Pencil Beam Proton Therapy for Head and Neck Cancer: Lessons Learned, Current Applications, Future Directions

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PENN RADIATION ONCOLOGY

Penn Medicine

Outline

- Rationale
- Patient selection
- Simulation/Treatment Planning
- Potential Benefits
- Current and Future Directions
- Conclusions

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- **Rationale**
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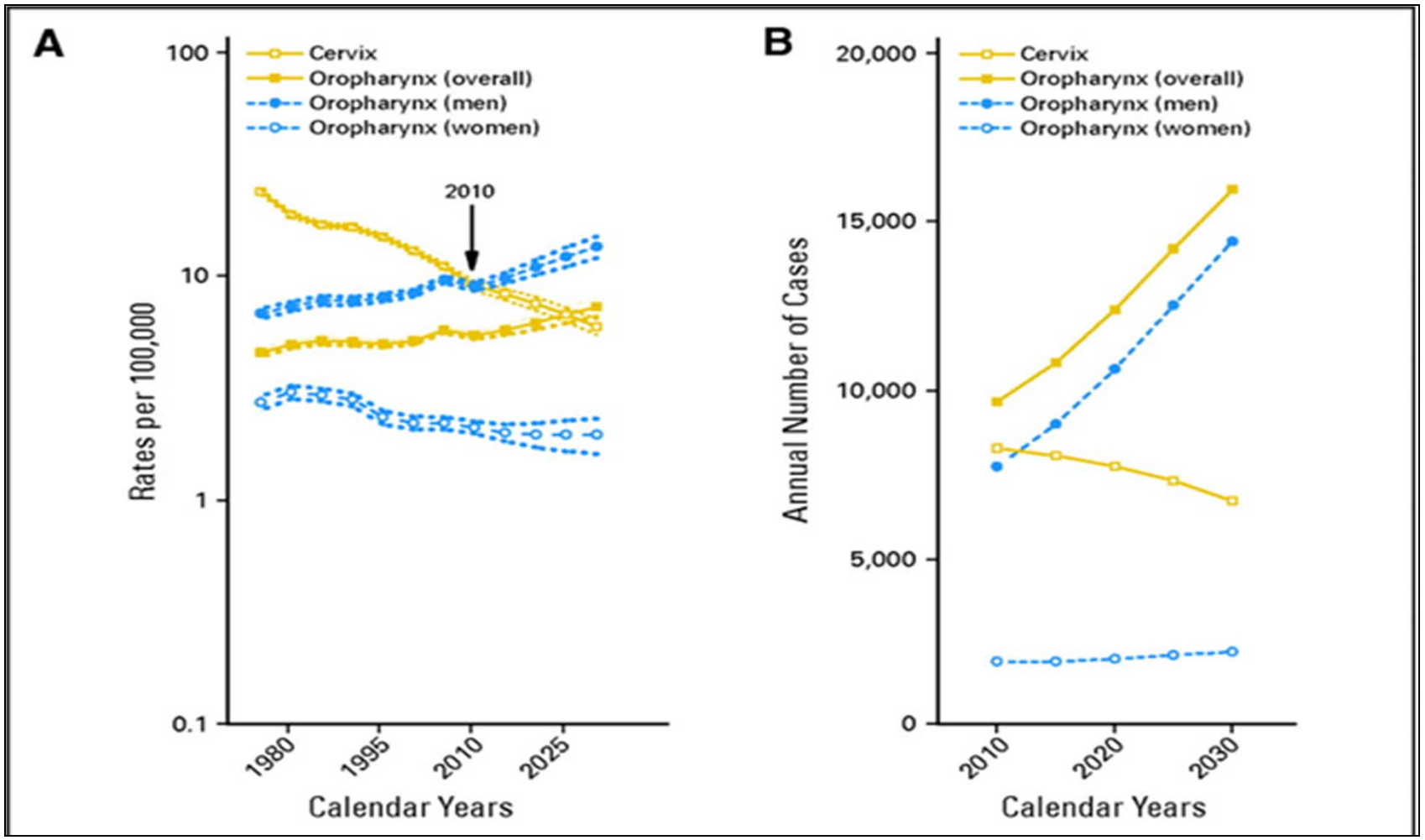
Why consider proton therapy for the head and neck cancer?

- **Treatment is morbid**

- **Side effects**
  - Acute
    - Mucositis
    - Dysgeusia
    - Dysphagia
    - Odynophagia (requiring opioids and/or supplemental nutrition)
    - Xerostomia
    - Weight loss, dehydration, malnutrition
  - Chronic
    - Dysgeusia
    - Xerostomia
    - Dysphagia (risk of feeding tube dependence)
    - Fibrosis
    - Lymphedema
    - Dental caries and Osteoradionecrosis
    - RT-induced malignancy
    - Cerebrovascular accident

Why consider proton therapy for the head and neck cancer?

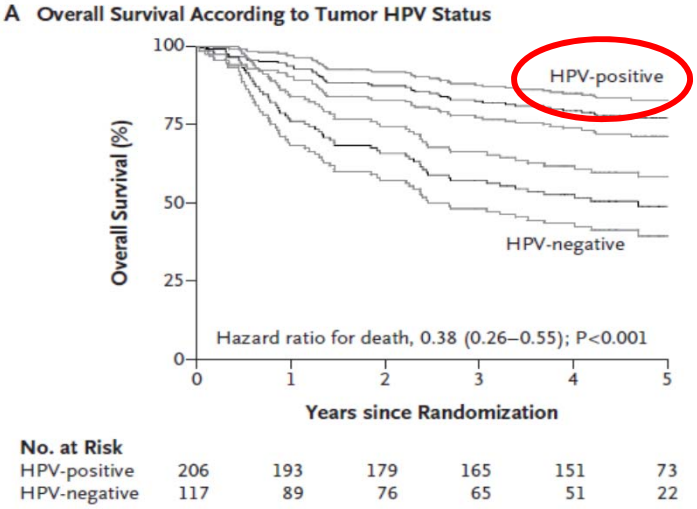
- **Treatment is morbid**
- **Increasing incidence**

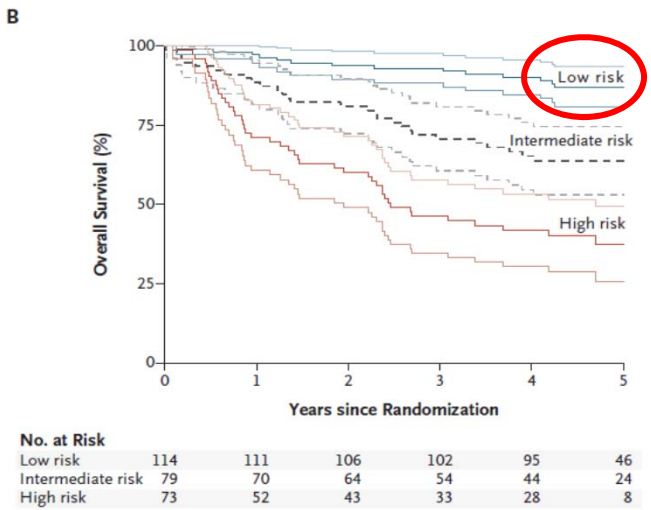


Chaturvedi, JCO 2011

Why consider proton therapy for the head and neck cancer?

- **Treatment is morbid**
- **Increasing incidence**
- **Improving disease outcomes**
  - Many people cured, living longer after treatment
  - Late toxicities are important





Ang et al., NEJM 2010

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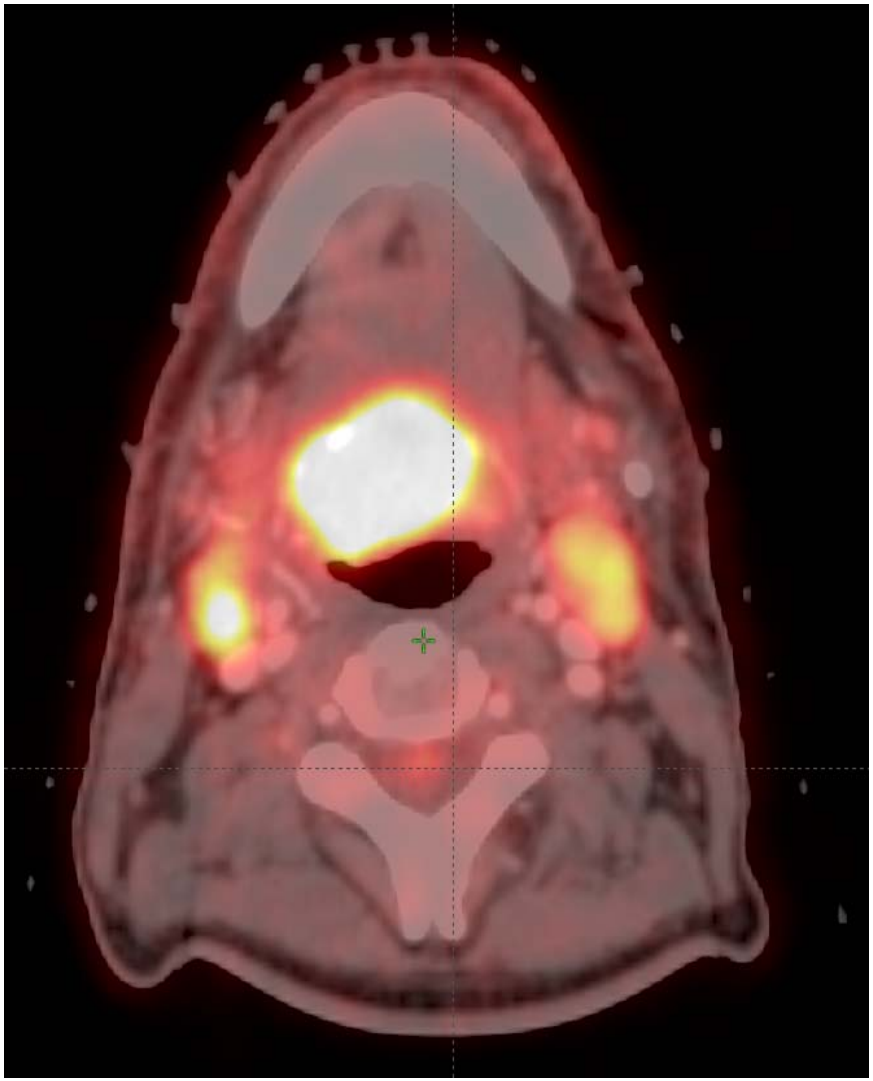
Selecting Patients for HN Proton RT

