Application of PET Data in Radiotherapy

Target Definition
in Head and Neck Tumours

M Wada

Radiation Oncologist

Austin Health Radiation Oncology

Tech team

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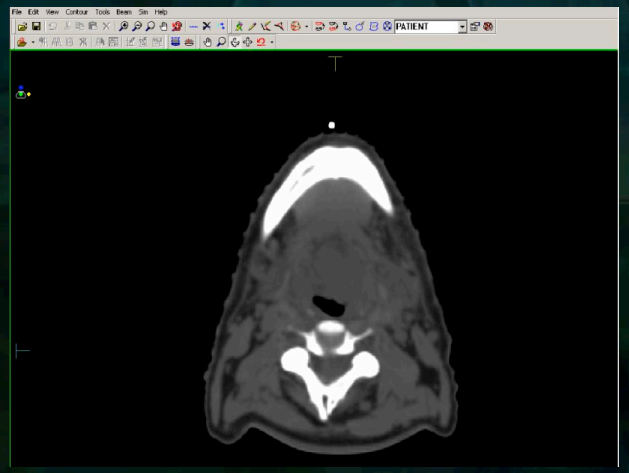
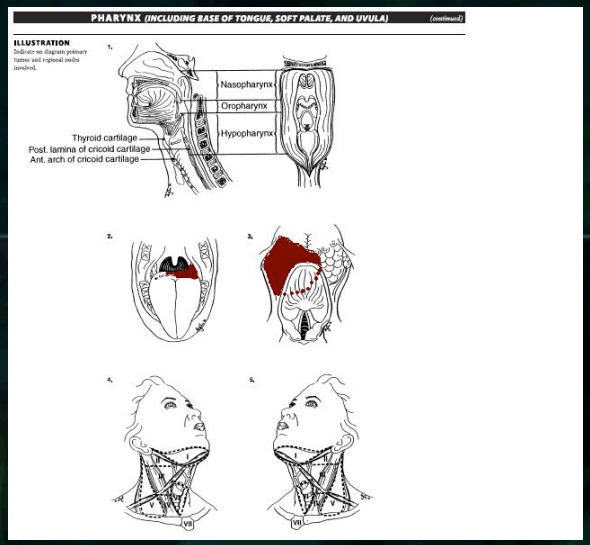
  - Dish Gunawardana
  - Andrew Scott
  - Aurora Poon

- **BAROC**
  - Nick Bennie
  - Michael Lim Joon
  - Andrew See

Case Study – Mr KC

- Mr. K.C.
- 54yo
- PHx
  - Ischaemic Heart Disease, CAGS
- HOPC
  - 3/12 L sided throat pain
  - swallowing & articulation difficulty
- O/E
  - L sided tongue base firmness crossing midline
  - Extends onto L tonsillar fossa
- Staging CT



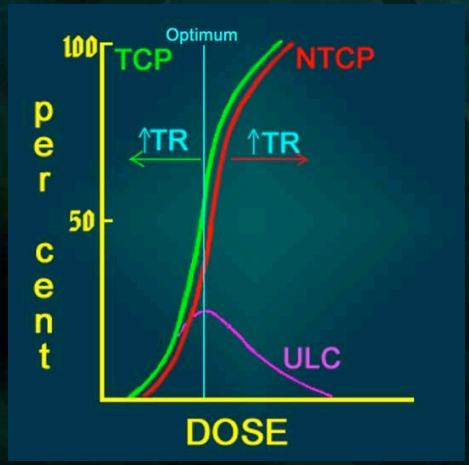


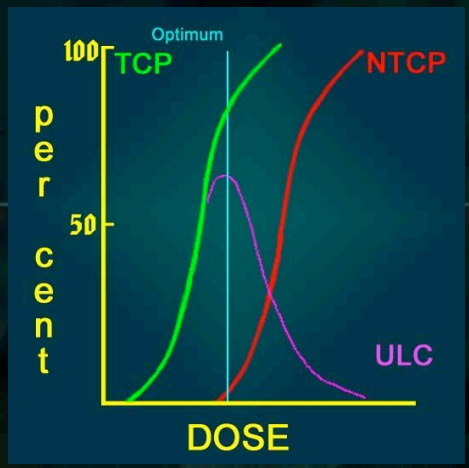
Case Study – Mr KC

- EUA
  - Confirmed the above
- Biopsy
  - MD SCC
- Assigned clinical stage
  - T3N0M0
  - PET / MRI

