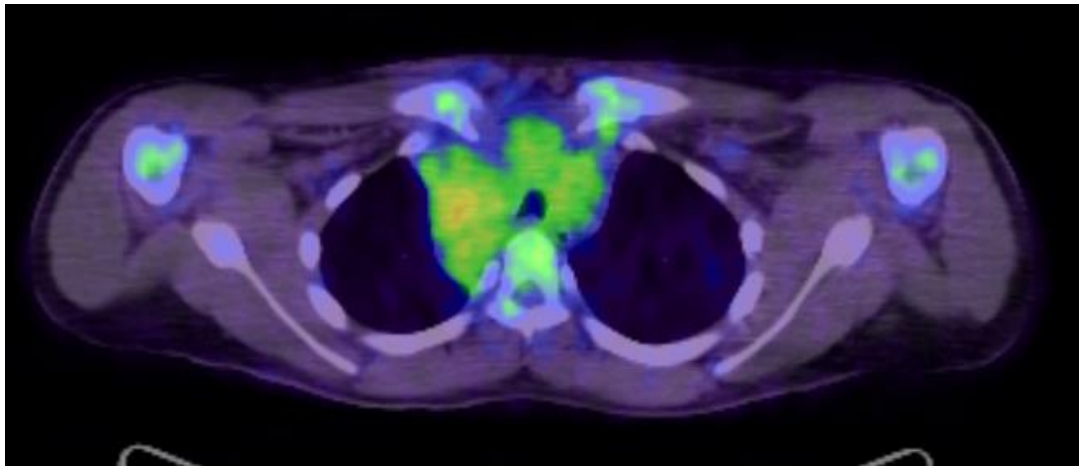
- 25 y/o man with stage IIA classic HL
- PET2: Deauville 4 (SER)
- EST-PET: Deauville 2 (CMR)

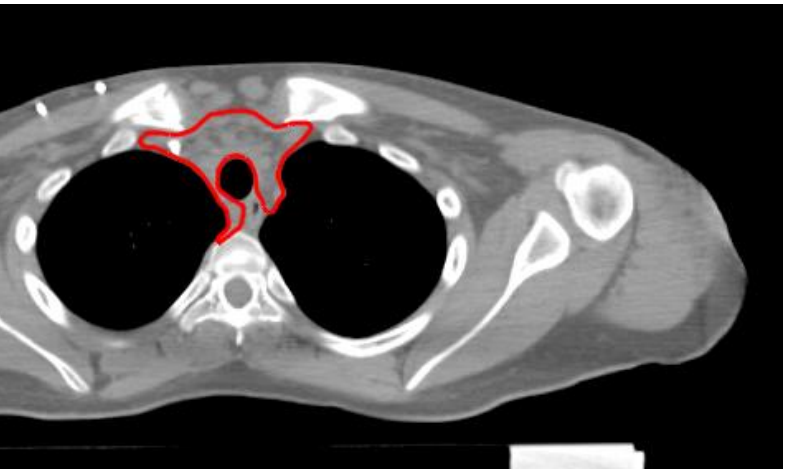
- ISRT: 30 Gy in 15 fractions

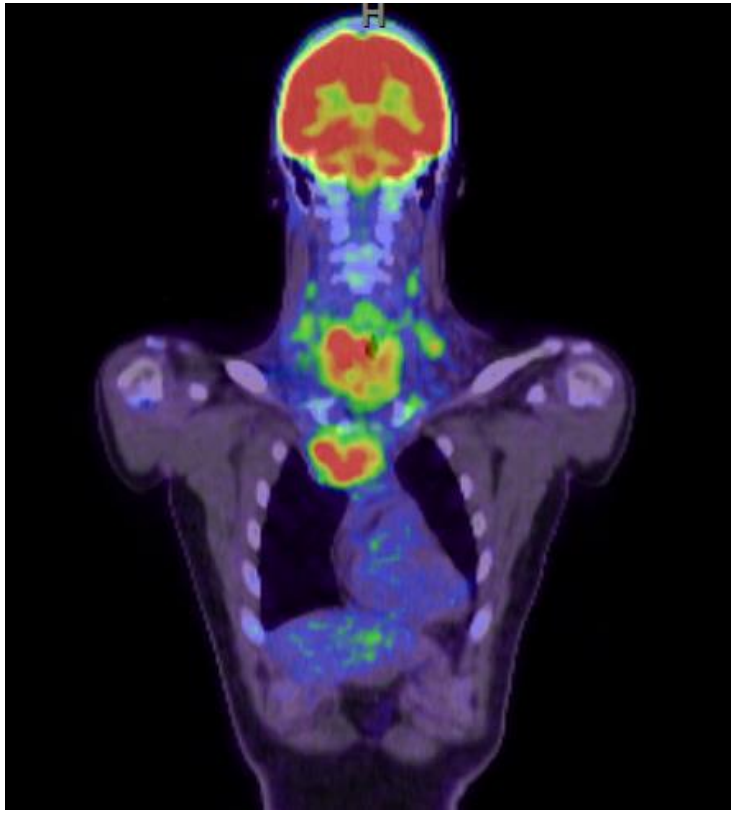


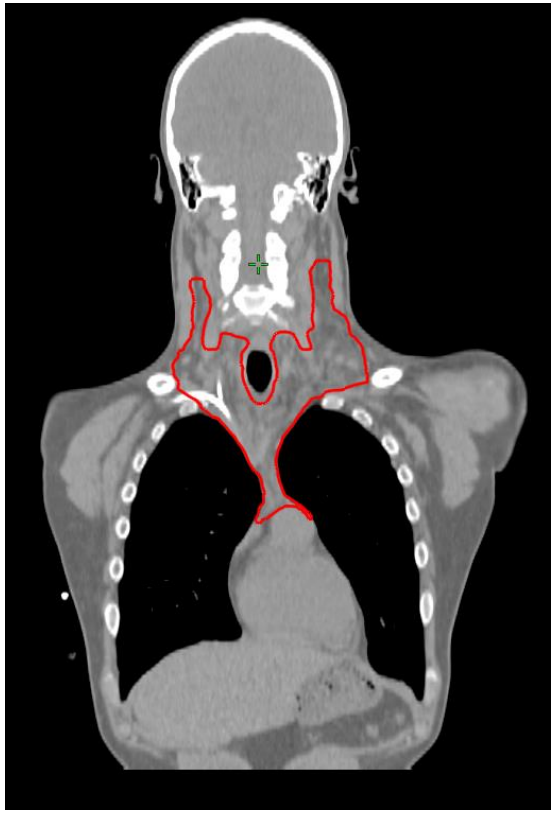
Baseline PET

CTVisrt

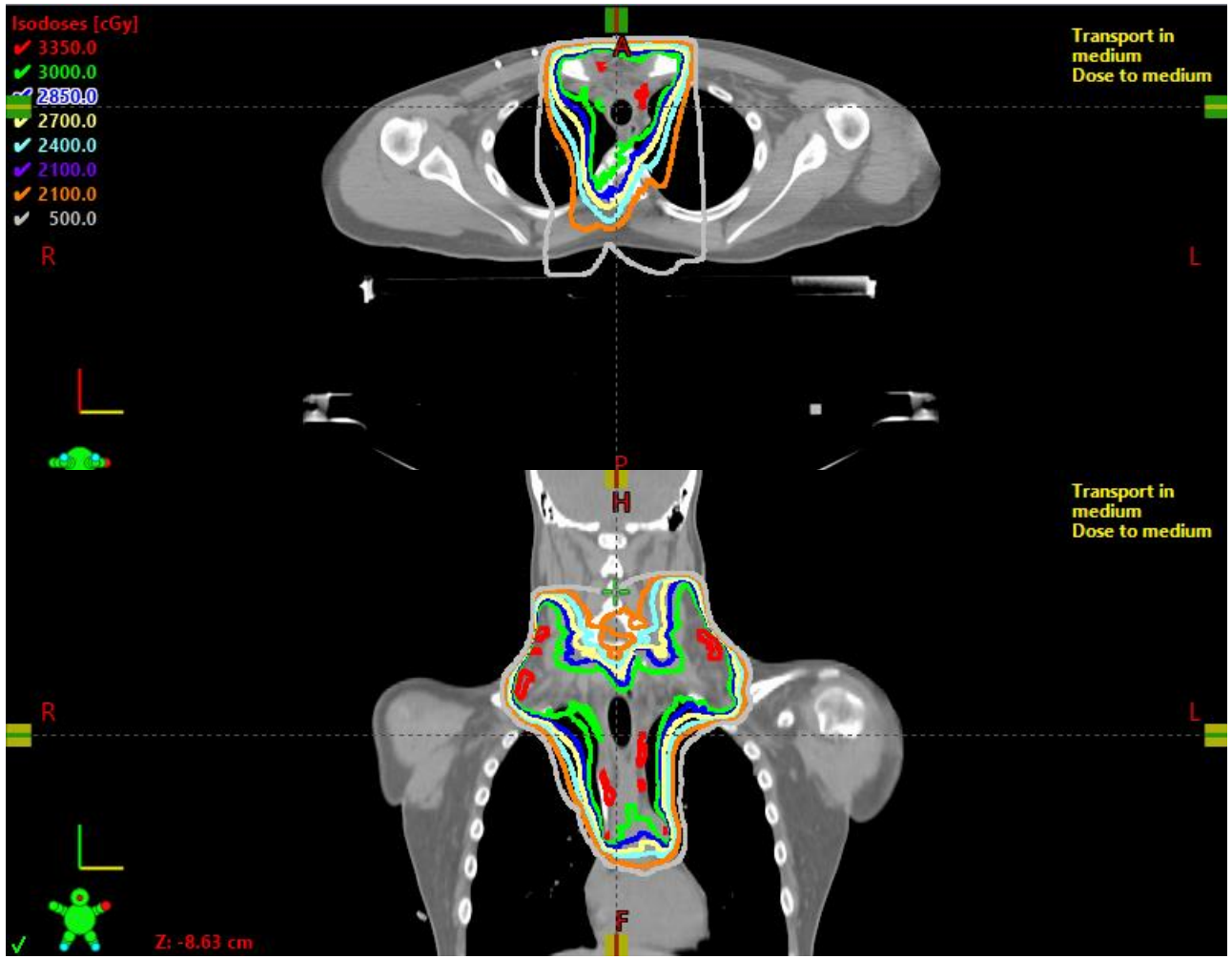








IMRT Plan Using DIBH & Butterfly Arrangement*



* Voong et al. Radiat Oncol. 2014 Apr 15:9:94

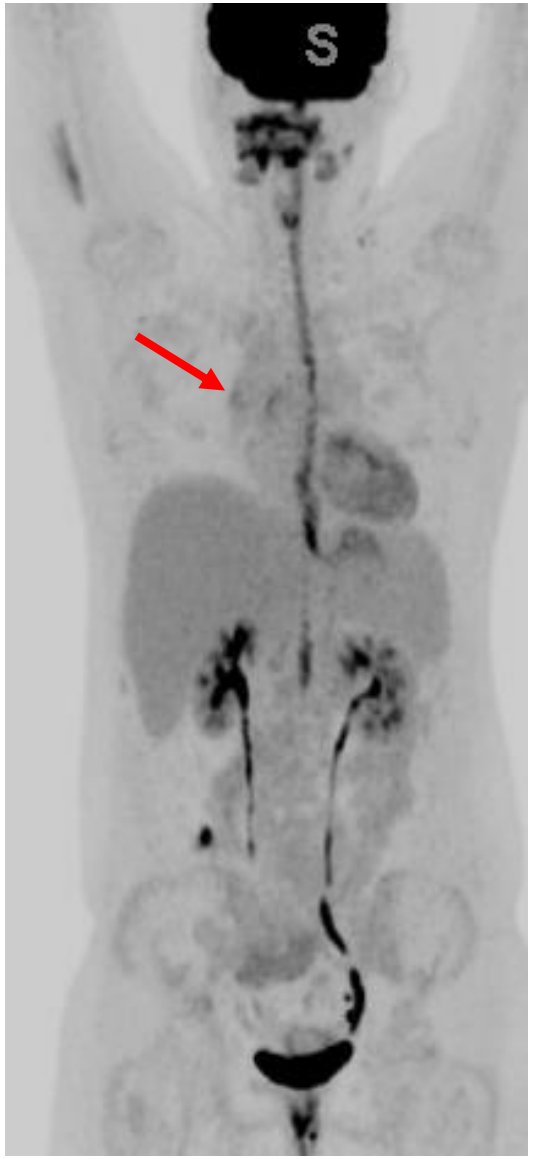
AHOD2131 Case #2

- 45 y/o woman with stage IIA bulky classic HL
- PET2: Deauville 4 (SER)
- EST-PET: Deauville 4 (PMR)