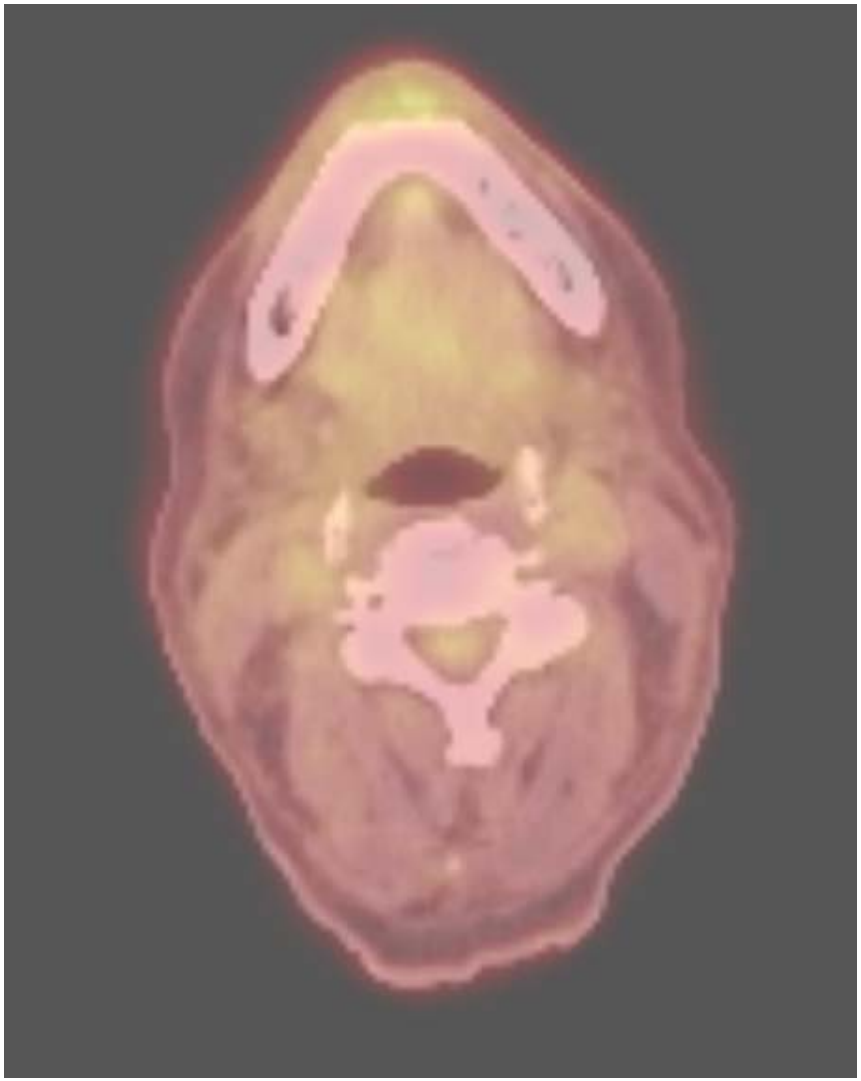
- **Definitive CRT**
  - Challenges:
    - Anatomic changes due to disease response
      - Need for soft tissue imaging (CBCT)
      - Resources required (contouring, replanning)

- **Postoperative, HPV+, oropharynx cancer**
  - Advantages:
    - Excellent disease outcomes, long-term f/u
    - Anatomy favorable for proton therapy
    - Anatomic changes during treatment limited to weight loss

Impact of anatomic changes during proton therapy?



Baseline



12 weeks post-CRT

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Simulation (previous approach)

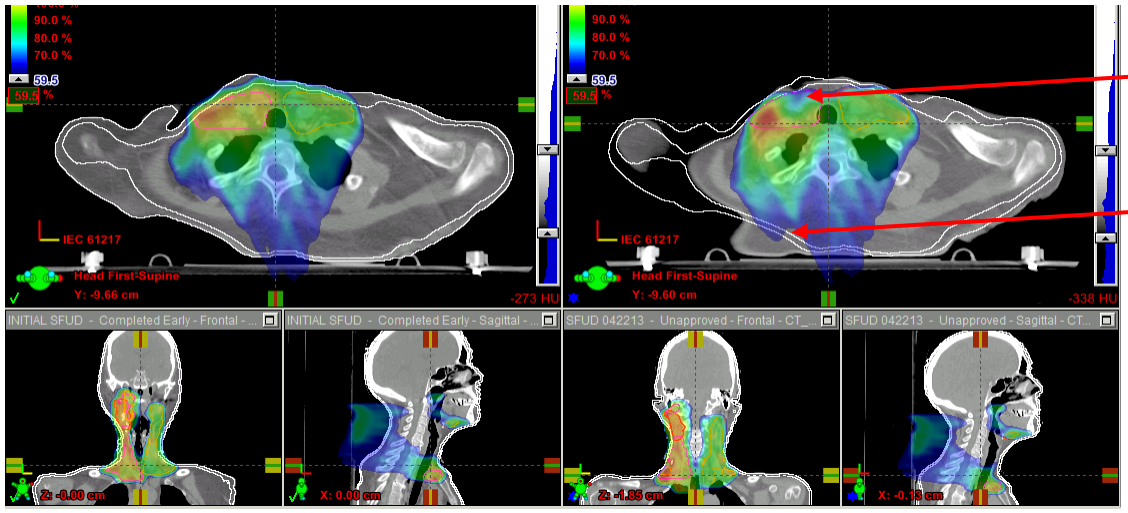
- Supine, head extended
- Thermoplastic mask (3-pt)
- Shoulders immobilization with rope pulls
- Non-contrast scan

CT verification

- **Through verification CT scans we find the most uncertainty in the lower neck:**
  - Loose skin
  - Shoulder positioning
  - Inability to see neck skin position with kV-kV setup