Mr K. C. - Aim of Management

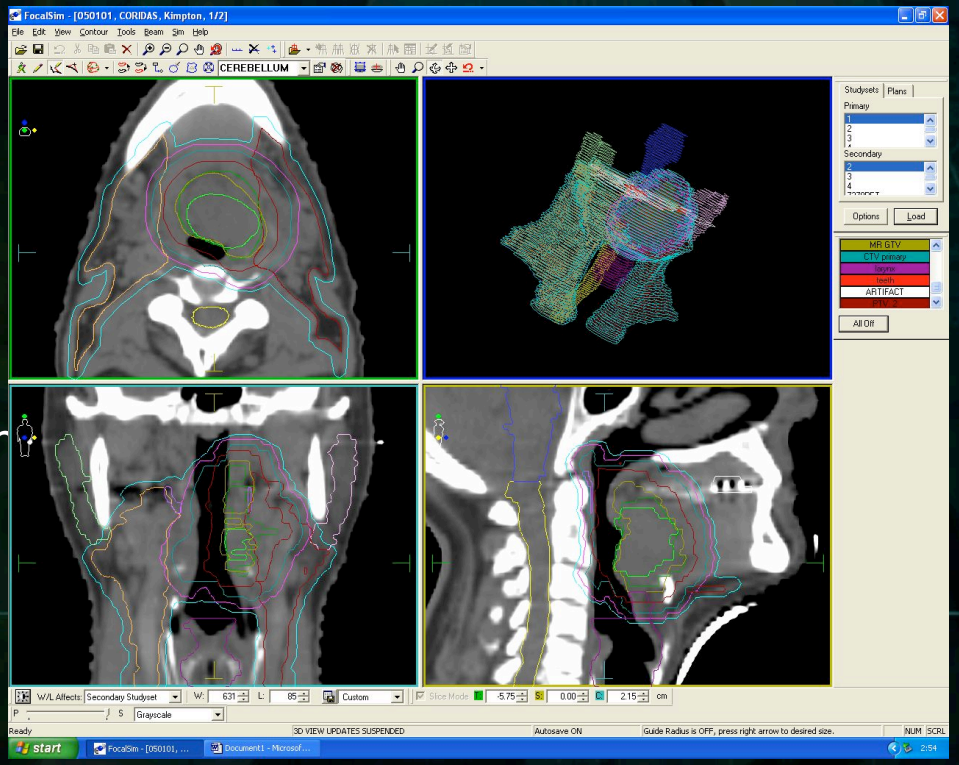
- Durable loco-regional tumour control
  - Cure / palliation / prevention of progressive loco regional disease
- Functional preservation, QoL
- Therapeutic ratio
- Double sigmoid curve
  - Balance between probability of tumour control probability and normal tissue complication probability
- Strategies
  - Correct management intent, selection of most appropriate modality/program
  - Fractionation
  - Chemo-radiotherapy
  - Dose conformation, escalation, normal tissue avoidance
  - Selective radiation protectors