- ISRT: 30 Gy in 15 fractions
- Sequential boost to area with a PMR at completion of systemic therapy: 8 Gy in 4 fractions

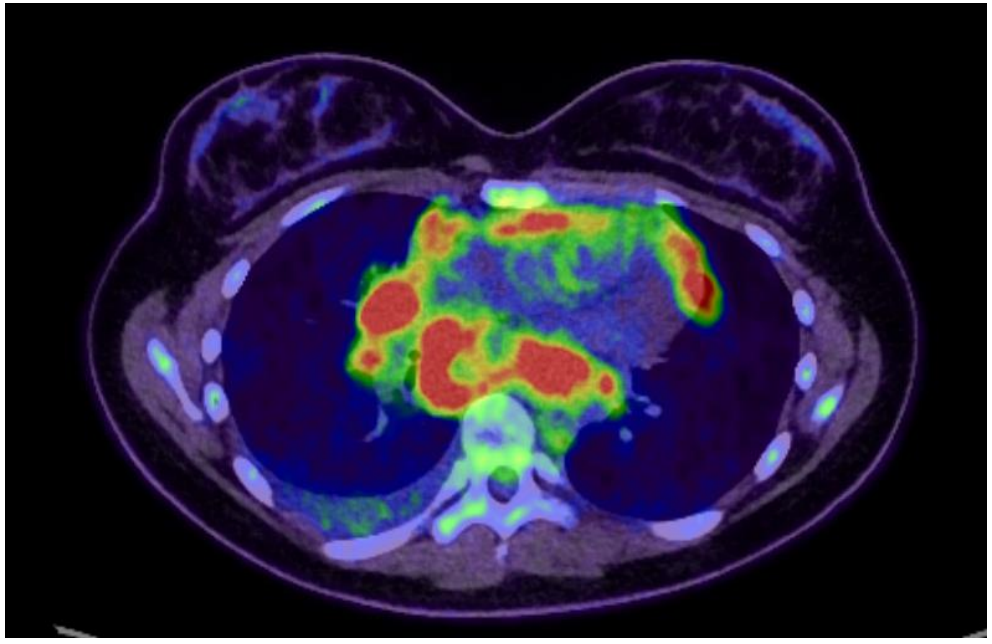
Baseline PET

PET2: 5-point score 4



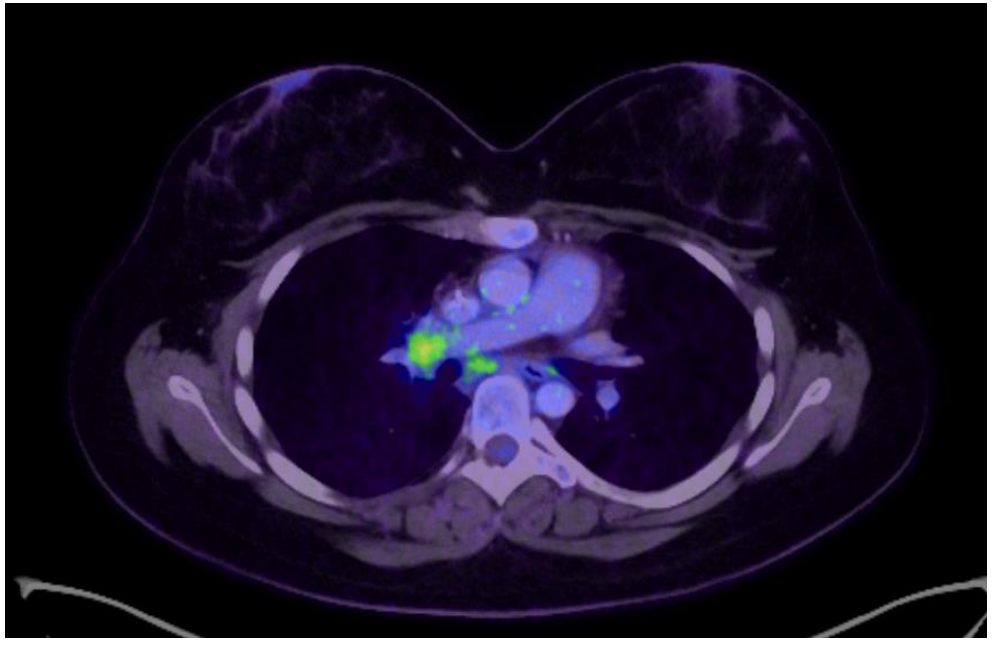
EST-PET: 5-point score 4

Baseline PET

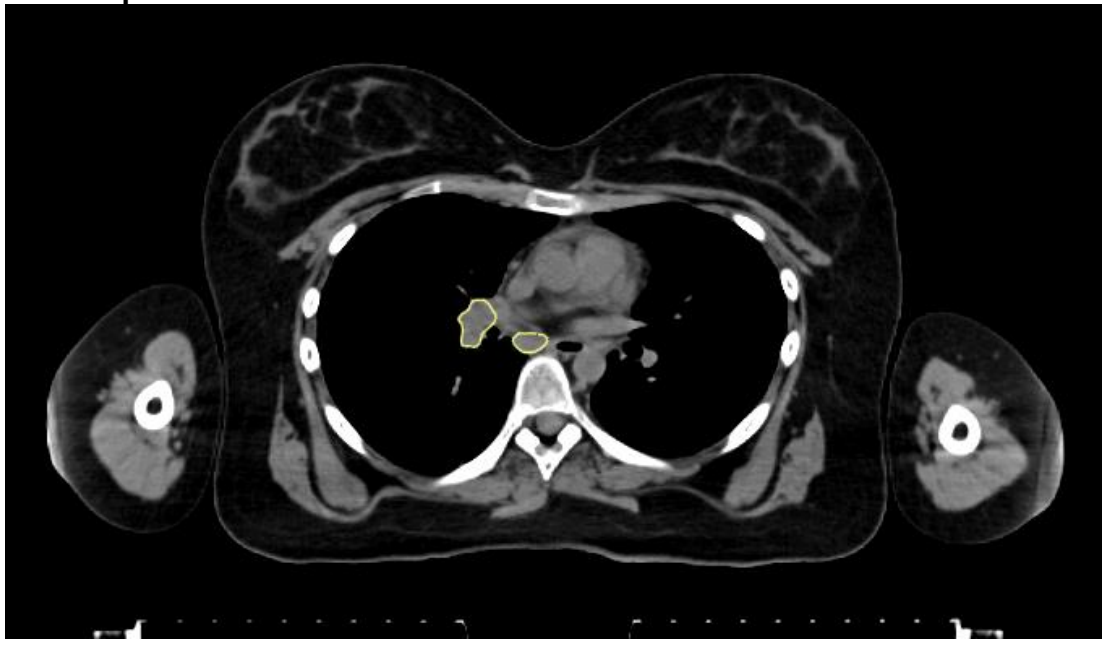


CTVisrt

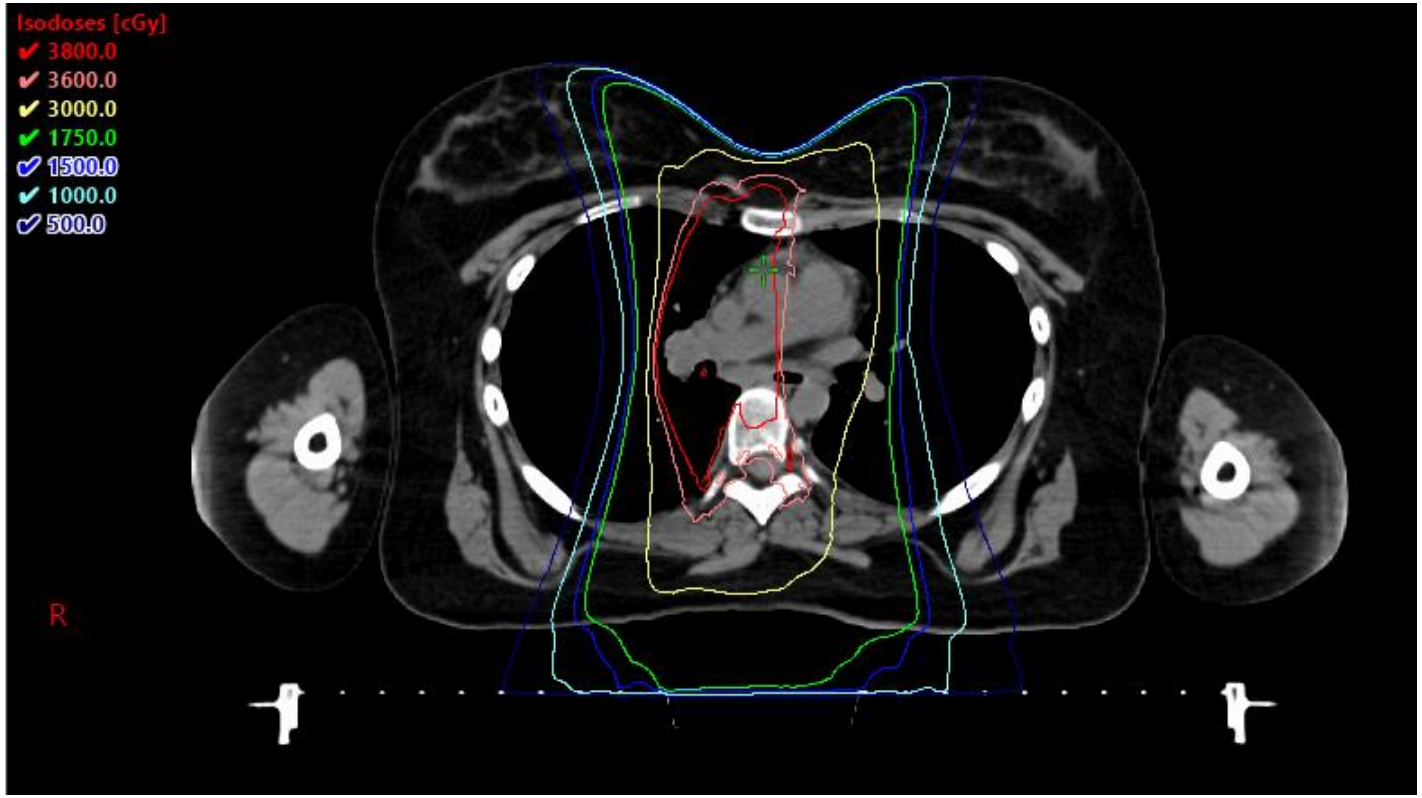
EST-PET

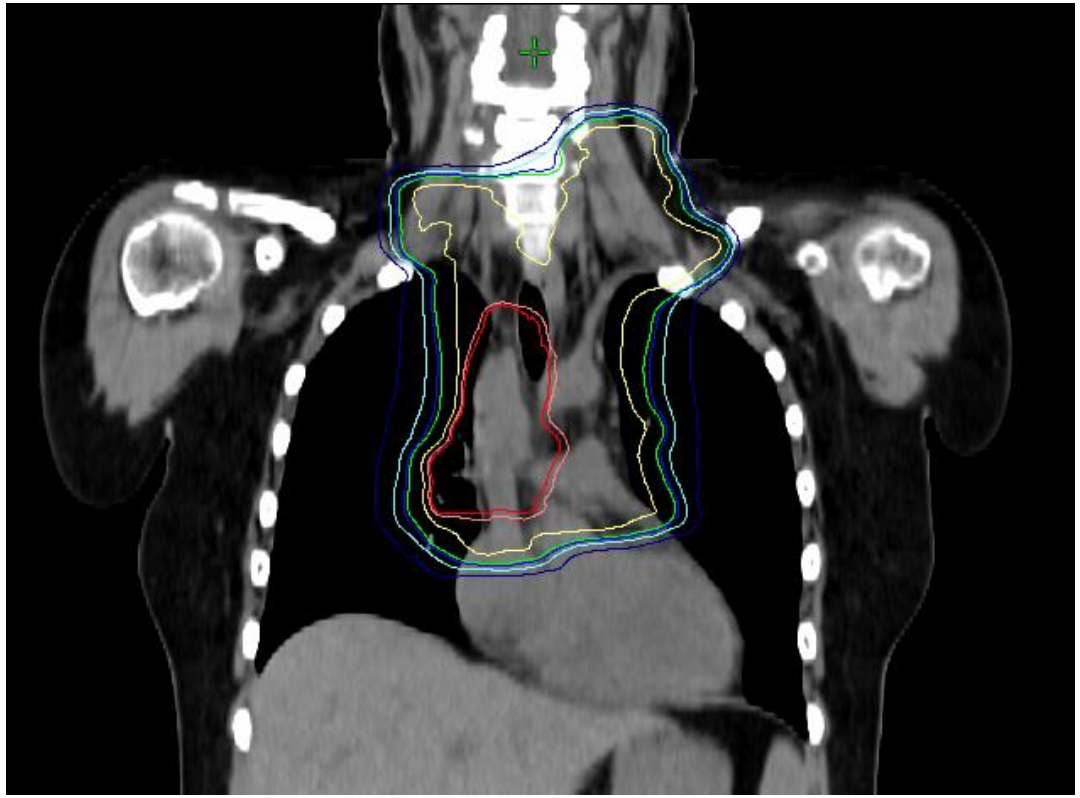


CTVpr



IMRT Plan Using DIBH & Butterfly Arrangement*