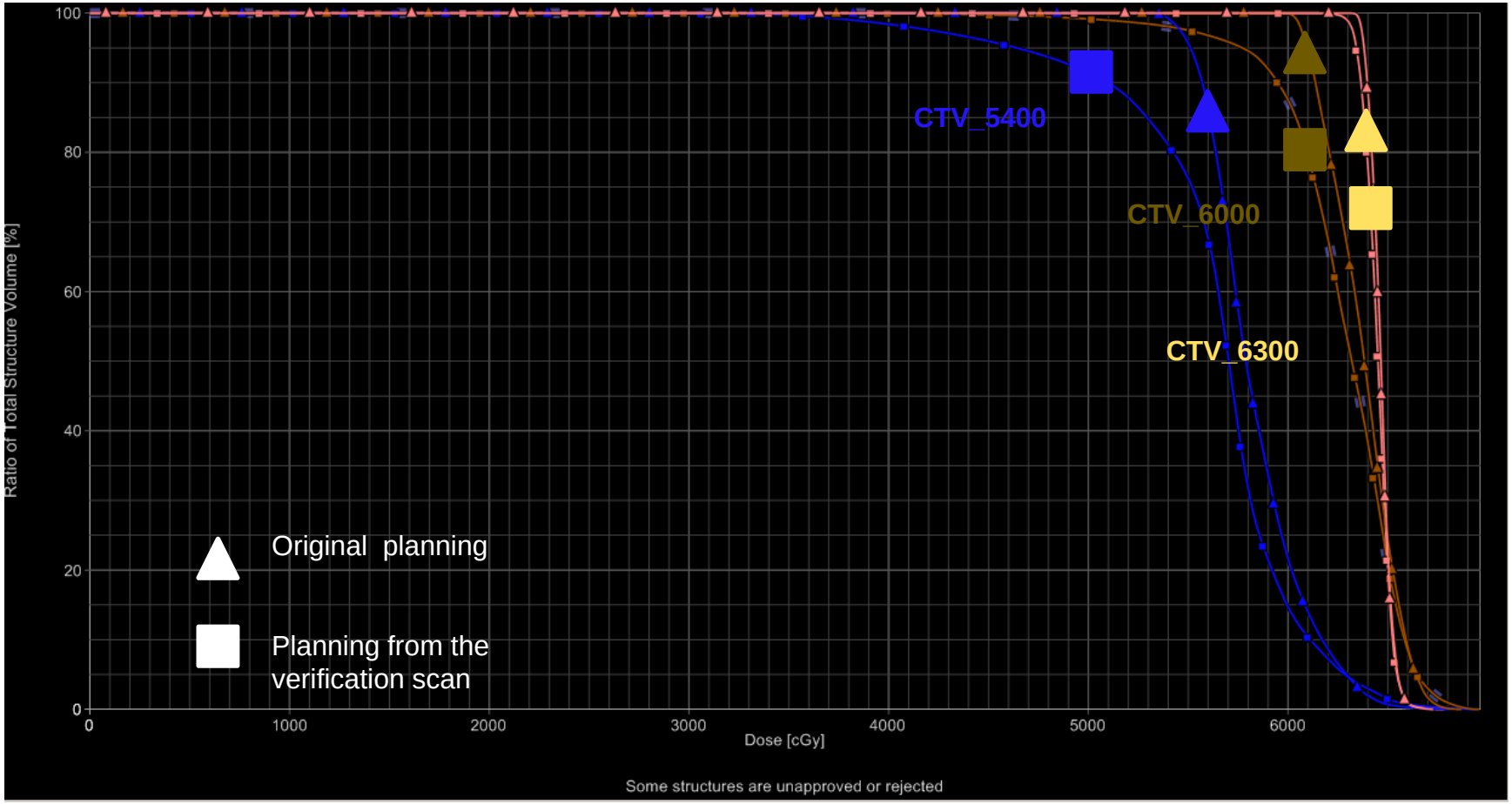
Nominal plan

Verification plan



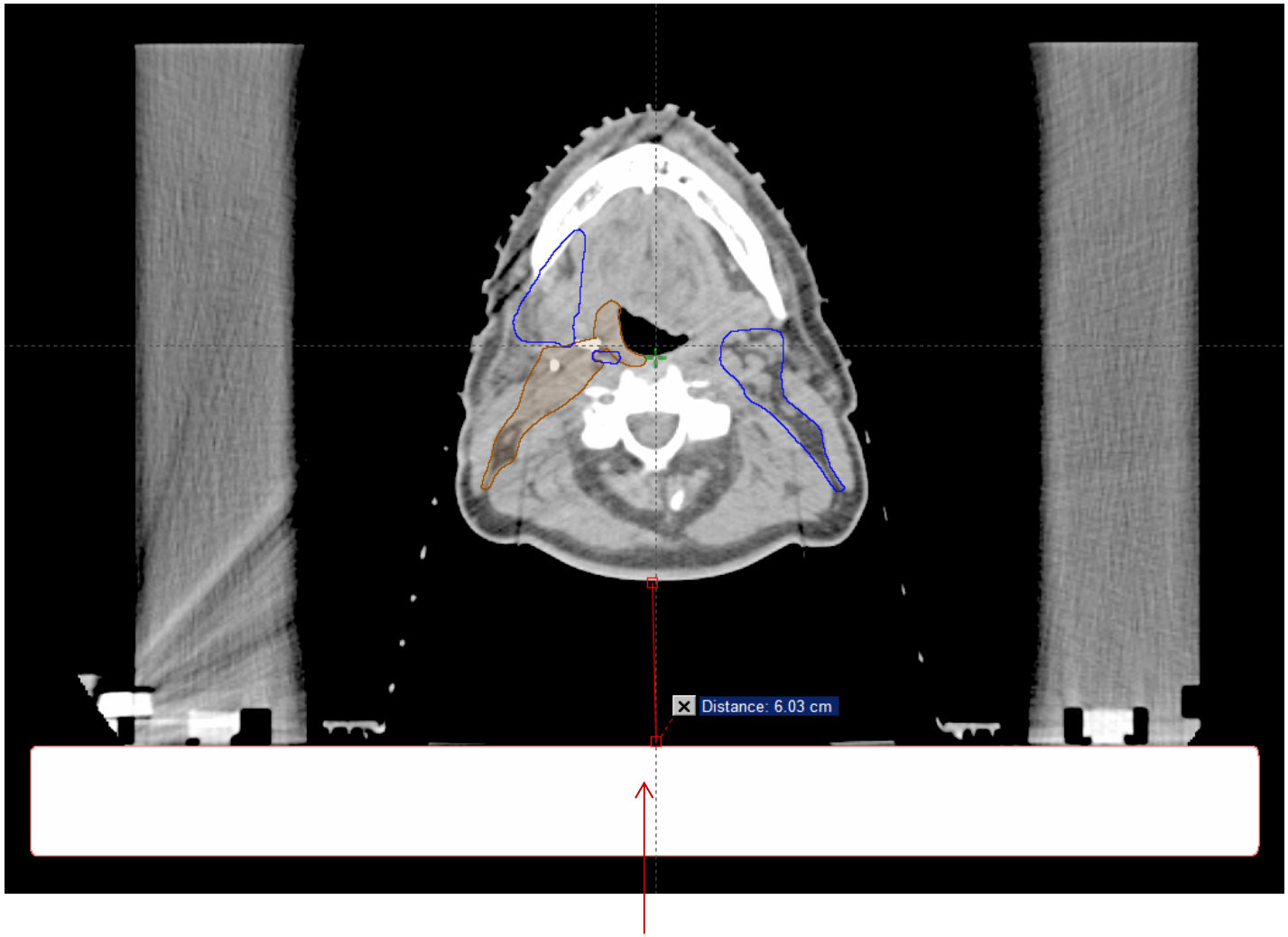
Loss of target coverage

Original skin contour


100
80
60
40
20
0
Ratio of Total Structure Volume [%]
0
1000
2000
3000
4000
5000
6000
Dose [cGy]
CTV_5400
CTV_6000
CTV_6300
Original planning
Planning from the verification scan
Some structures are unapproved or rejected

Simulation (current approach)

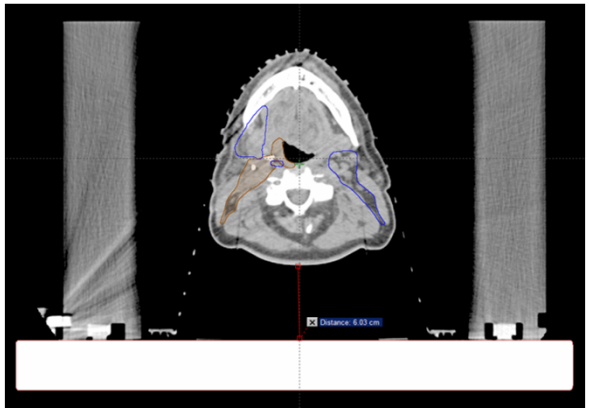
- Supine, head extended
- Thermoplastic mask (5-pt), extending to superior thorax
- Customized mold for the soft tissues of the head, neck, and shoulders
- Shoulders immobilization reinforced with a U-bolus
- Non-contrast scan



Universal Bolus

Choosing Beam Arrangement

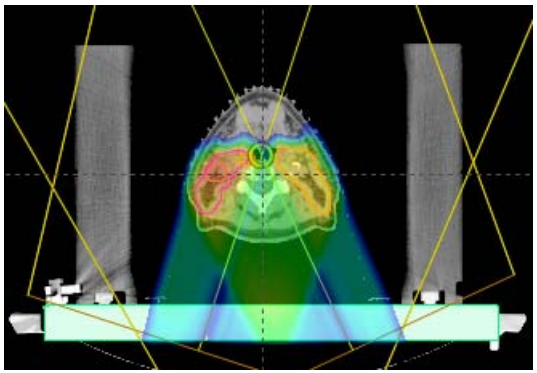
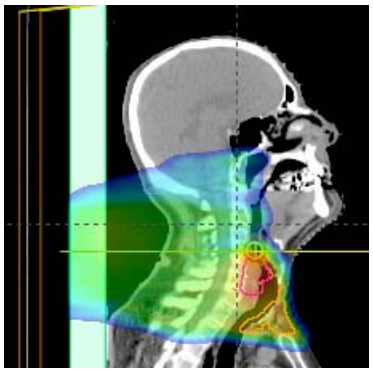
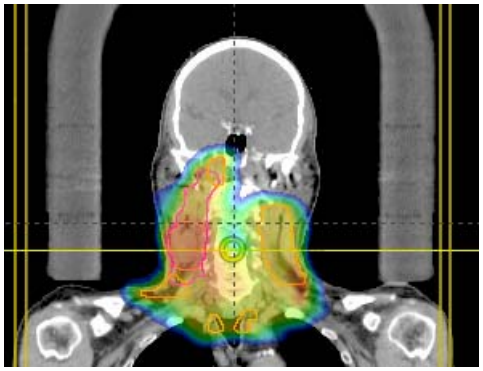
- **Need a reproducible beam path which minimizes uncertainties**



- **Anterior beam should be avoided**
  - Uncertainty caused by dental artifacts and implants
  - Goal of decreasing dose to oral cavity (mucositis, additional sparing of taste buds, minor salivary glands

Choosing Beam Arrangement

- **Best option:**
  - High density table used as a range shifter
  - Two posterior oblique beams

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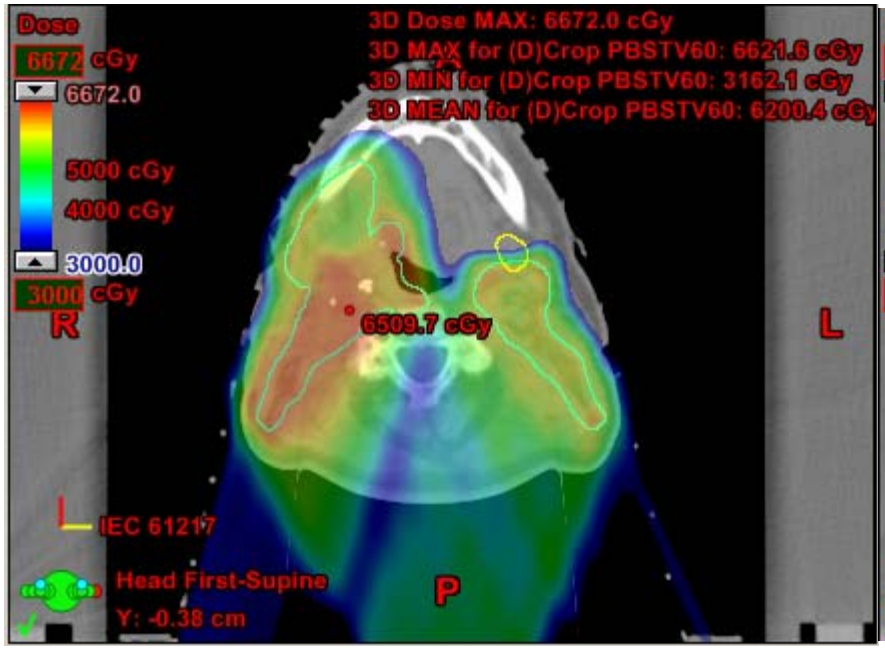
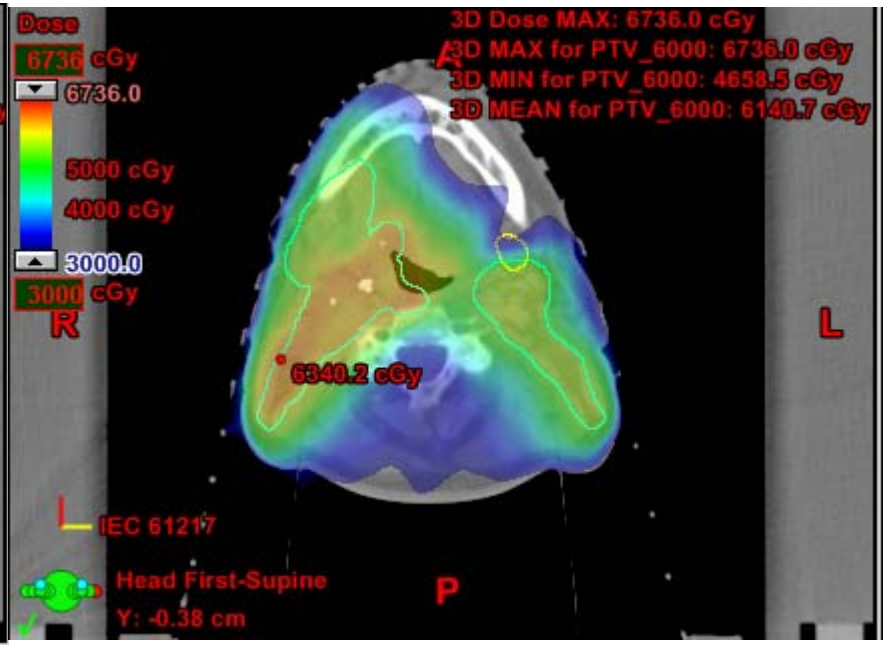
Contralateral Submandibular Gland