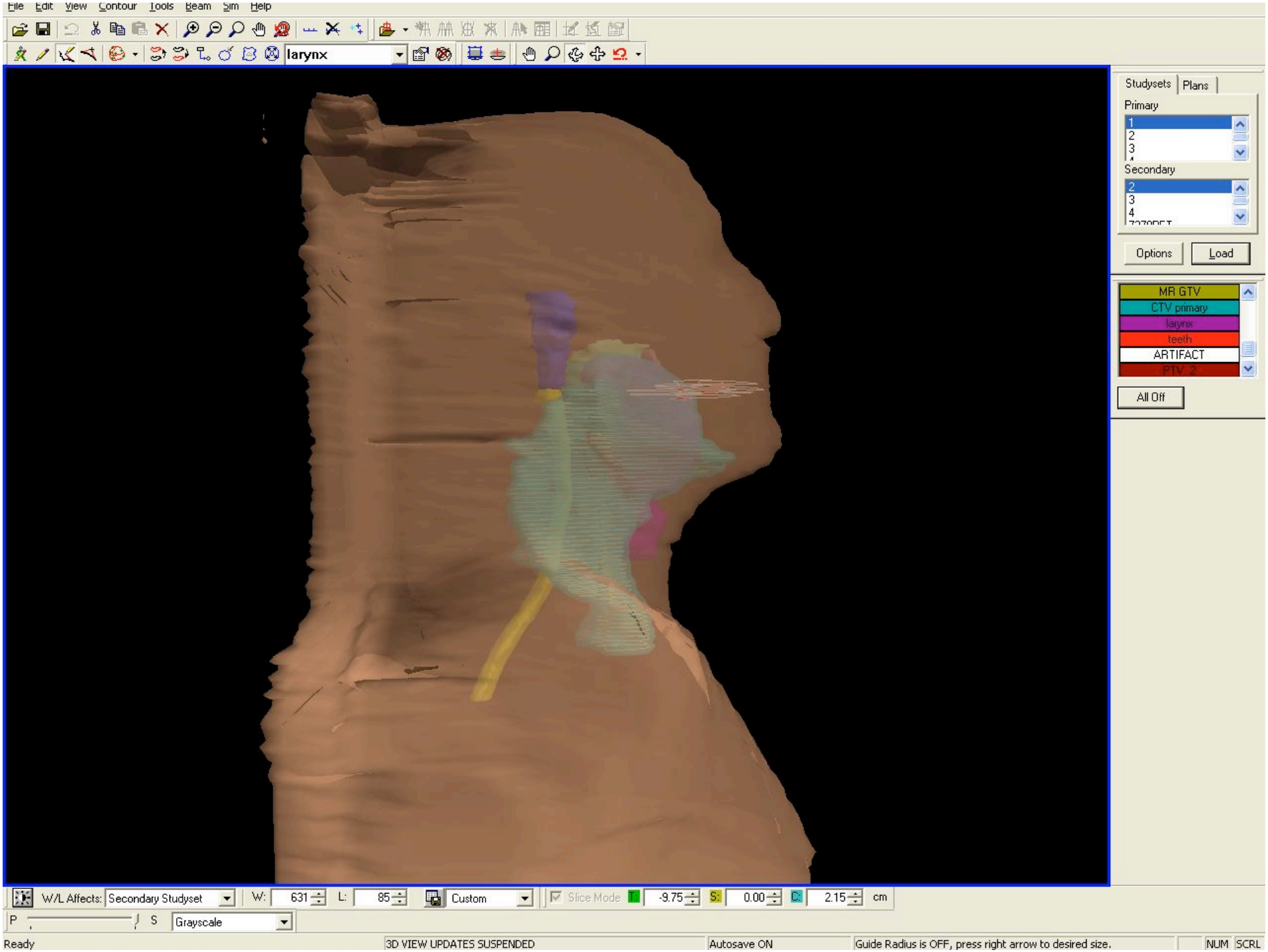




Mr. K.C – Planning Goals, Constraints

- Standard fractionation
  - GTV – 70Gy in 2Gy fractions
  - CTV – high risk 60Gy
  - CTV – microscopic disease 50Gy
- Normal tissue tolerance
  - Parotid glands 26Gy mean
  - Spinal cord 45-50Gy maximal dose
  - Mandible 70Gy max
  - Larynx V>50Gy to <33%
- ICRU 50 / 62