CHILDREN'S ONCOLOGY GROUP

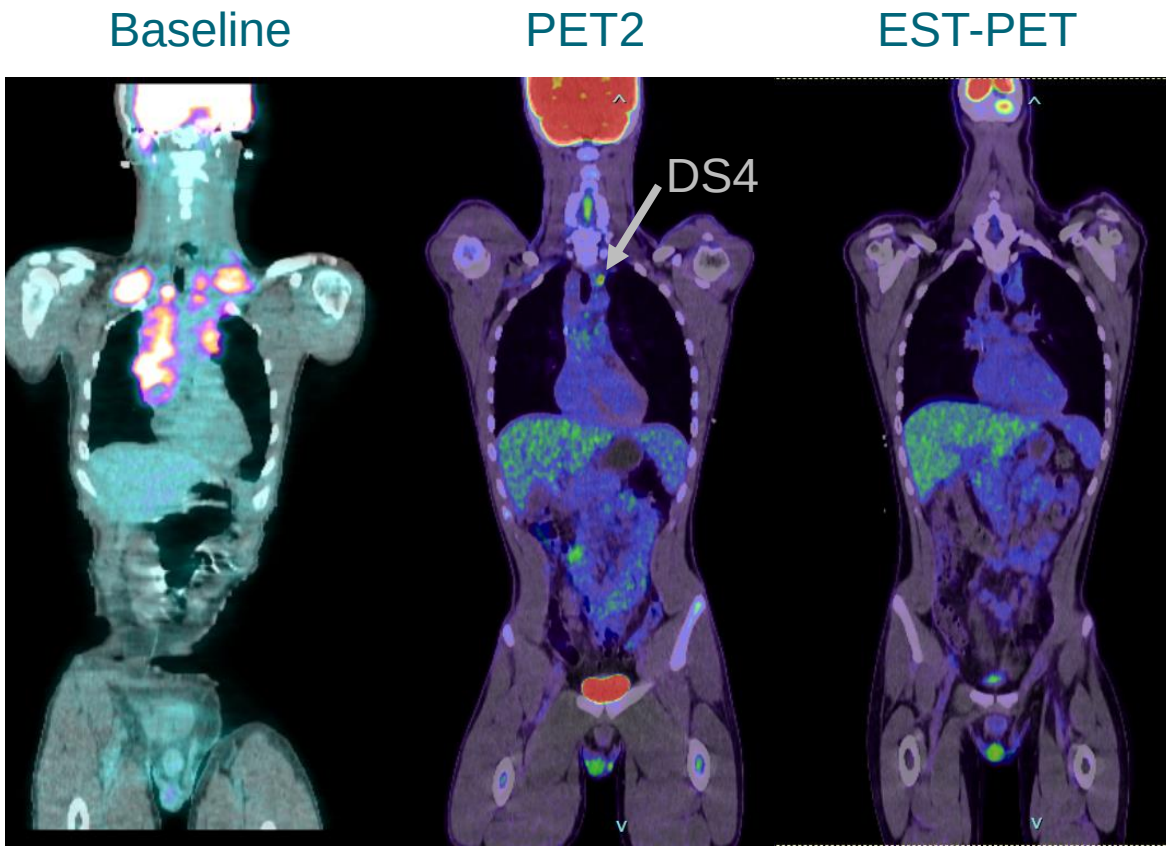
The world's childhood cancer experts

* Voong et al. Radiat Oncol. 2014 Apr 15:9:94

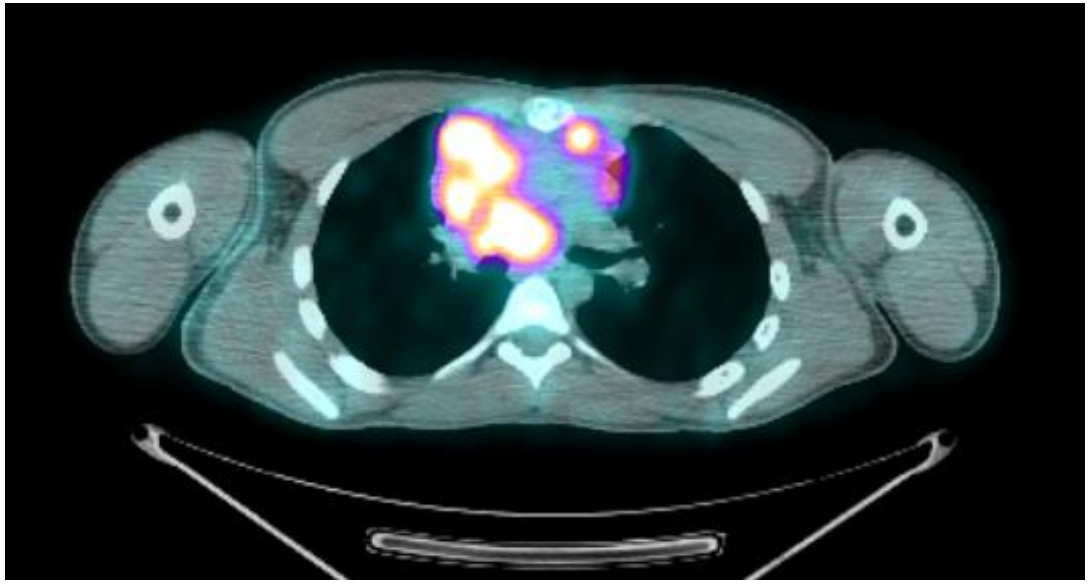
AHOD2131 Case #3

- 14 y/o boy with stage II cHL
- PET2: Deauville 4 (SER)
- EST-PET: Deauville 3 (CMR)

- In CMR & <16 y/o →
  - ISRT: 21 Gy/14 fractions
  - Boost to SER site: 9 Gy/6 fractions

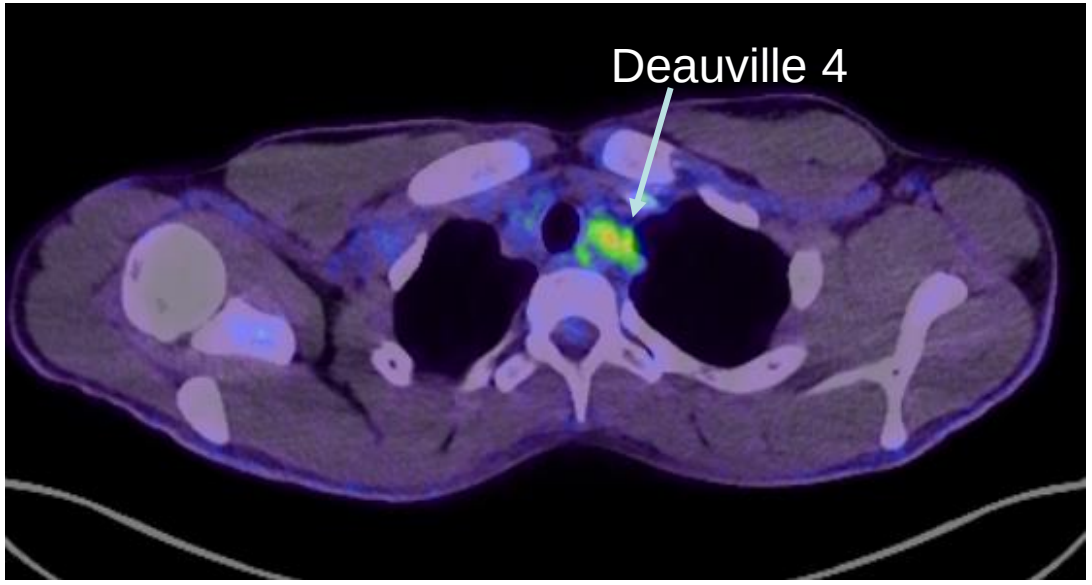


Baseline PET

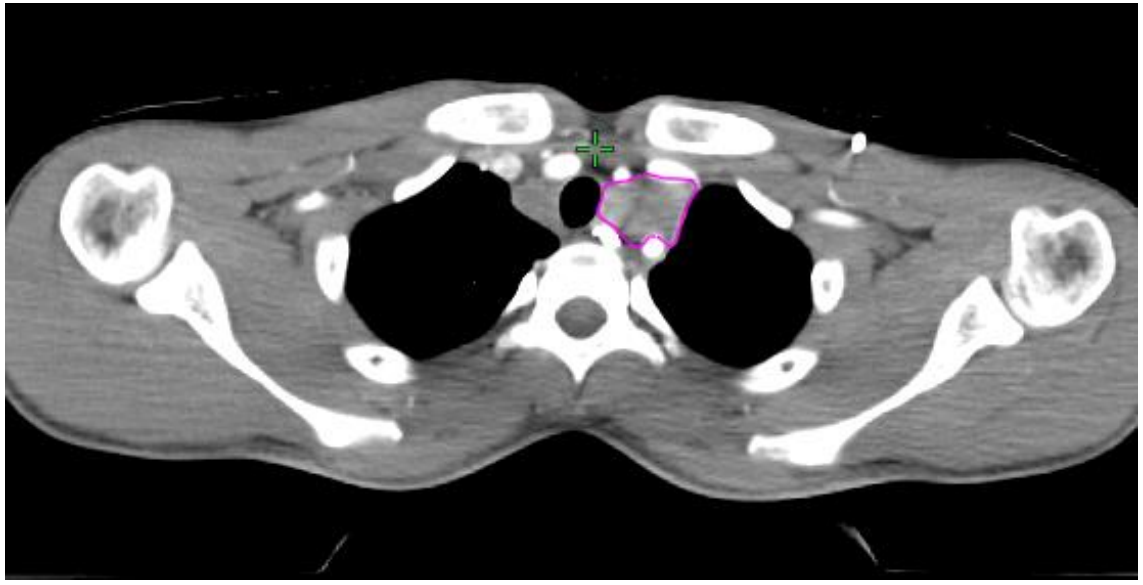


CTVisrt (21Gy)