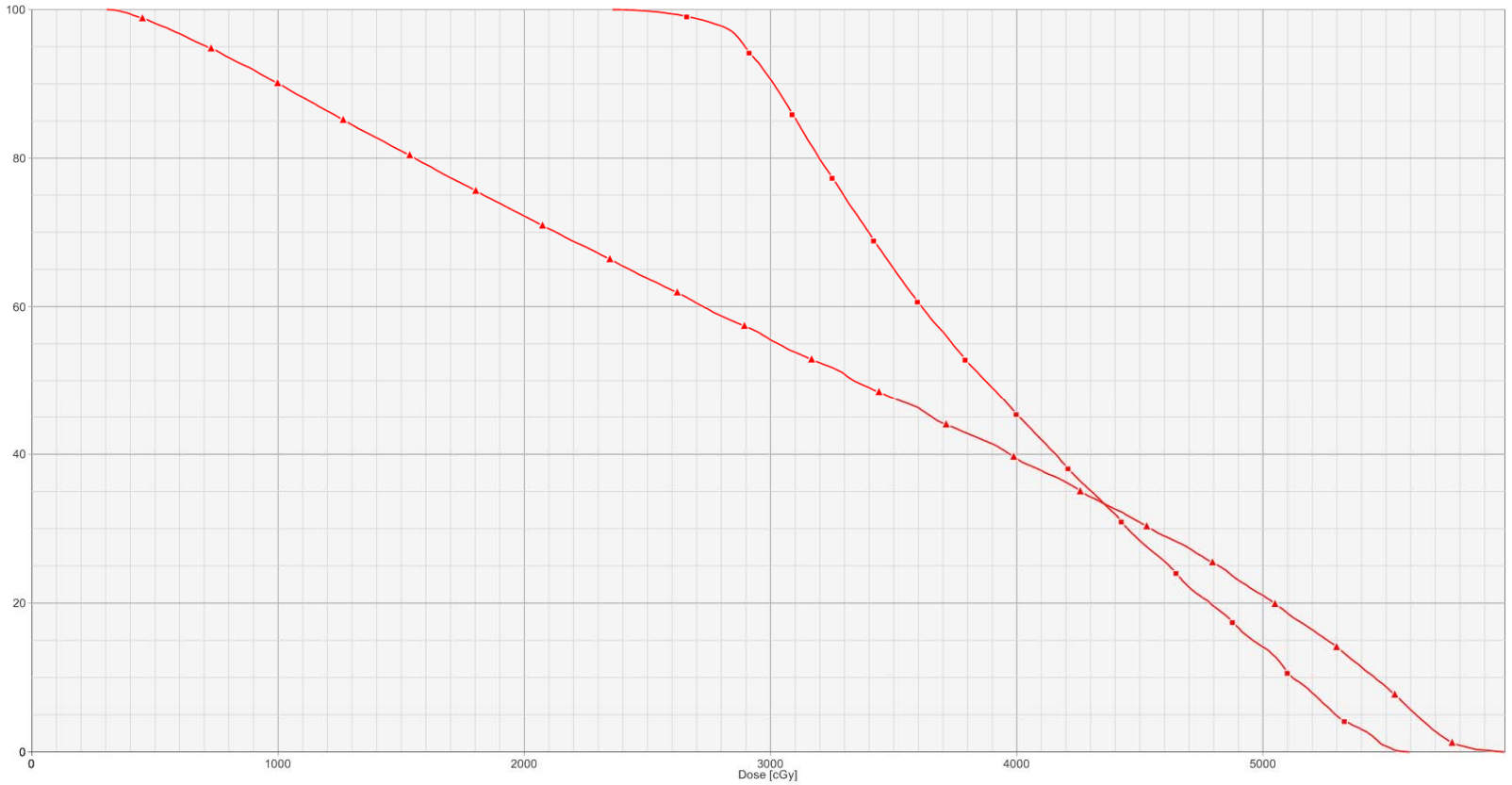


PBS



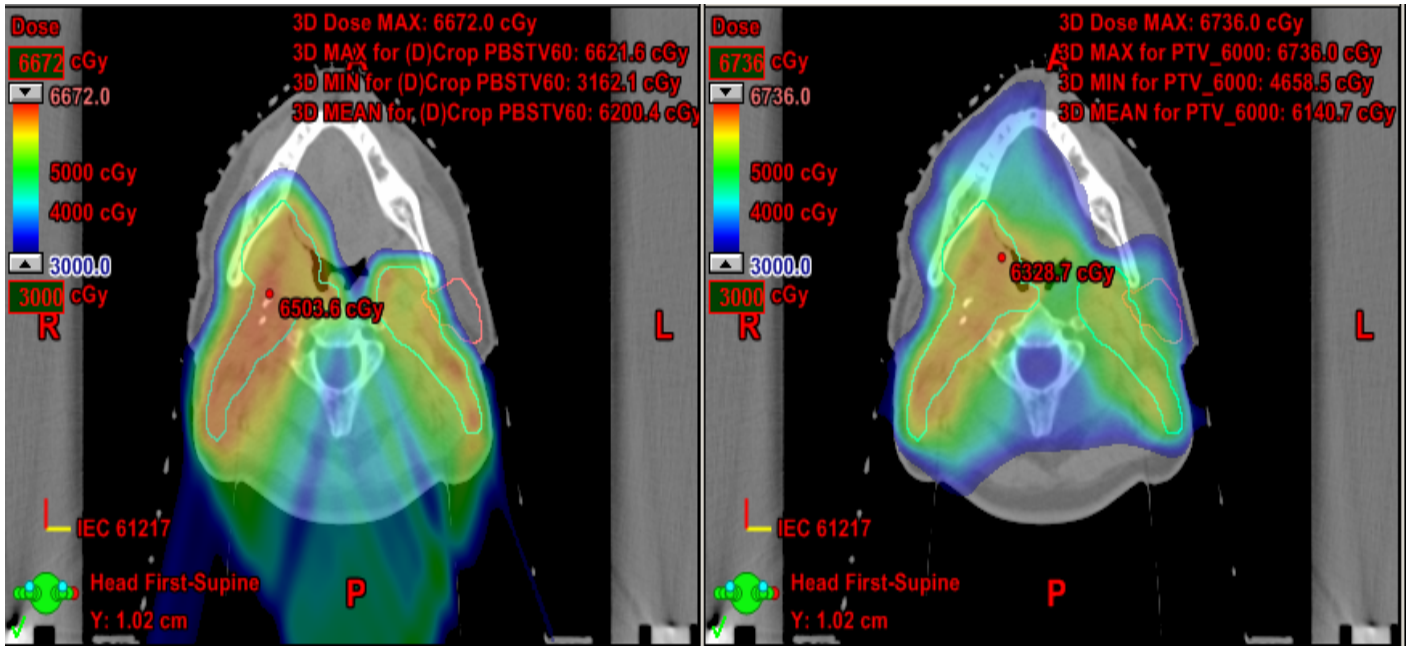
Rapid Arc IMRT: Backup plan

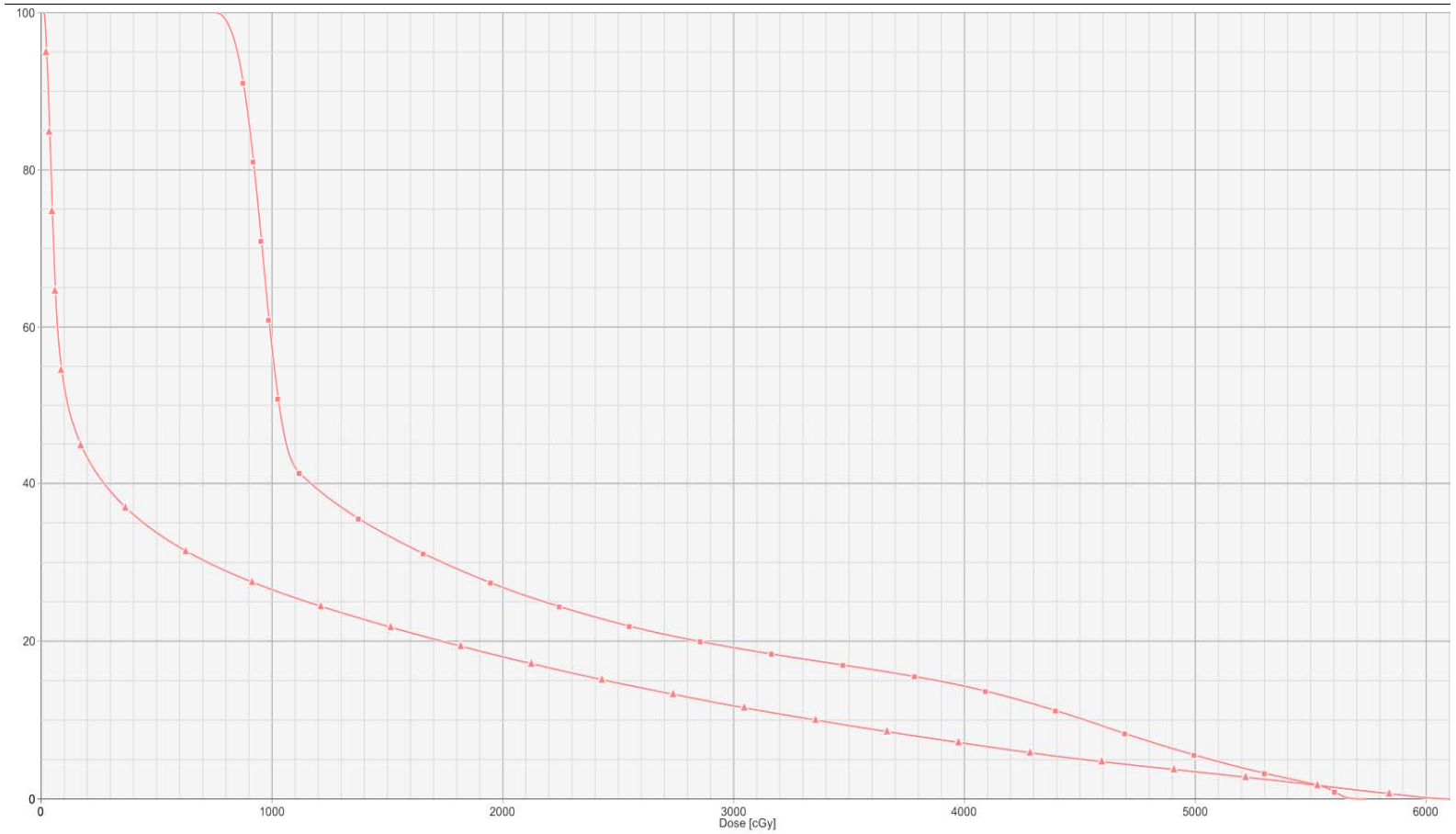
Stage 4a, T1N2b, HPV+, R tonsil SCCA



Mean Doses: IMRT (40 Gy), PBS (33 Gy)