PET2



CTVser (9Gy boost)



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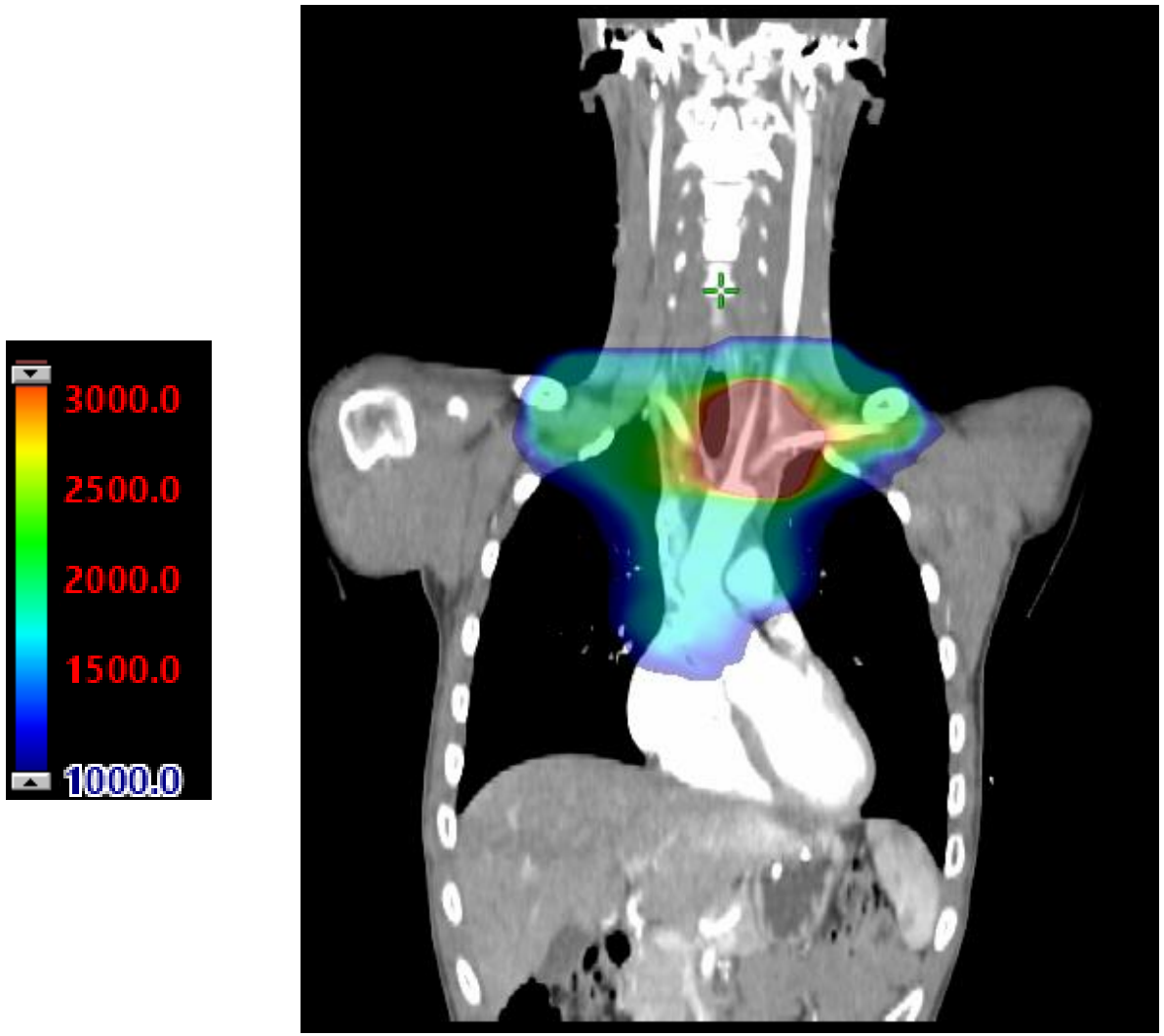


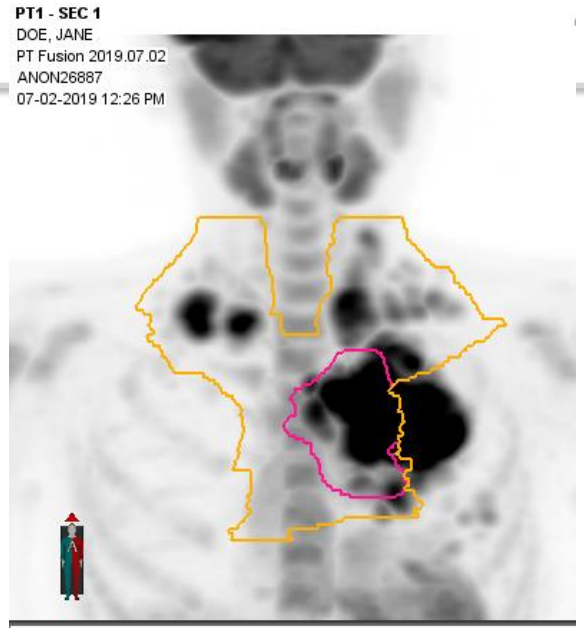
* Voong et al. Radiat Oncol. 2014 Apr 15:9:94

Case 4

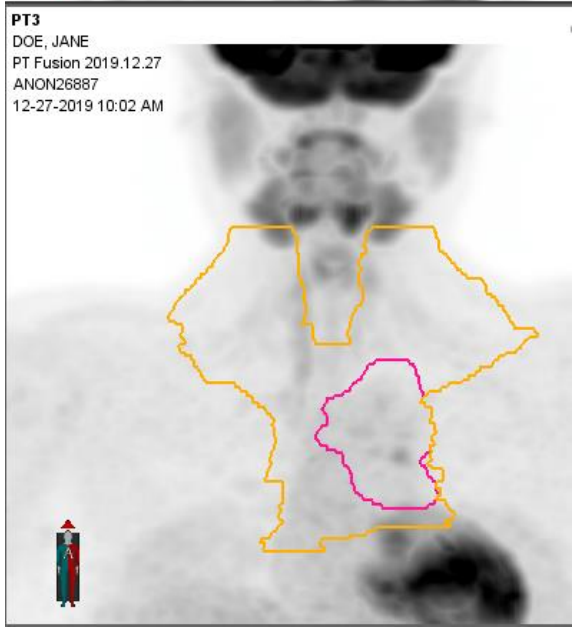
- 30 y/o F with stage IIA Hodgkin lymphoma
- PET2: Deauville 4
- EST-PET: Deauville 4
- ISRT: 3000 cGy in 15 fractions
- Sequential boost to area with a PR at completion of systemic therapy: 600 cGy in 3 fractions

Contours

- Orange
  - ♦ CTVisrt – 30 Gy
    - All initial sites
- Magenta
  - ♦ CTVpr – 9 Gy
    - Partially responding site (EST-PET+)

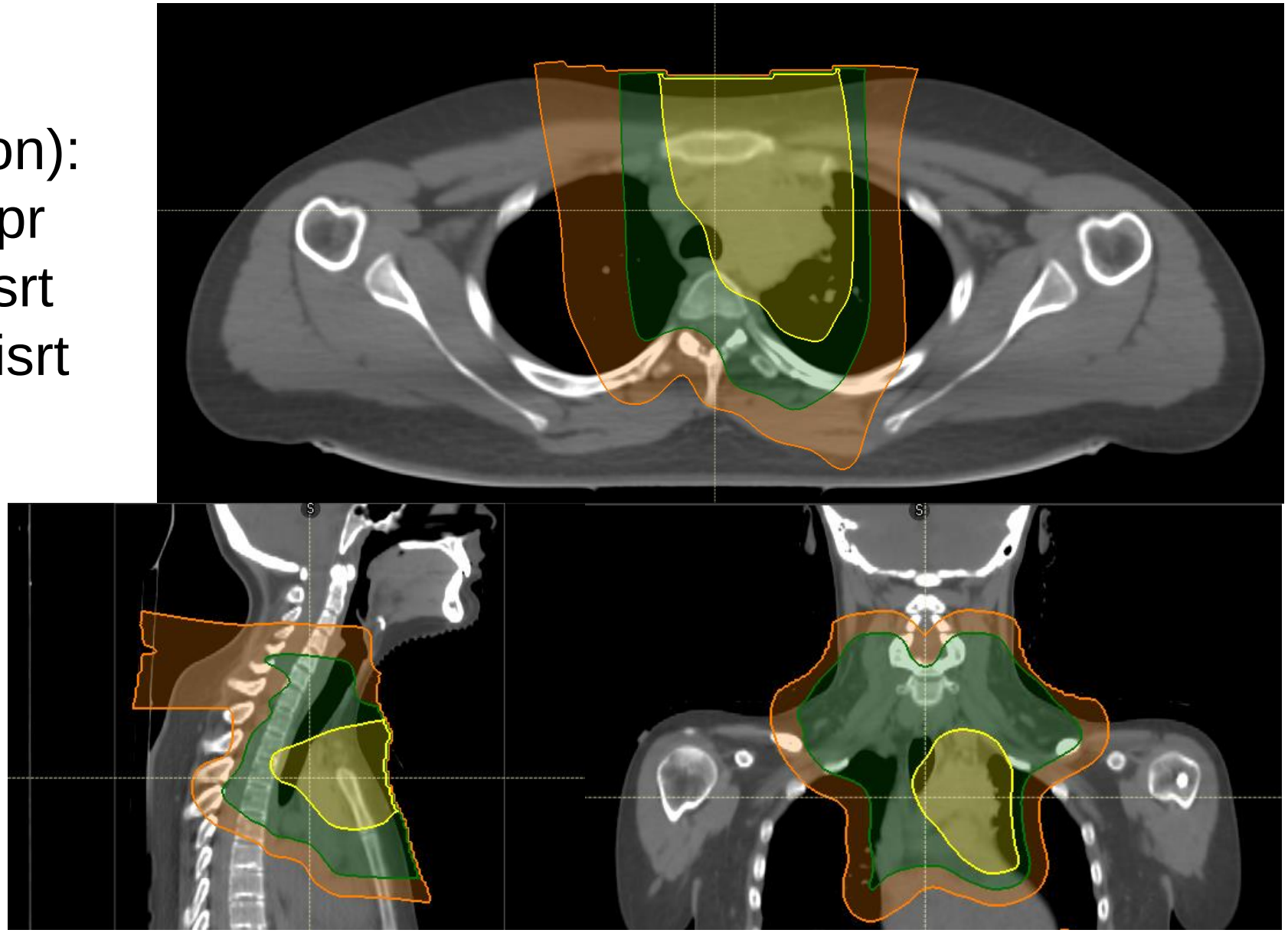


Pre-chemo PET



EST-PET

Dose (% of prescription):
Yellow: 95% of CTVpr
Green: 95% of CTVisrt
Orange: 10% of CTVisrt

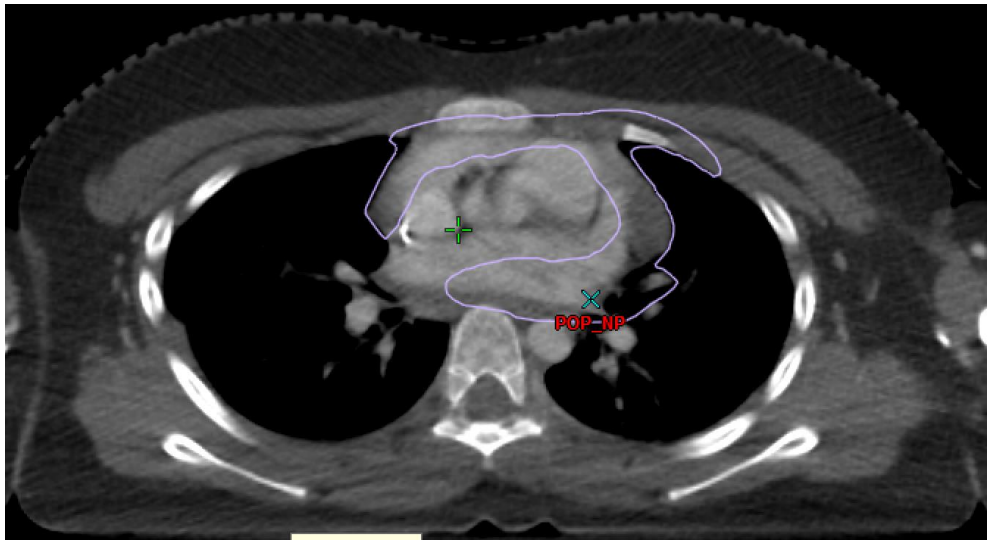


Case 5

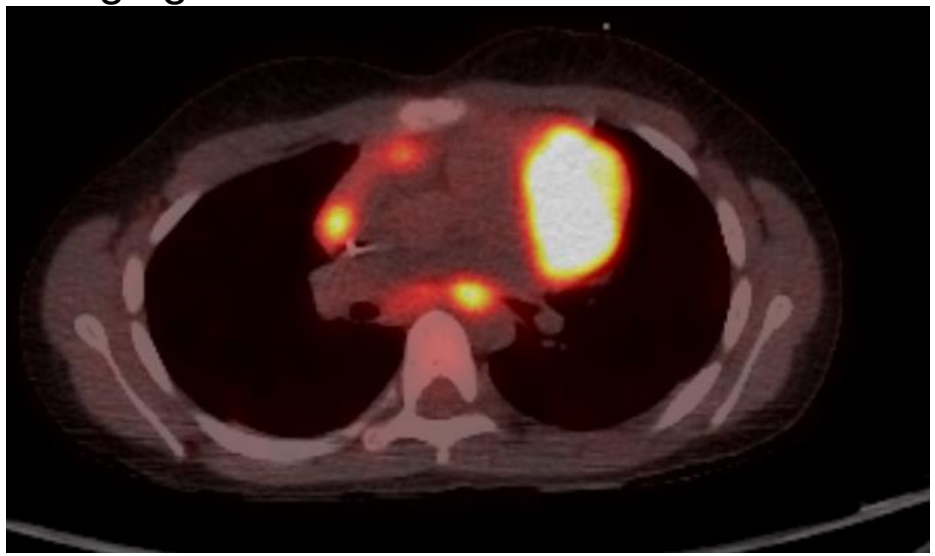
- 11 y/o boy with stage IIB classical Hodgkin lymphoma
- PET2: Deauville 4
- EST-PET: Deauville 3

- In CR after chemo & under 15 y/o → 21 Gy ISRT + 9 Gy boost to the slowly responding site
  - ISRT: 2100cGy/14 fractions
  - Boost to PET SER disease: 900cGy/6 fractions