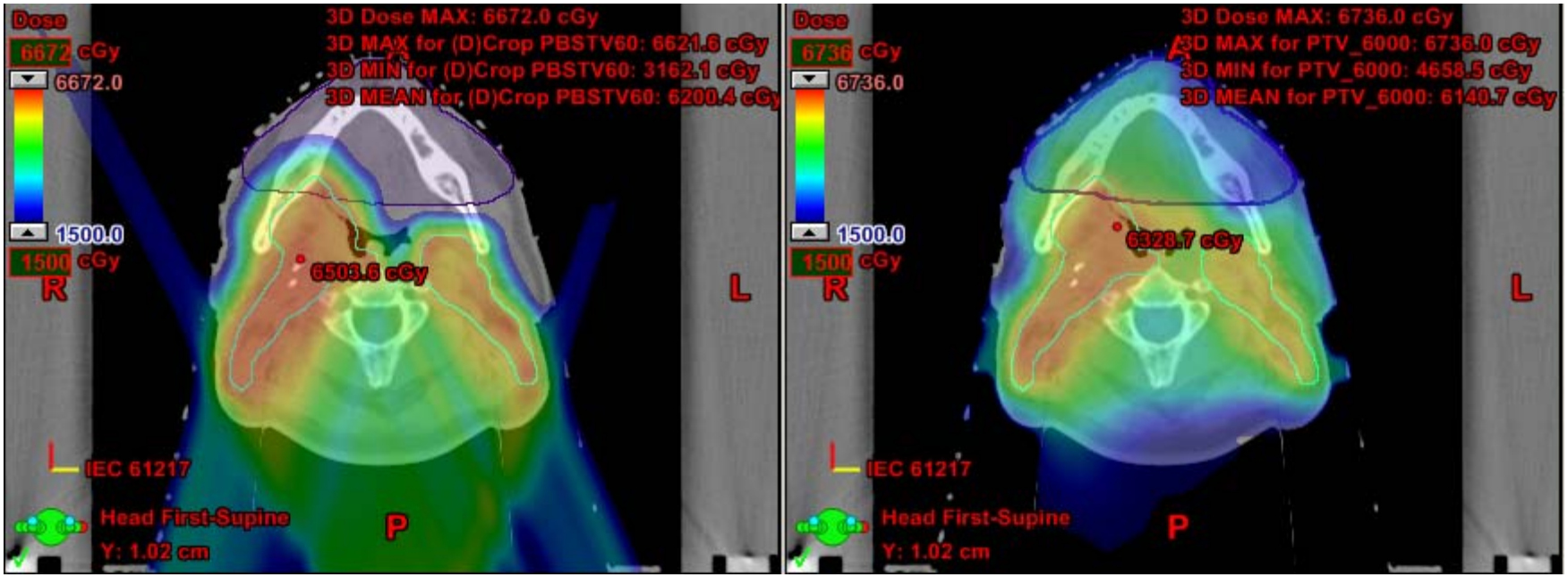
Contralateral parotid

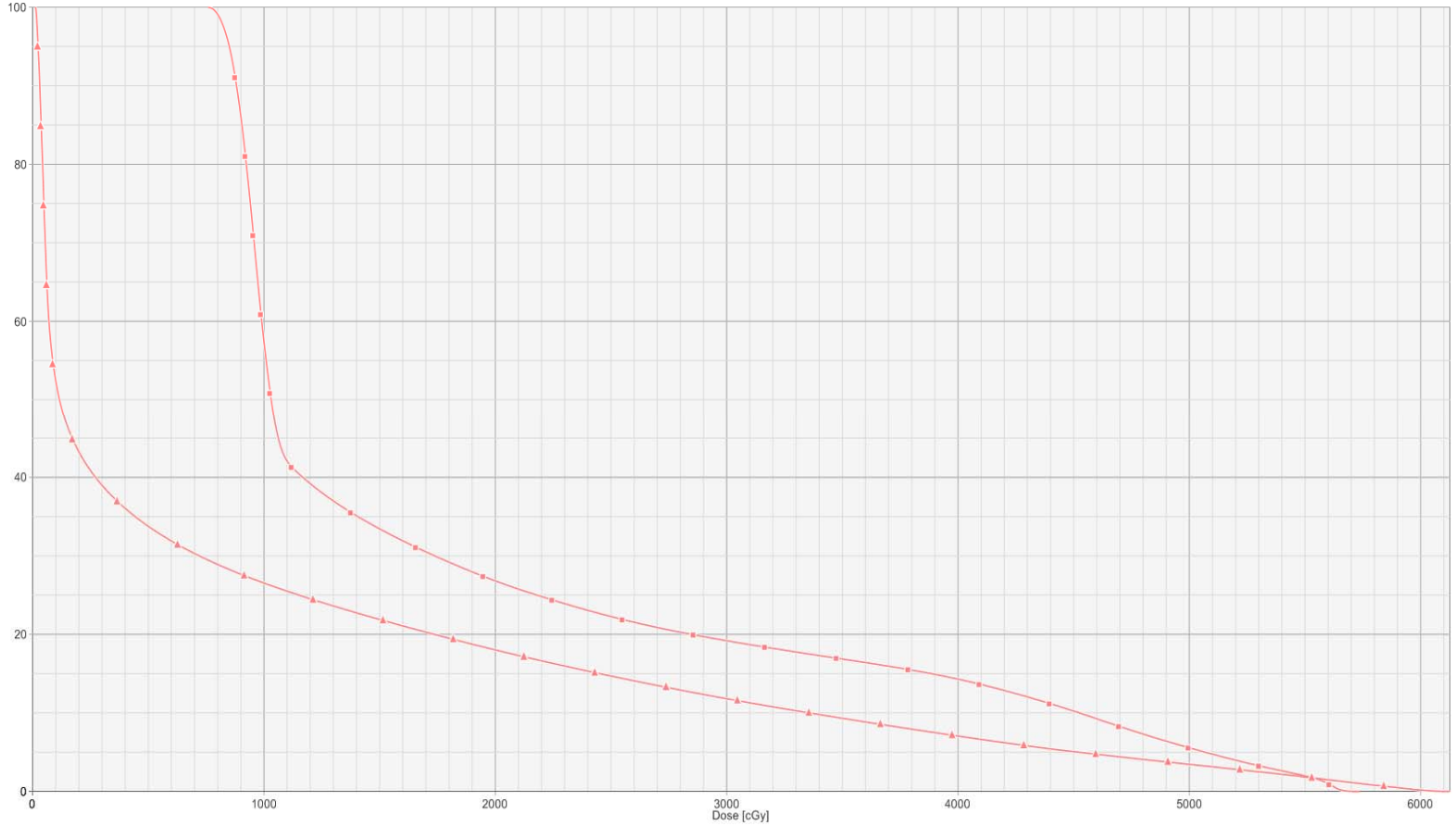




Mean Doses: IMRT (18 Gy), PBS (9 Gy)

Oral Cavity


Dose
6672 cGy
6672.0
1500.0
1500 cGy
R
3D Dose MAX: 6672.0 cGy
3D MAX for (D)Crop PBSTV60: 6621.6 cGy
3D MIN for (D)Crop PBSTV60: 3162.1 cGy
3D MEAN for (D)Crop PBSTV60: 6200.4 cGy
6503.6 cGy
L
IEC 61217
Head First-Supine
Y: 1.02 cm
P
Dose
6736 cGy
6736.0
1500.0
1500 cGy
R
3D Dose MAX: 6736.0 cGy
3D MAX for PTV_6000: 6736.0 cGy
3D MIN for PTV_6000: 4658.5 cGy
3D MEAN for PTV_6000: 6140.7 cGy
6328.7 cGy
L
IEC 61217
Head First-Supine
Y: 1.02 cm
P



Mean Doses: IMRT (19 Gy), PBS (3 Gy)