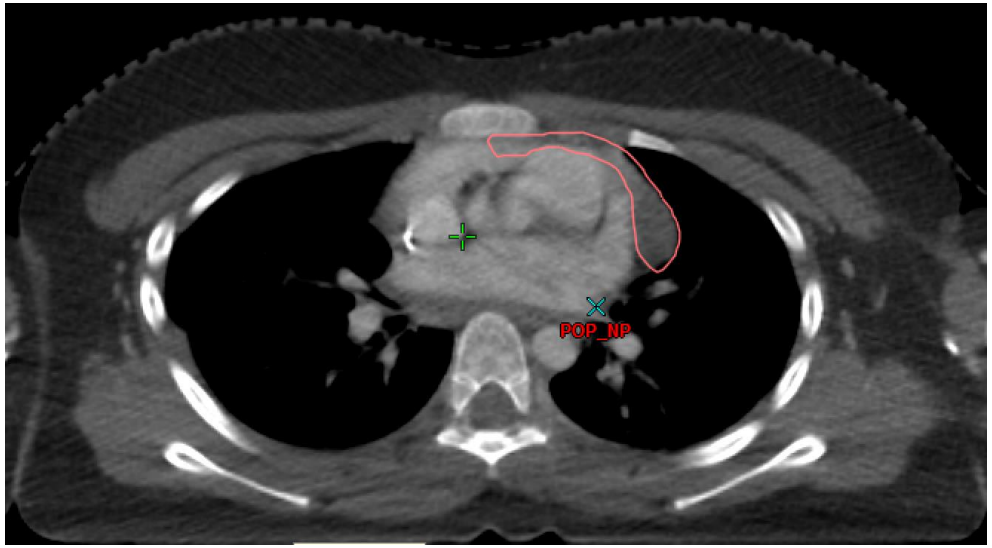
CTV 21Gy



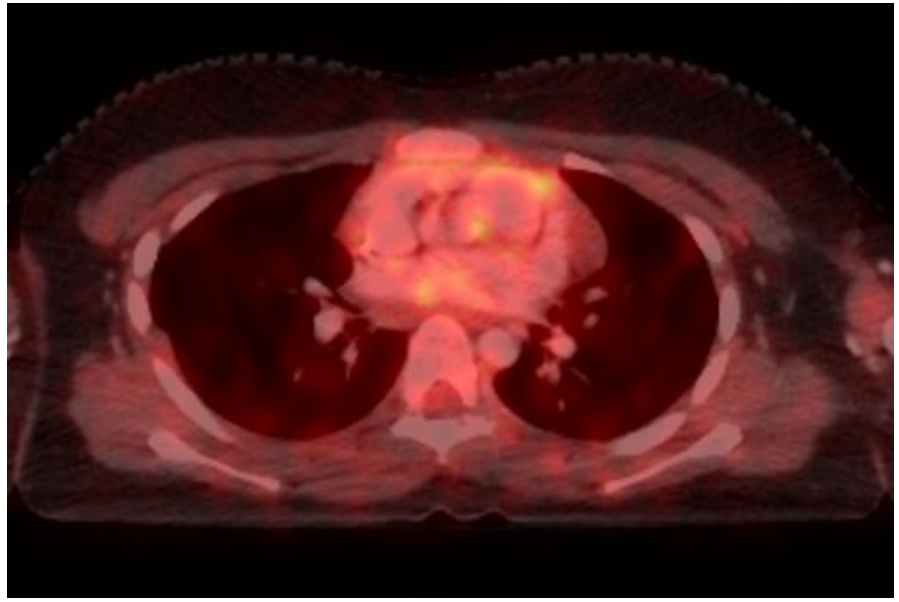
Staging PET



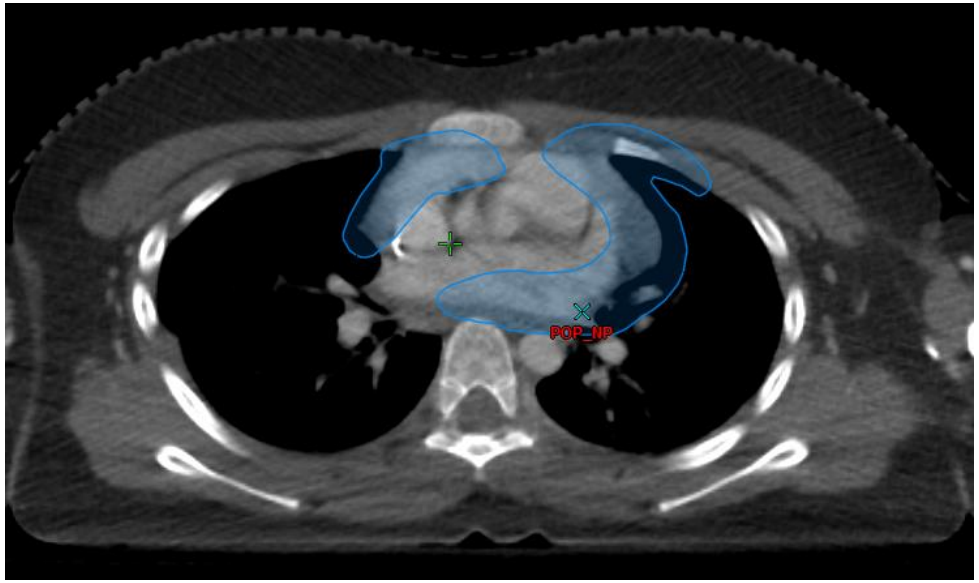
CTV 9Gy Boost



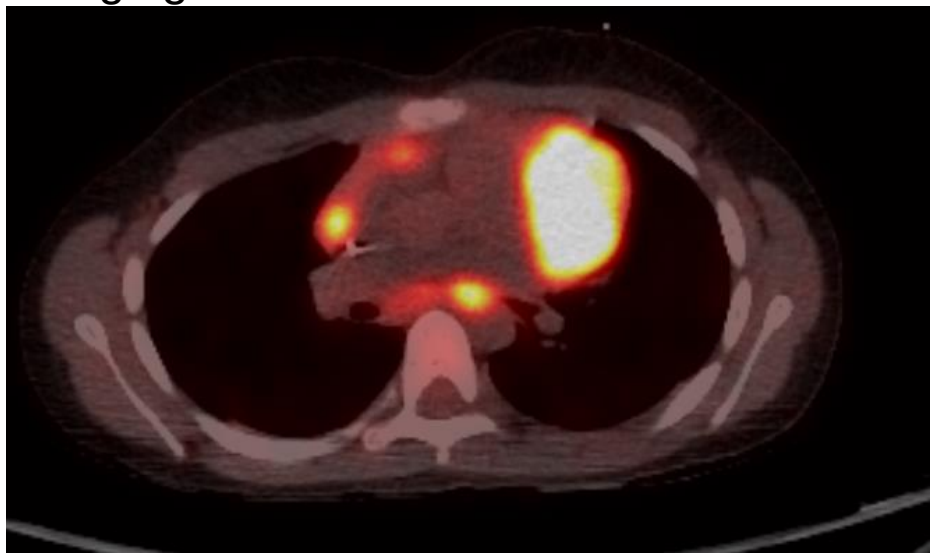
PET2



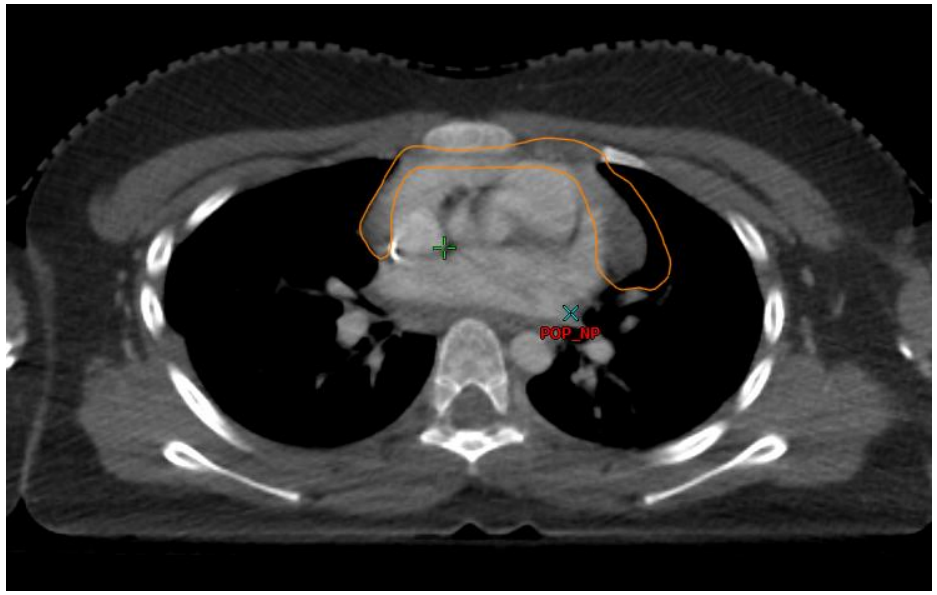
ITV 21Gy



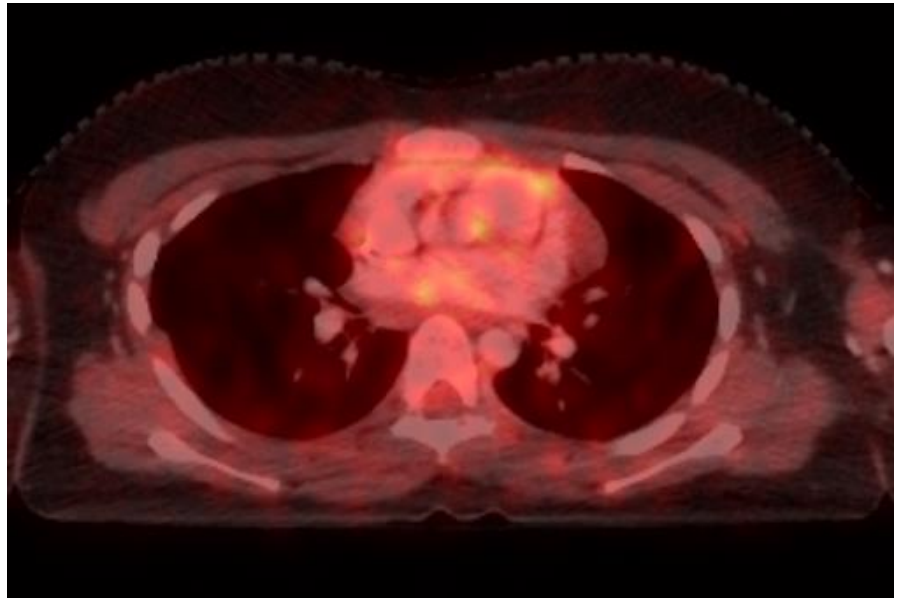
Staging PET

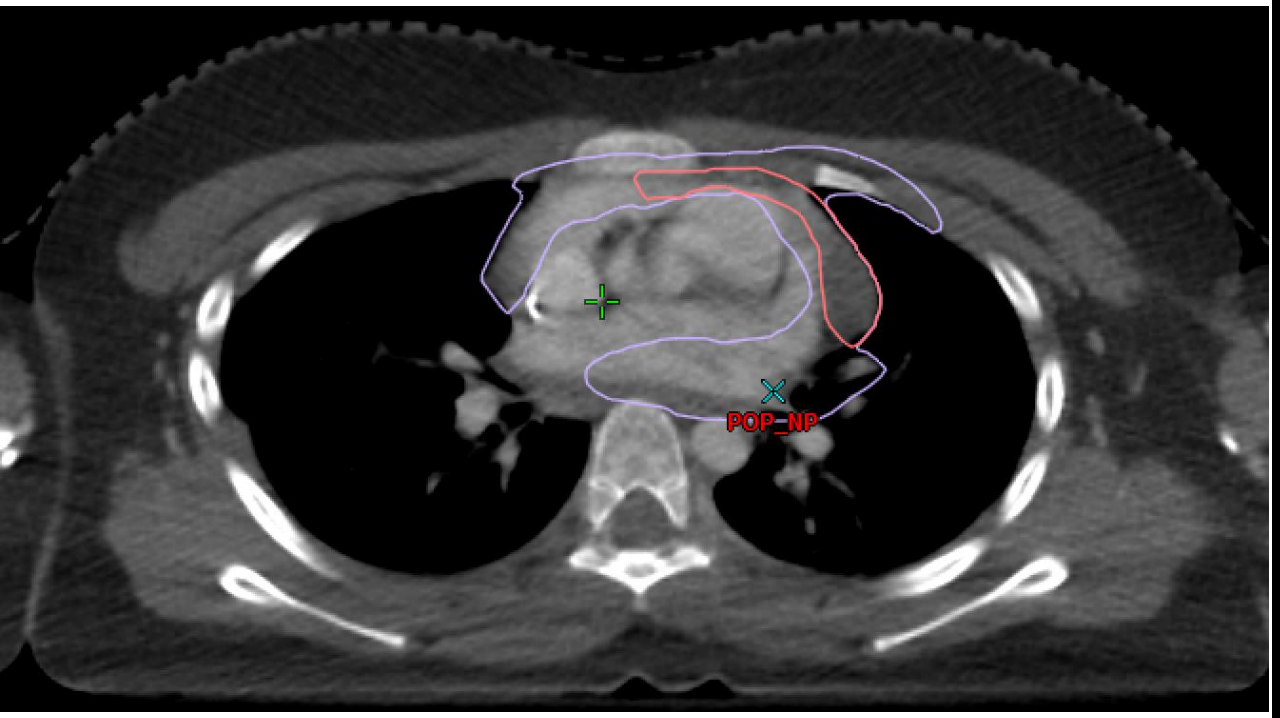


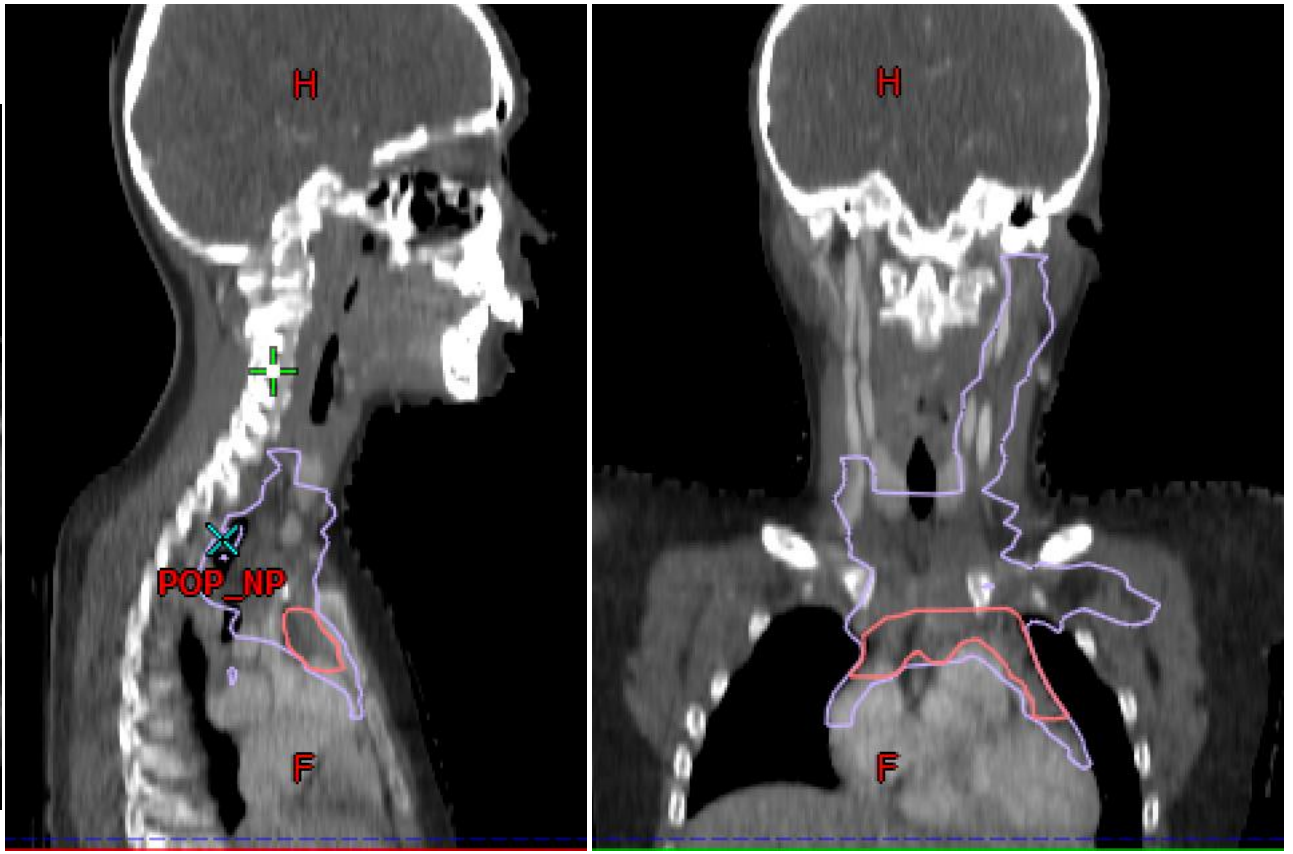
ITV 9Gy Boost



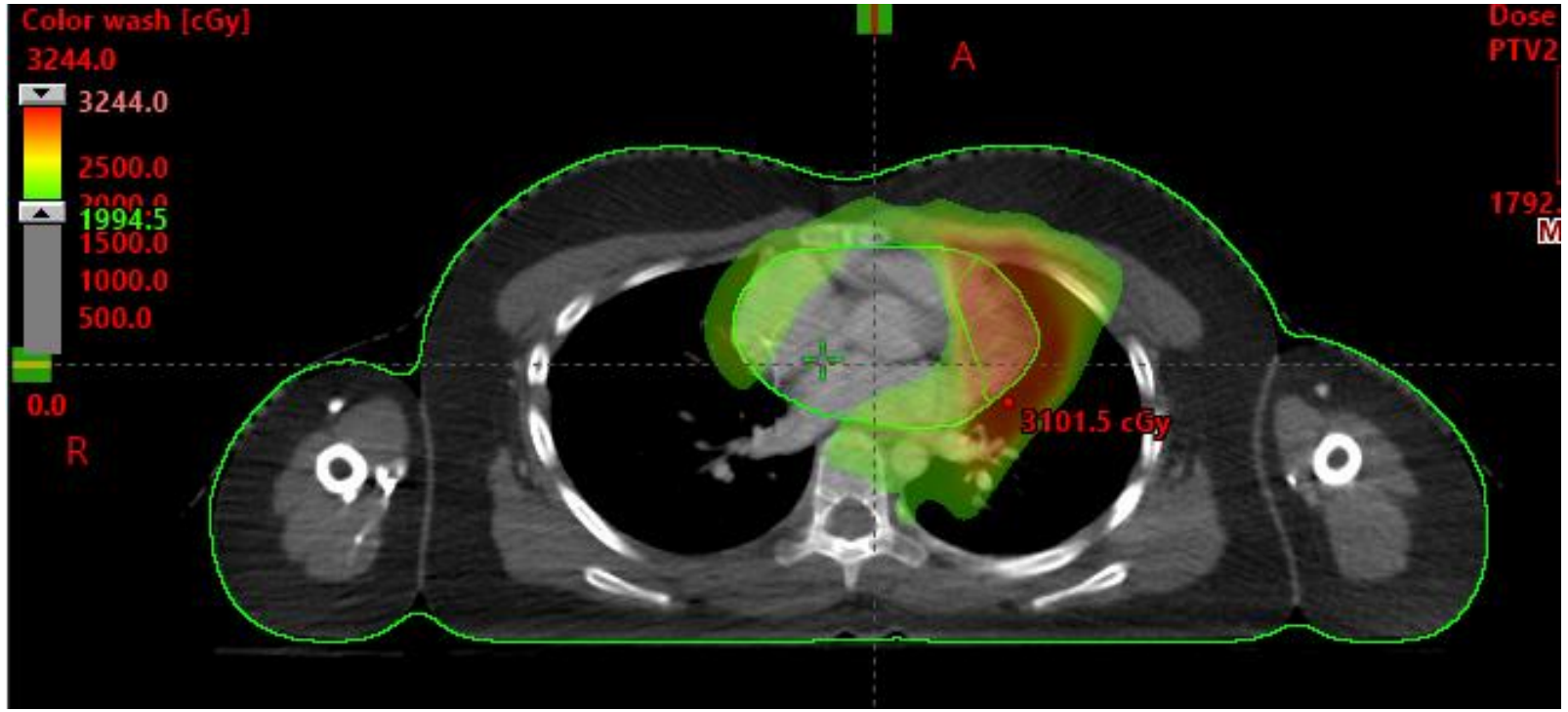
PET2



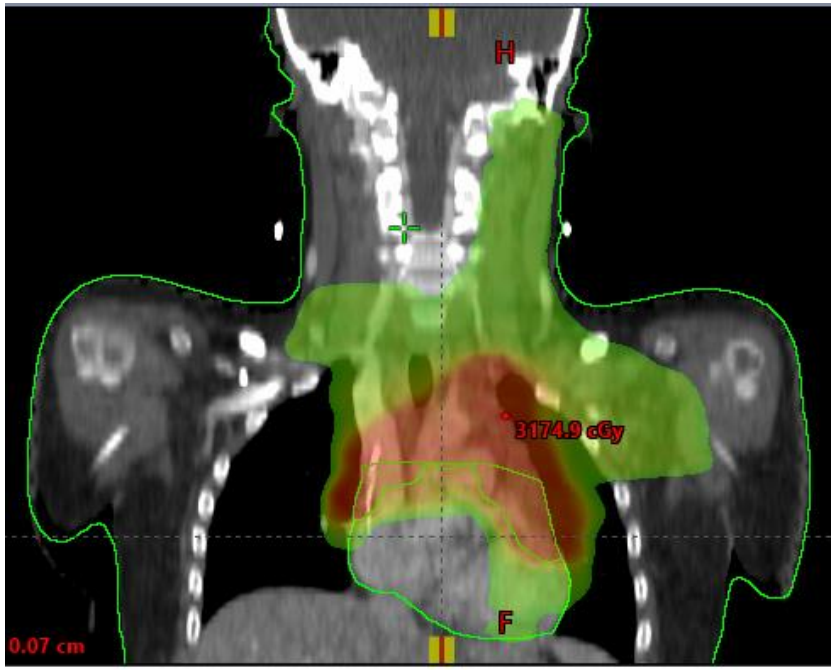




Purple = CTVisrt (21Gy)
Pink= CTVser (9Gy)

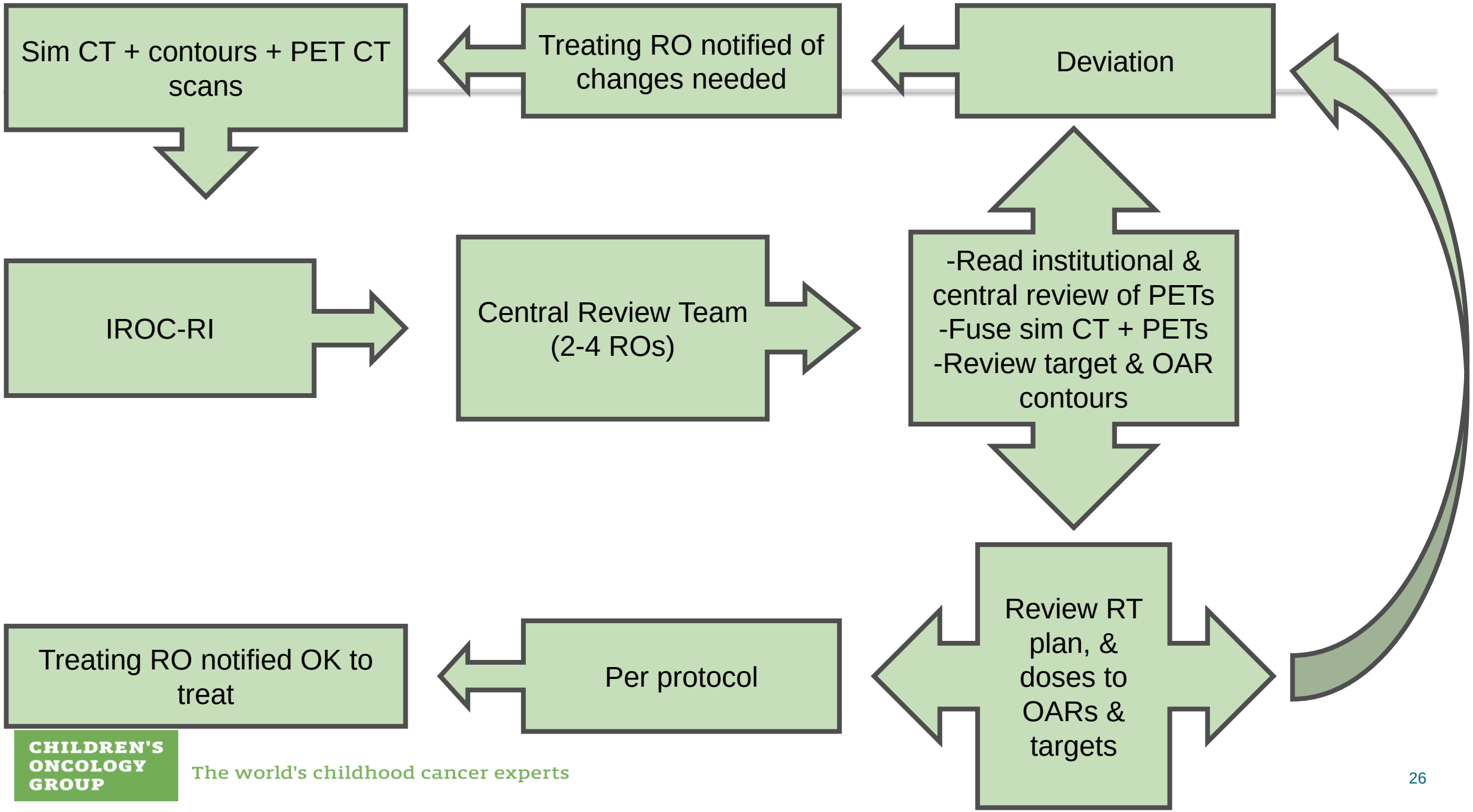

Color wash [cGy]
3244.0
3244.0
2500.0
1994.5
1500.0
1000.0
500.0
0.0
R
A
Dose
PTV2
1792
M
3101.5 cGy


H
3156.3 cGy
F


H
3174.9 cGy
F
0.07 cm

AHOD2131 Radiation Approach: Central Review

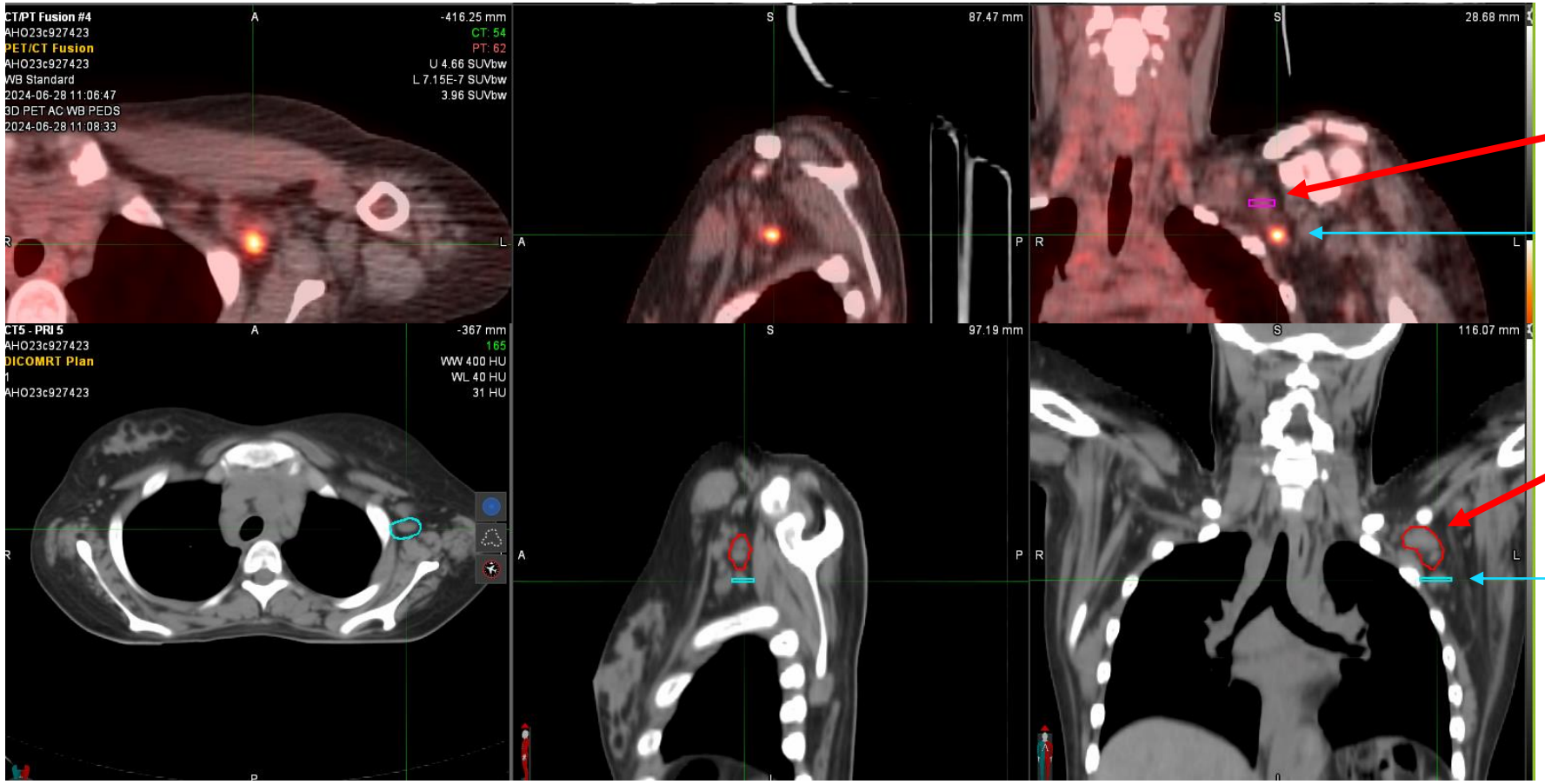
- All contours & RT plans undergo central review by the study team before the patient is treated
- Early referral to RO is highly recommended to allow time for treatment planning, submission for central review, contour/plan revision if required, and final approval
- **Goal:** rigorous, real-time central review, building upon QA performed on prior studies of early-stage HL
  - EORTC H10: retrospective QA, representative sample of INRT plans, no PET fusion
  - GHSG HD16/17: retrospective QA, all INRT plans & a representative sample of IFRT plans, no PET fusion
  - AHOD0031: prospective QA, all plans prior to treatment, APPA fields, no PET fusion