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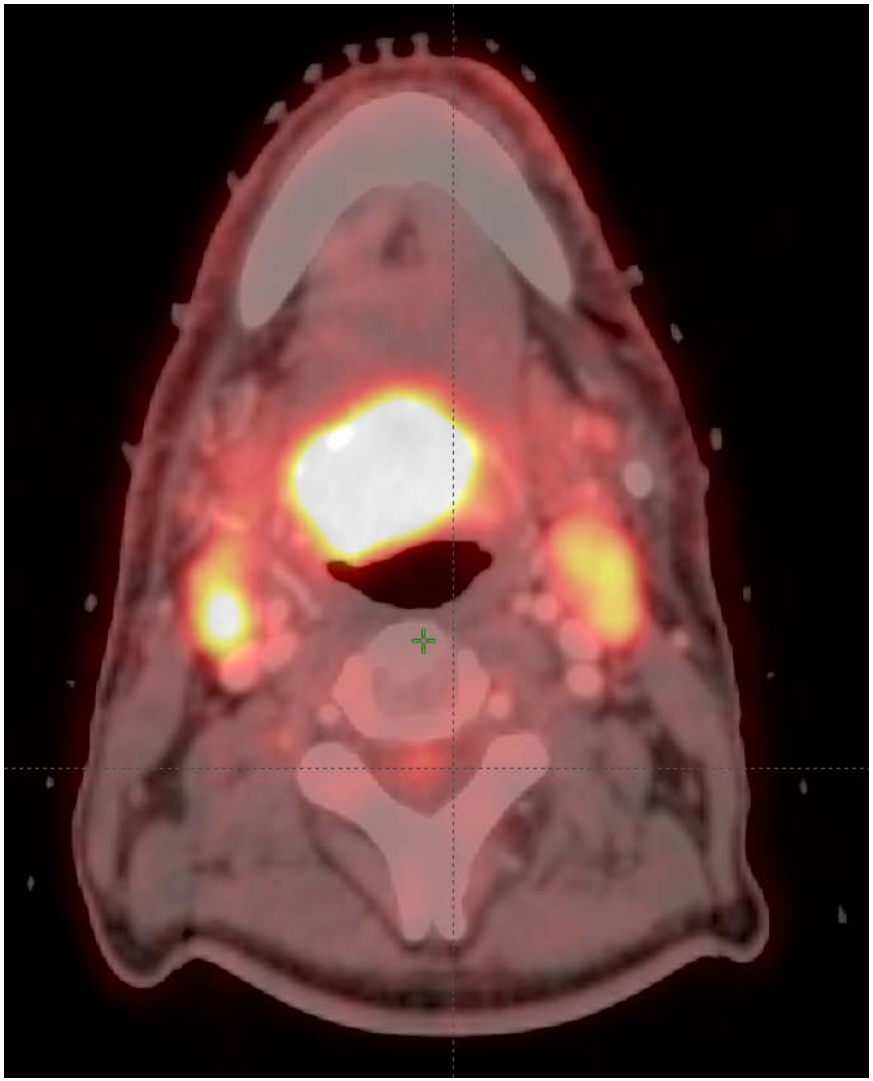
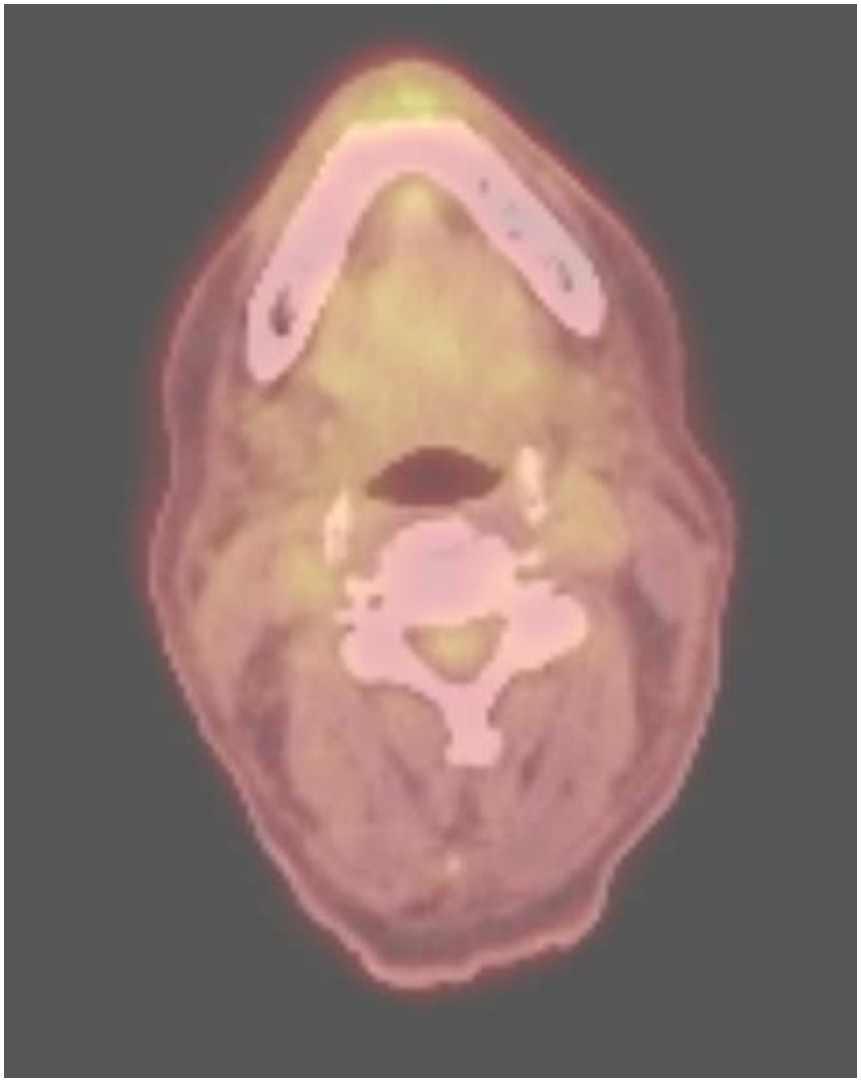
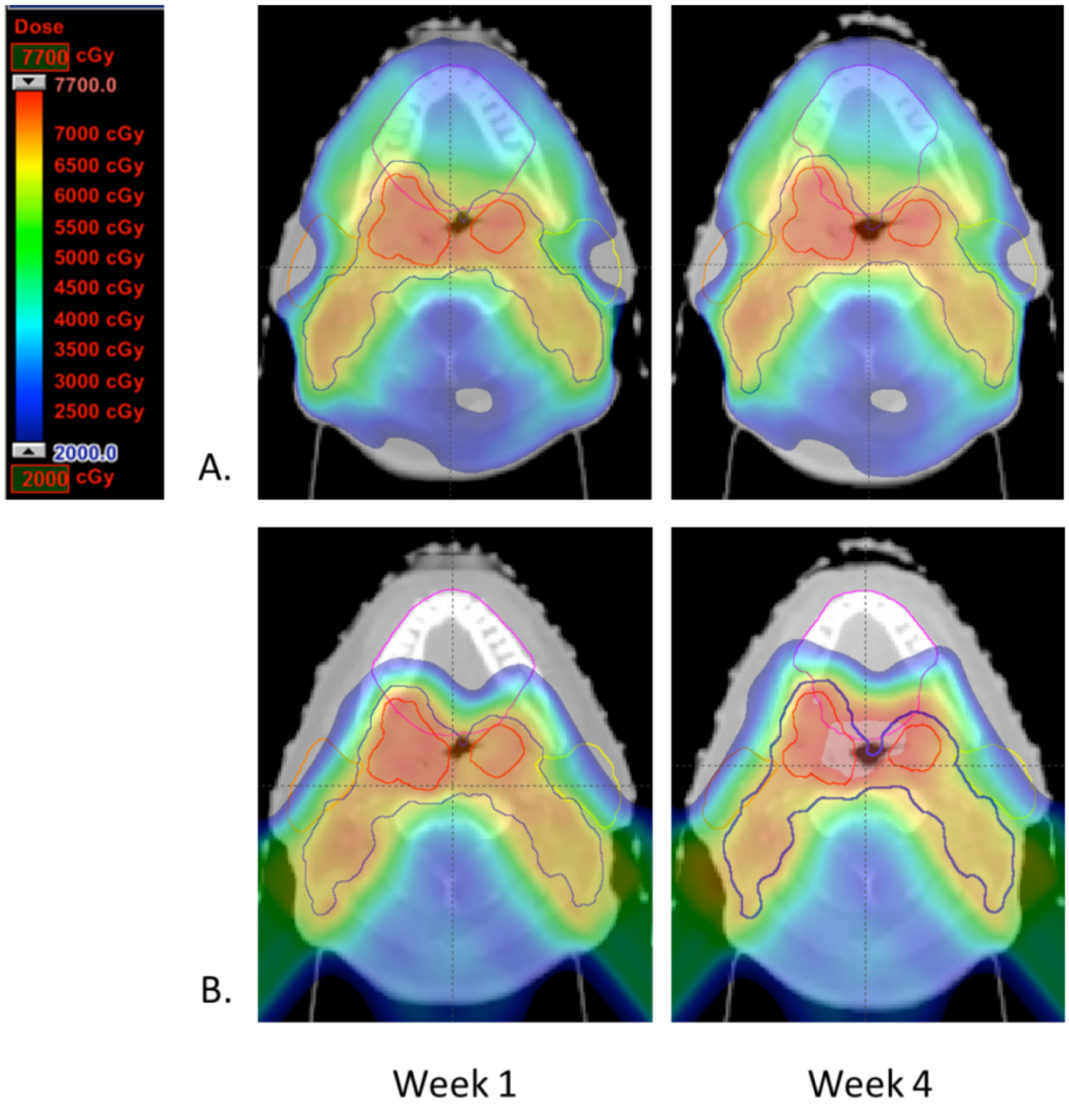
Definitive treatment of bulky, intact disease?



Baseline



12 weeks post-CRT


Dose
7700 cGy
7700.0
7000 cGy
6500 cGy
6000 cGy
5500 cGy
5000 cGy
4500 cGy
4000 cGy
3500 cGy
3000 cGy
2500 cGy
2000.0
2000 cGy
A.
B.
Week 1
Week 4

What is the impact of anatomic change?

- **If no adaptive changes are made:**
  - IMRT
    - No changes in coverage of targets
    - No changes in doses to organs at risk
  - PBS
    - No changes in coverage of targets
    - Increase in organs at risk (3-5 Gy increase in mean dose over course of treatment)
      - Oral cavity
      - Pharyngeal Constrictors
      - Salivary glands
      - Larynx
    - Changes most profound weeks 3-5

- **Quick, reliable methods to image, assess, adapt, and replan are therefore needed.**

CBCT Image Guidance for Proton Therapy

- **All the advantages of CBCT in photon therapy:**
  - Visualization of soft tissue, tumor size, or location
  - 3D anatomic matching
- **AND**

  (1) Assessment of dose delivery deviations due to anatomical change/setup error

  (2) Dose calculation using CBCT

  (3) Dose guided adaptive proton therapy

Challenges:

(1) CBCT HU variation: patient size, scatter, beam hardening

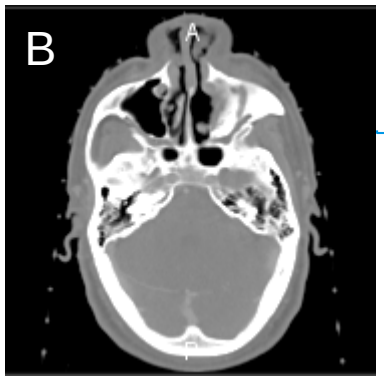
-->Large uncertainty in proton stopping power and thus calculated range

Solution: Use deformable image registration tools to map HU of Planning CT to CBCT

CBCT Image Intensity Correction

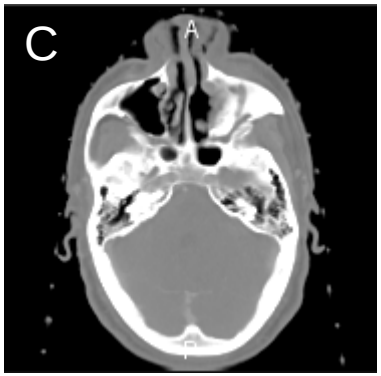
*Linac CBCT is used in this study. Proton CBCT under development.

Original CBCT



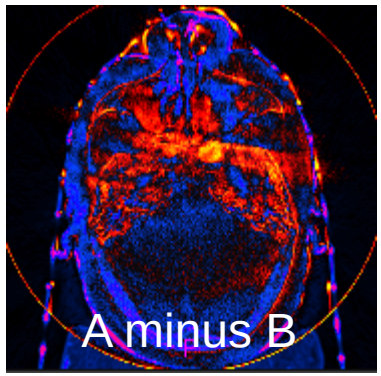
Planning CT

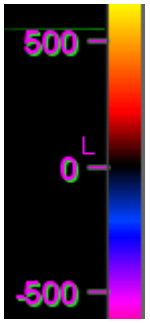
Advanced Normalization Tools



Intensity Corrected CBCT
=Deformed planning CT

Image Difference (uncorrected)





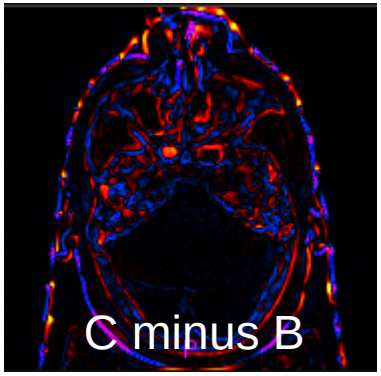
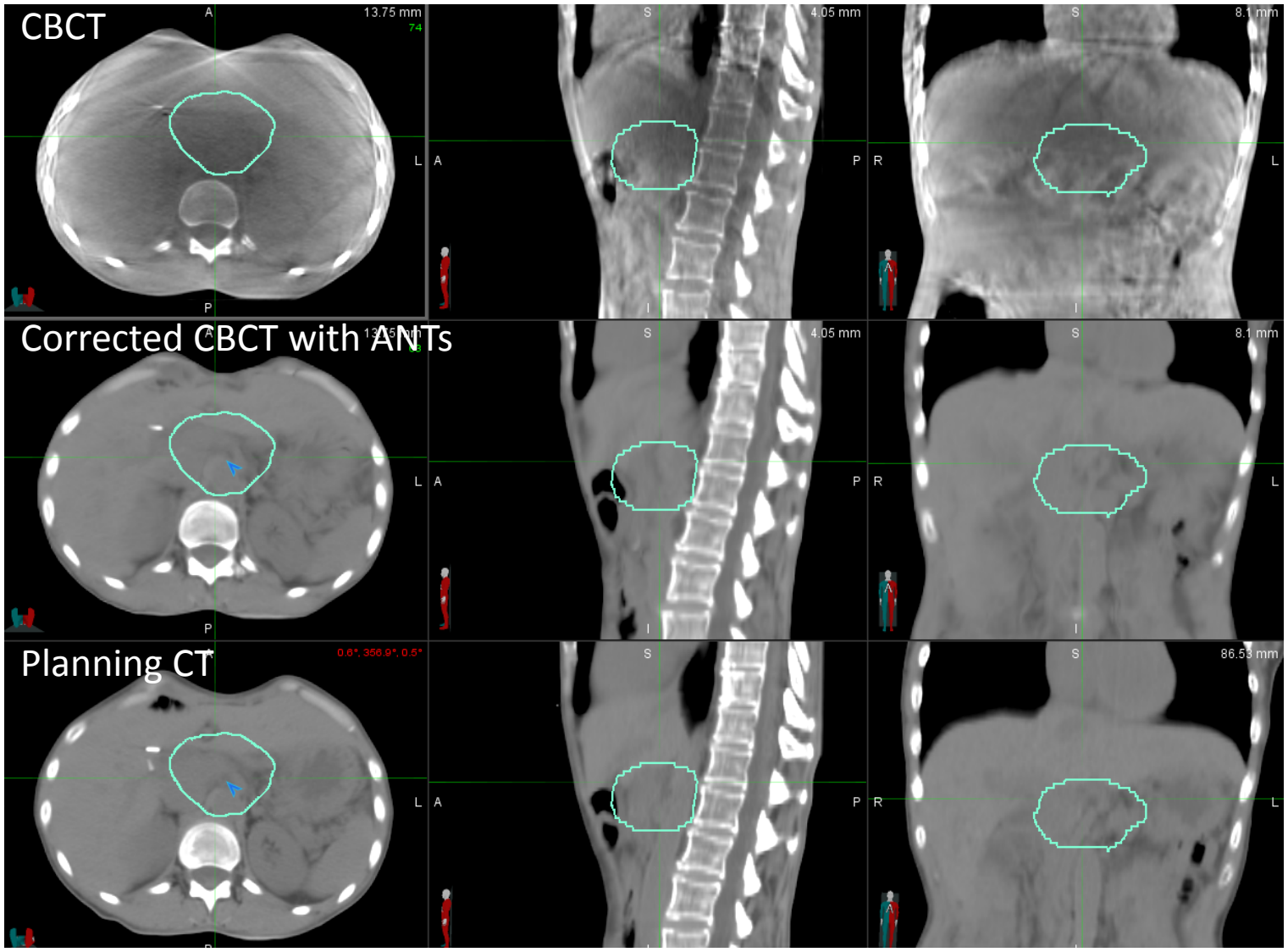
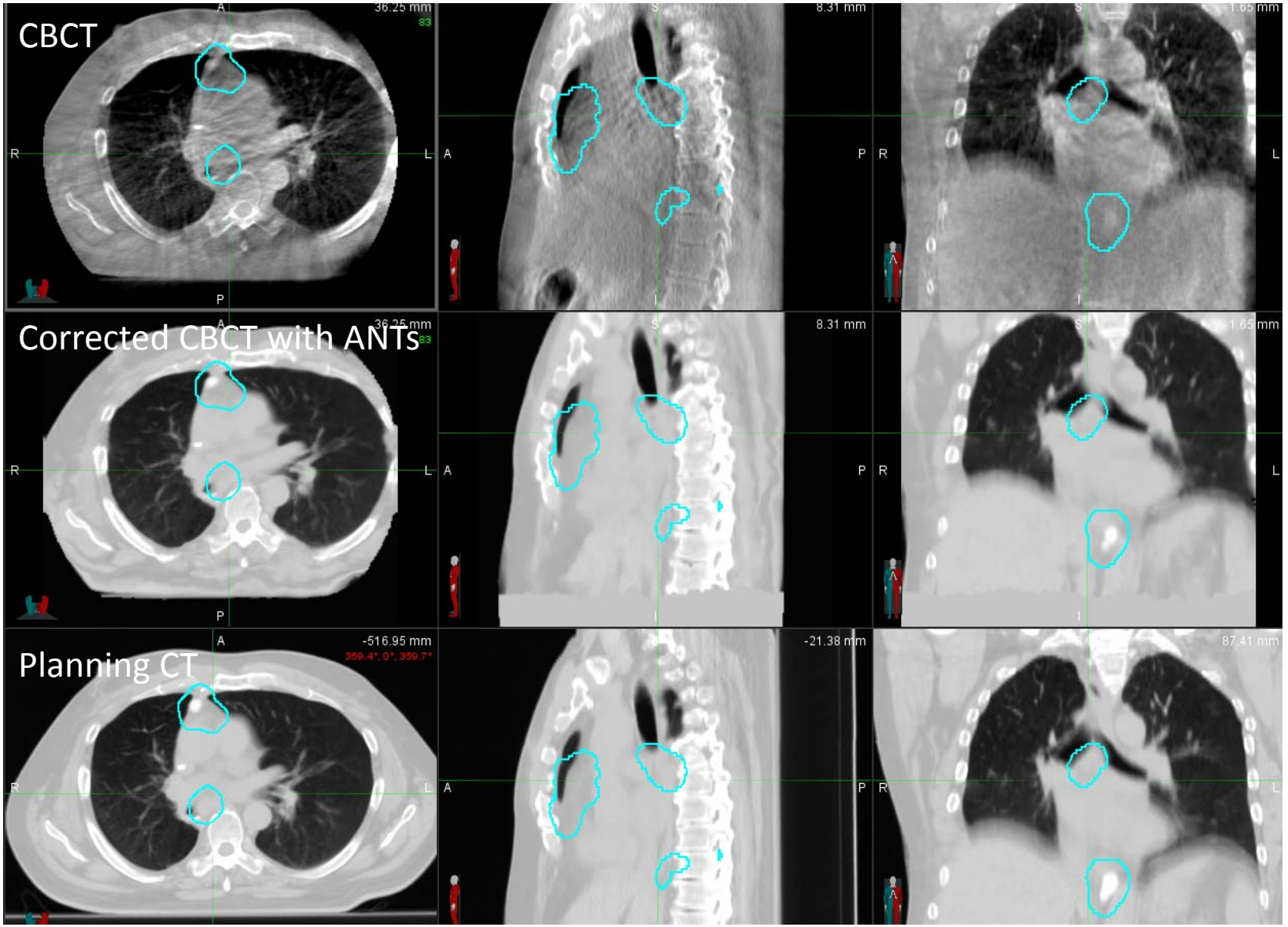


Image Difference (corrected)

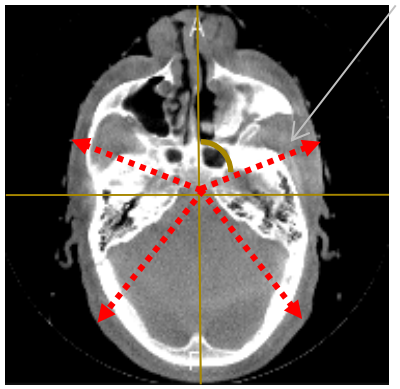
Pelvis CBCT

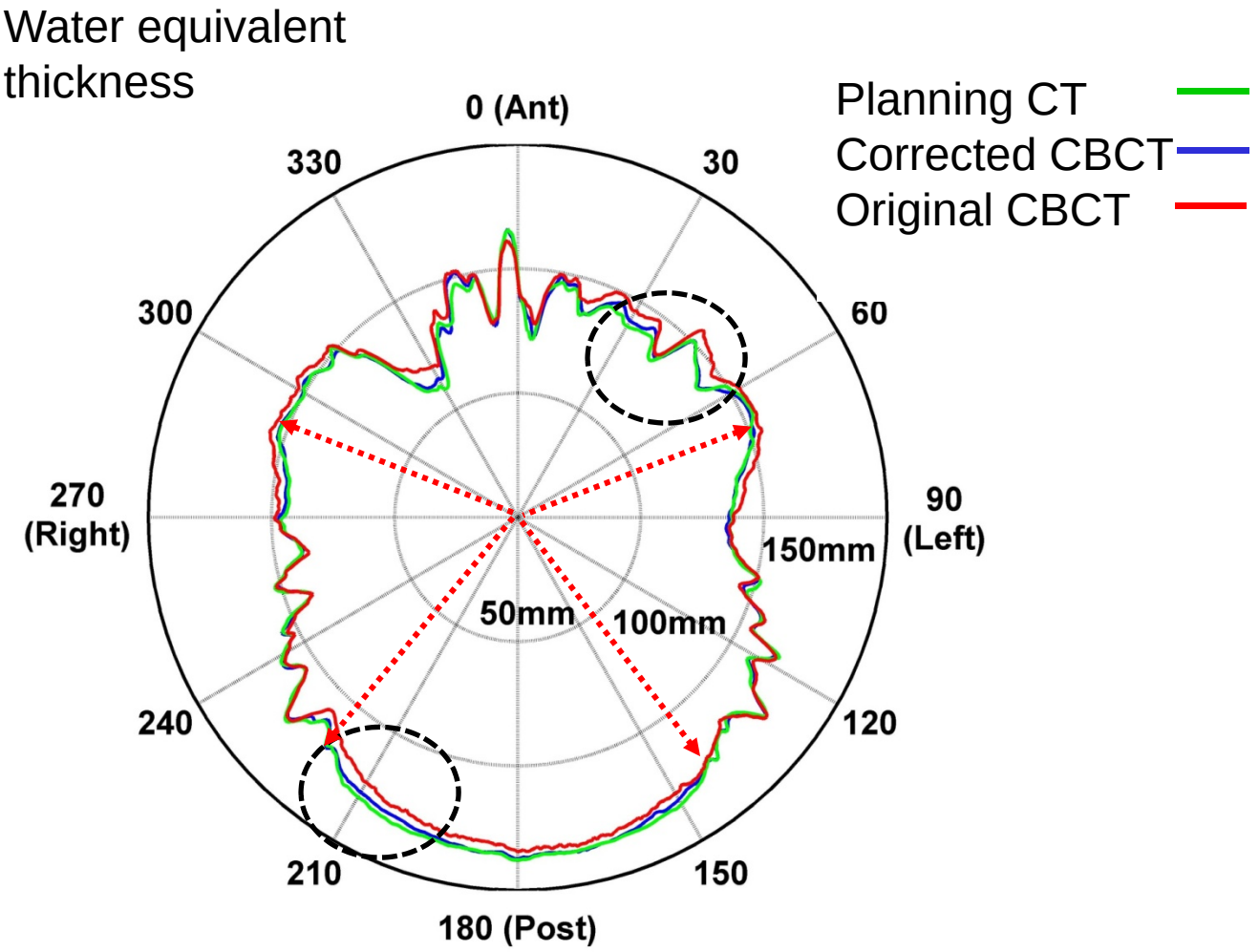


Lung CBCT



Polar Plot of Water Equivalent Thickness (WET)