Sim CT + contours + PET CT scans
Treating RO notified of changes needed
Deviation
IROC-RI
Central Review Team (2-4 ROs)
-Read institutional & central review of PETs
-Fuse sim CT + PETs
-Review target & OAR contours
Treating RO notified OK to treat
Per protocol
Review RT plan, & doses to OARs & targets

AHOD2131 Radiation Approach: Central Review

- Written feedback with screenshots provided to treating RO regarding the contours & RT plan
- Average time from receiving RT data at IROC-RI to sending feedback to investigator: 1.8 days
  - Thank you, IROC-RI team!
- Deviations (revision required):
  - Contours: disease missed
  - Plan: dose to targets or OARs defined as “Deviation Unacceptable” in protocol
- Variation acceptable (revision optional):
  - Contours: targets over-contoured
  - Plan: doses to targets or OARs defined as “Variation Acceptable” in protocol

Challenge #1: Fusion Confusion

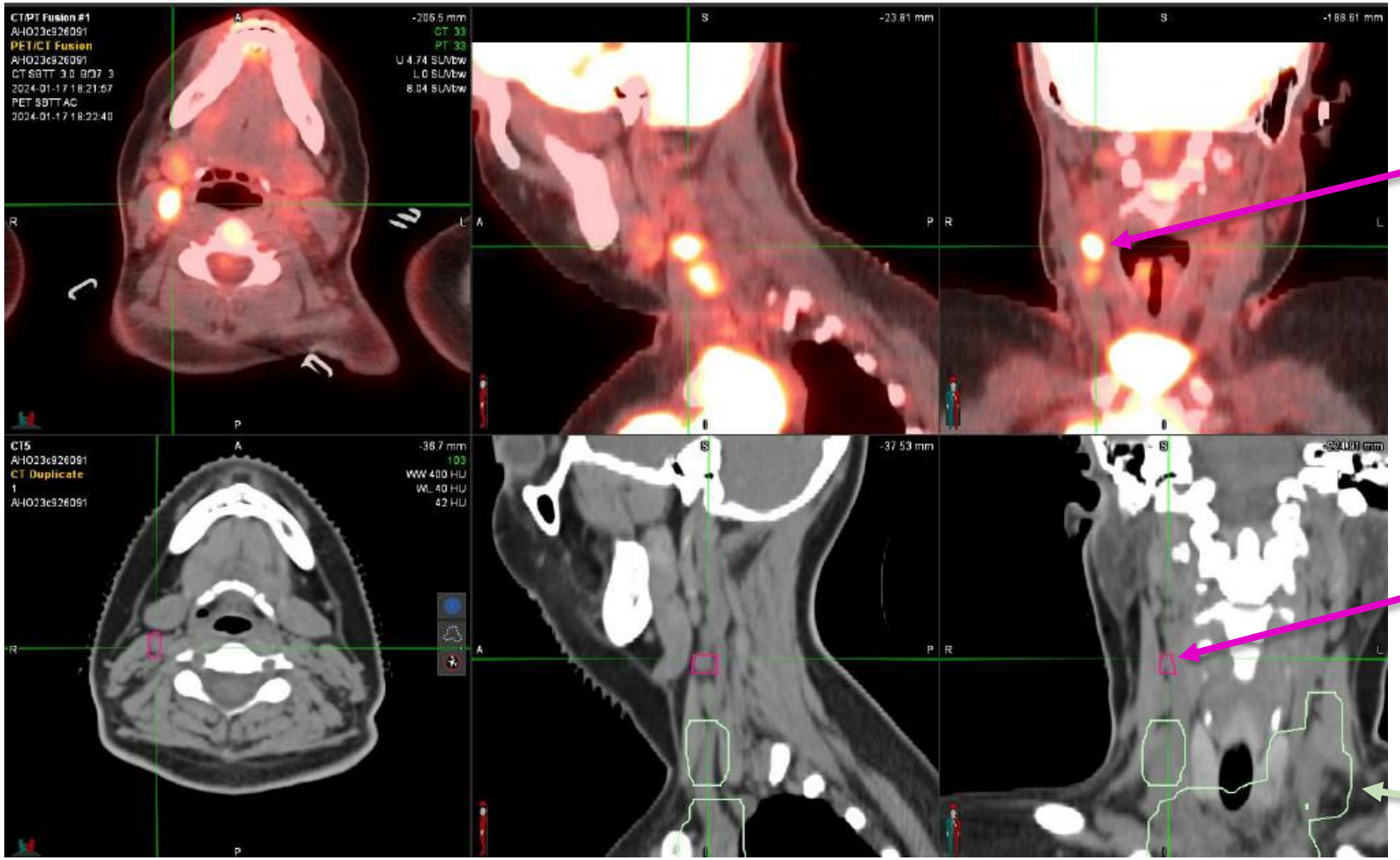


- PET-directed boost for node with PMR
- Sim performed with arms up, PET with arms down
- Contoured superior LN, meant to contour inferior LN

Challenge #1: Fusion Confusion

- Differences in body positioning for PET and sim CT complicate interpretation of registered images
  - Arms up vs. down
  - Differences in neck flexion
- Suggestions:
  - Try to sim with the same body position that was used for the PET, if it is acceptable for RT
  - A “mental fusion” may be valuable

Challenge #2: Site Omission

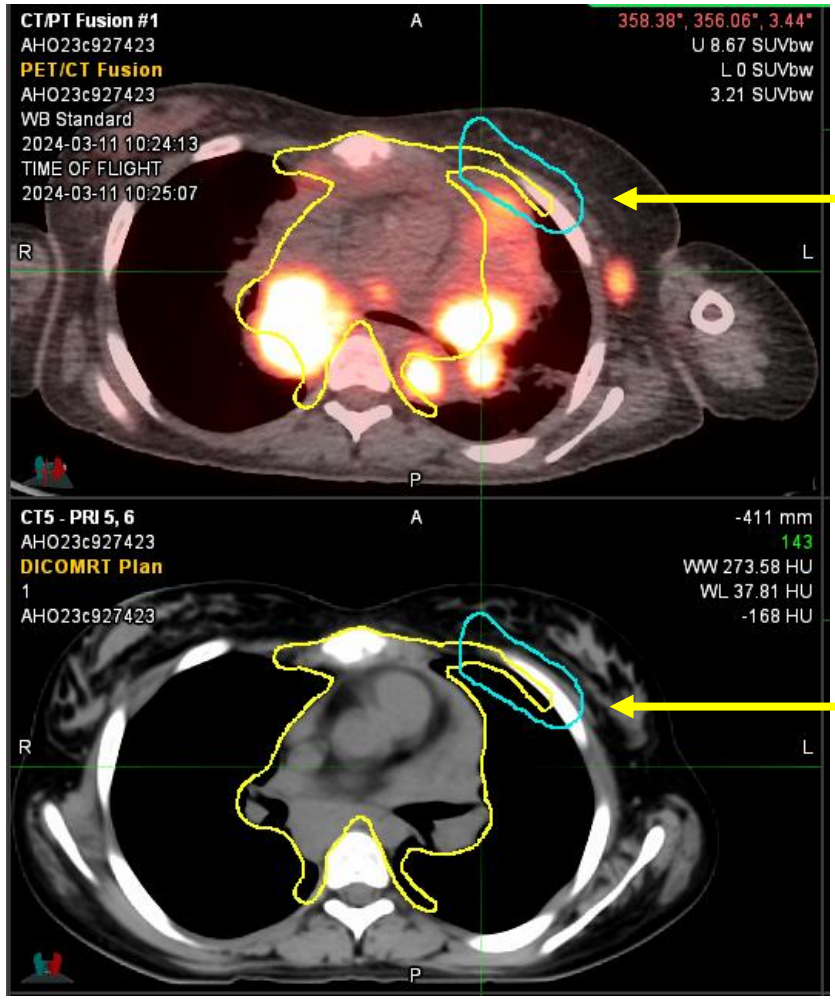


- Initially involved nodes in R neck extended more superiorly than CTVisrt

Challenge #2: Site Omission

- All sites of initial involvement should be included in CTVisrt, even if they respond completely to systemic therapy
- There might not be an obvious residual abnormality on the sim CT
- Suggestions:
  - Carefully review baseline imaging & reports
  - Review PET central review findings in case of discrepancies between institutional & central review

Challenge #3: Adjusting for Anatomic Changes



Contoured as CTVisrt

Contoured as CTVisrt

- Bulky mediastinal mass contacted, but did not invade, anterior chest wall
  → chest wall does not need to be included in CTV

Challenge #3: Adjusting for Anatomic Changes

- CTV
  - Should account for anatomic changes that occur with chemotherapy
  - Should include tissues that were infiltrated by lymphoma at diagnosis
  - Should not include tissues that were only contacted/displaced
- Suggestions:
  - Carefully review imaging & reports
  - Consider whether normal tissues were infiltrated (include in CTV) or contacted/displaced (exclude from CTV)

Final Thoughts

- AHOD2131
  - Employs a modern, individualized RT approach
  - Prescribes RT for a small subset of patients with the greatest risk of relapse
  - Incorporates rigorous pre-treatment RT review
- Please contact the AHOD2131 RO investigators if you have questions:
  - Brad Hoppe: hoppe.bradford@mayo.edu
  - Andrea Lo: andrea.lo@bccancer.bc.ca
  - Ray Mailhot: rbmailhot@floridaproton.org
  - David Hodgson: david.hodgson@uhn.ca
  - Sarah Milgrom: sarah.milgrom@CUAnschutz.edu