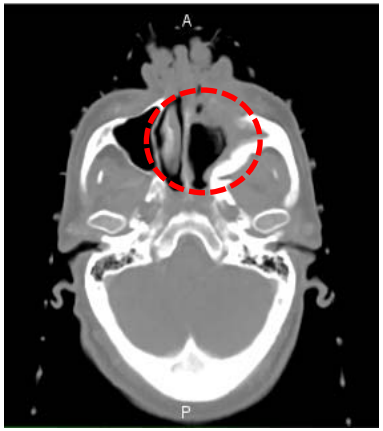
- **Good Agreement of WETs in regions with minimum physiological changes: Mean WET difference =1.26 mm (Corrected) vs 3.38 mm**

Detecting Proton Range Differences

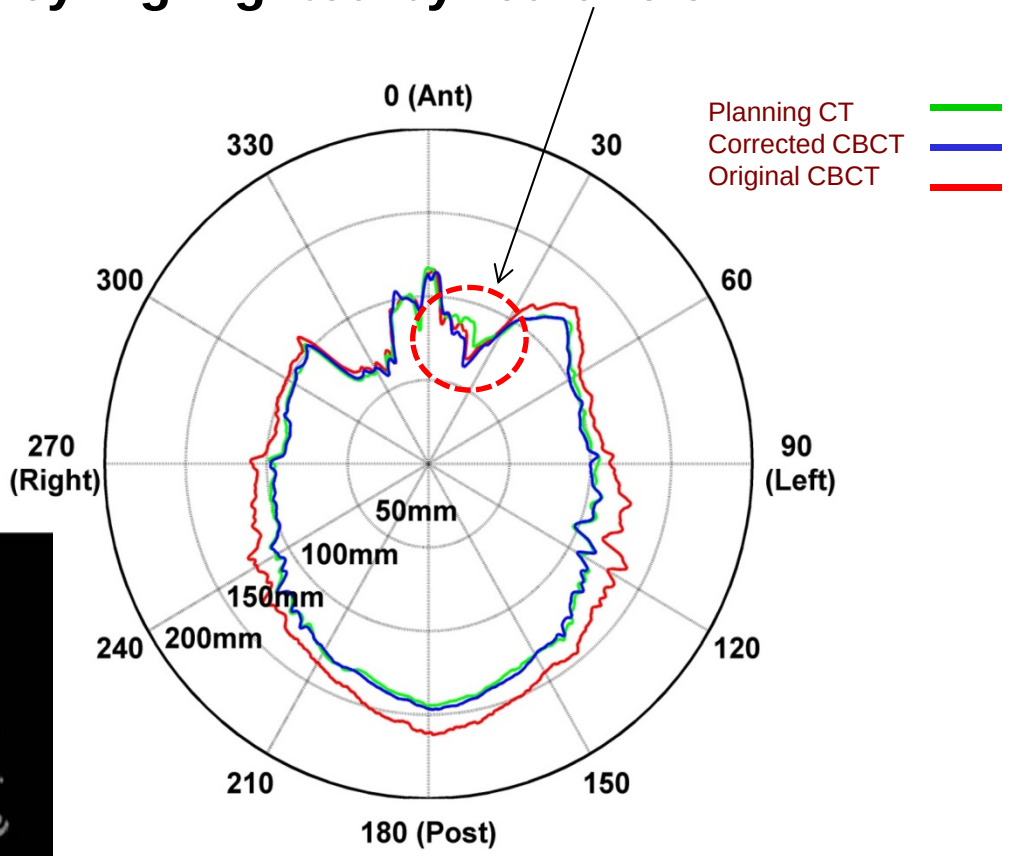
- **Identified range discrepancy highlighted by red circle**

Planning CT

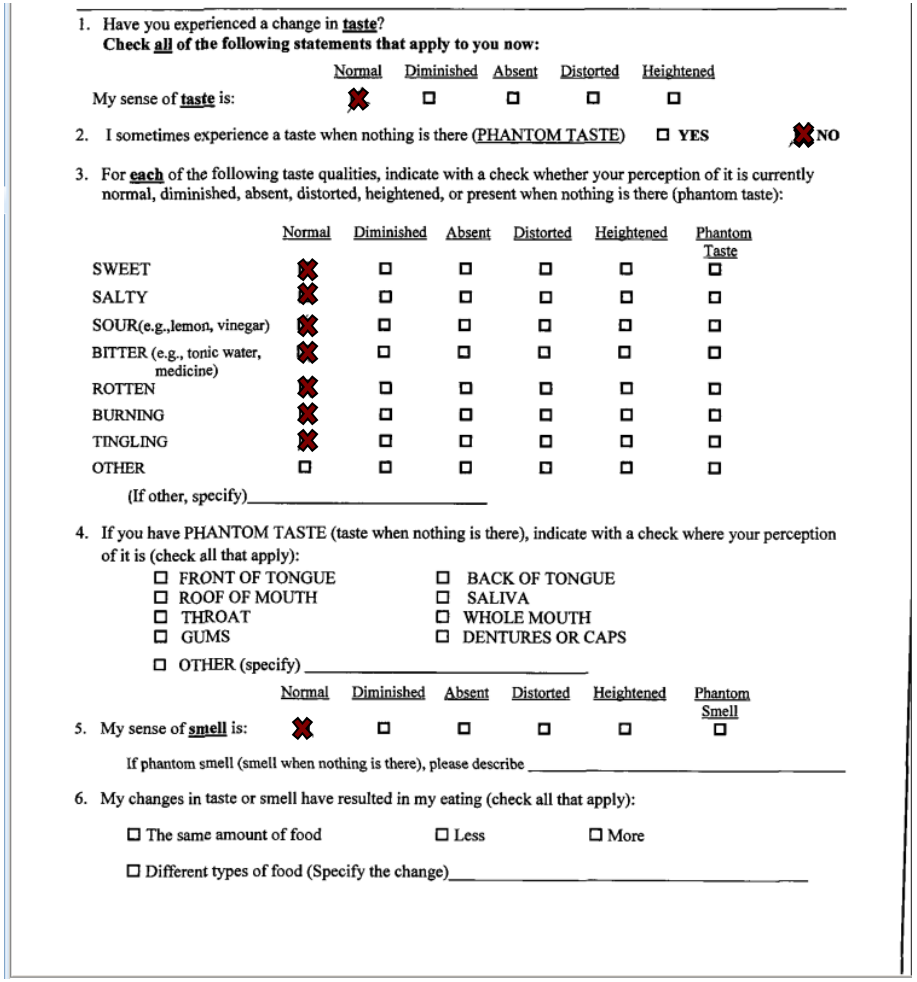
Original CBCT



Intensity corrected CBCT



Patient-reported toxicity/QOL



1. Have you experienced a change in **taste**?
   Check all of the following statements that apply to you now:

	Normal	Diminished	Absent	Distorted	Heightened
My sense of **taste** is:	☒	☐	☐	☐	☐

2. I sometimes experience a taste when nothing is there (PHANTOM TASTE) ☐ YES ☒ NO

3. For **each** of the following taste qualities, indicate with a check whether your perception of it is currently normal, diminished, absent, distorted, heightened, or present when nothing is there (phantom taste):

	Normal	Diminished	Absent	Distorted	Heightened	Phantom Taste
SWEET	☒	☐	☐	☐	☐	☐
SALTY	☒	☐	☐	☐	☐	☐
SOUR(e.g.,lemon, vinegar)	☒	☐	☐	☐	☐	☐
BITTER (e.g., tonic water, medicine)	☒	☐	☐	☐	☐	☐
ROTTEN	☒	☐	☐	☐	☐	☐
BURNING	☒	☐	☐	☐	☐	☐
TINGLING	☒	☐	☐	☐	☐	☐
OTHER	☐	☐	☐	☐	☐	☐

(If other, specify)_____

4. If you have PHANTOM TASTE (taste when nothing is there), indicate with a check where your perception of it is (check all that apply):

☐ FRONT OF TONGUE ☐ BACK OF TONGUE
☐ ROOF OF MOUTH ☐ SALIVA
☐ THROAT ☐ WHOLE MOUTH
☐ GUMS ☐ DENTURES OR CAPS
☐ OTHER (specify) _____

	Normal	Diminished	Absent	Distorted	Heightened	Phantom Smell
5. My sense of **smell** is:	☒	☐	☐	☐	☐	☐

If phantom smell (smell when nothing is there), please describe _____

6. My changes in taste or smell have resulted in my eating (check all that apply):

☐ The same amount of food ☐ Less ☐ More

☐ Different types of food (Specify the change)_____

Collected at baseline, 3, 6, 12, and 24 mos

Conclusions

- **Pencil-beam scanning: promising approach to improve the therapeutic ratio for our patients**
- **Head and neck: ideal disease site for proton therapy, often in a multimodal setting**
- **Need for comparative evidence generation, reporting patient outcomes**
  - Collaborative efforts
- **Technical advances required for further improvements**
  - Soft tissue imaging (CBCT)
  - Adaptive methods (dose calculation, plan analysis, replanning)

Acknowledgements

- **Clinical**
  - Steve Hahn
  - Jim Metz
  - Zelig Tochner

- **Physics**
  - Tim Solberg
  - Jim McDonough
  - Maura Kirk
  - Kevin Teo
  - Richard Maughan
  - Stefan Both