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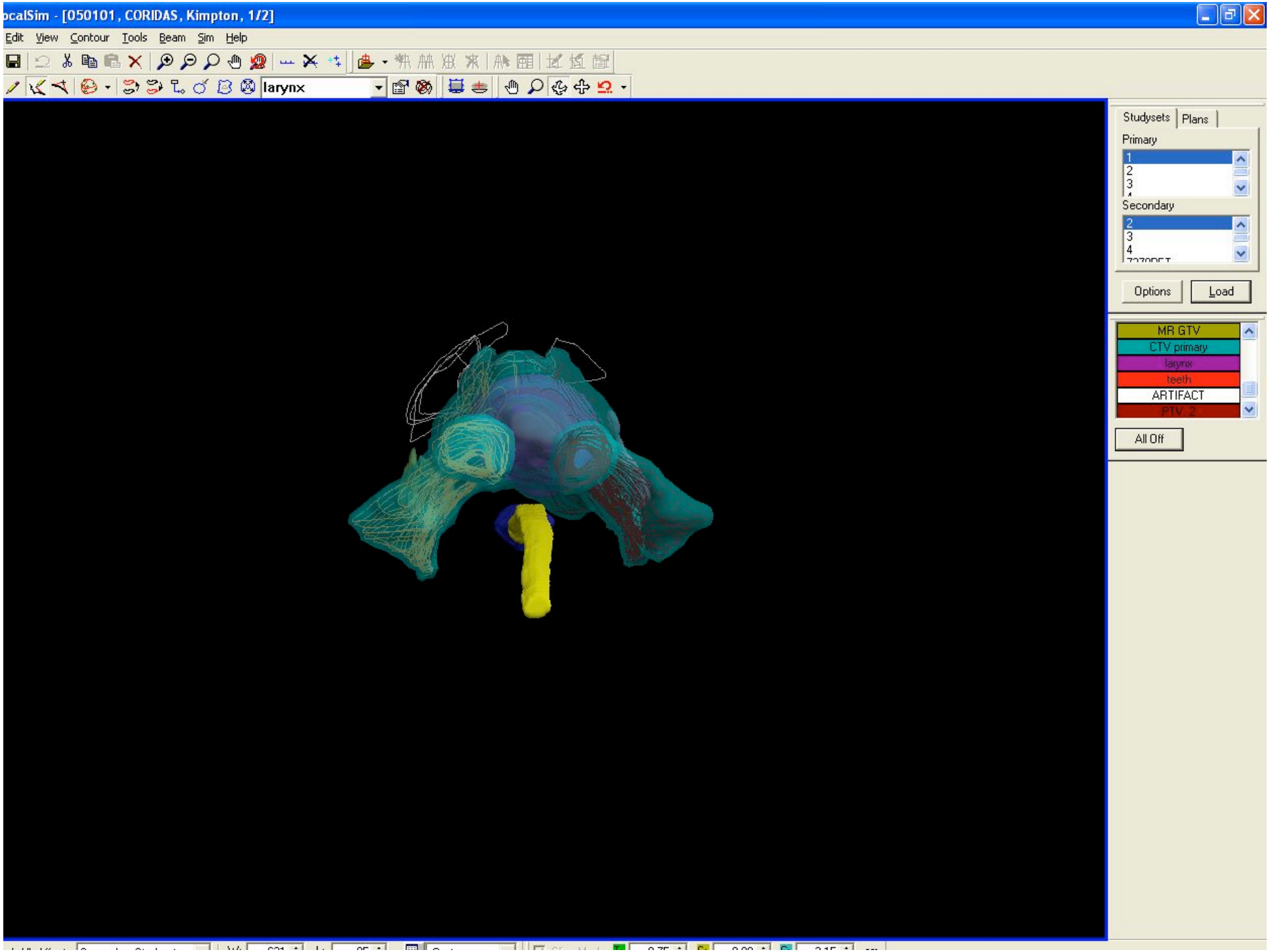
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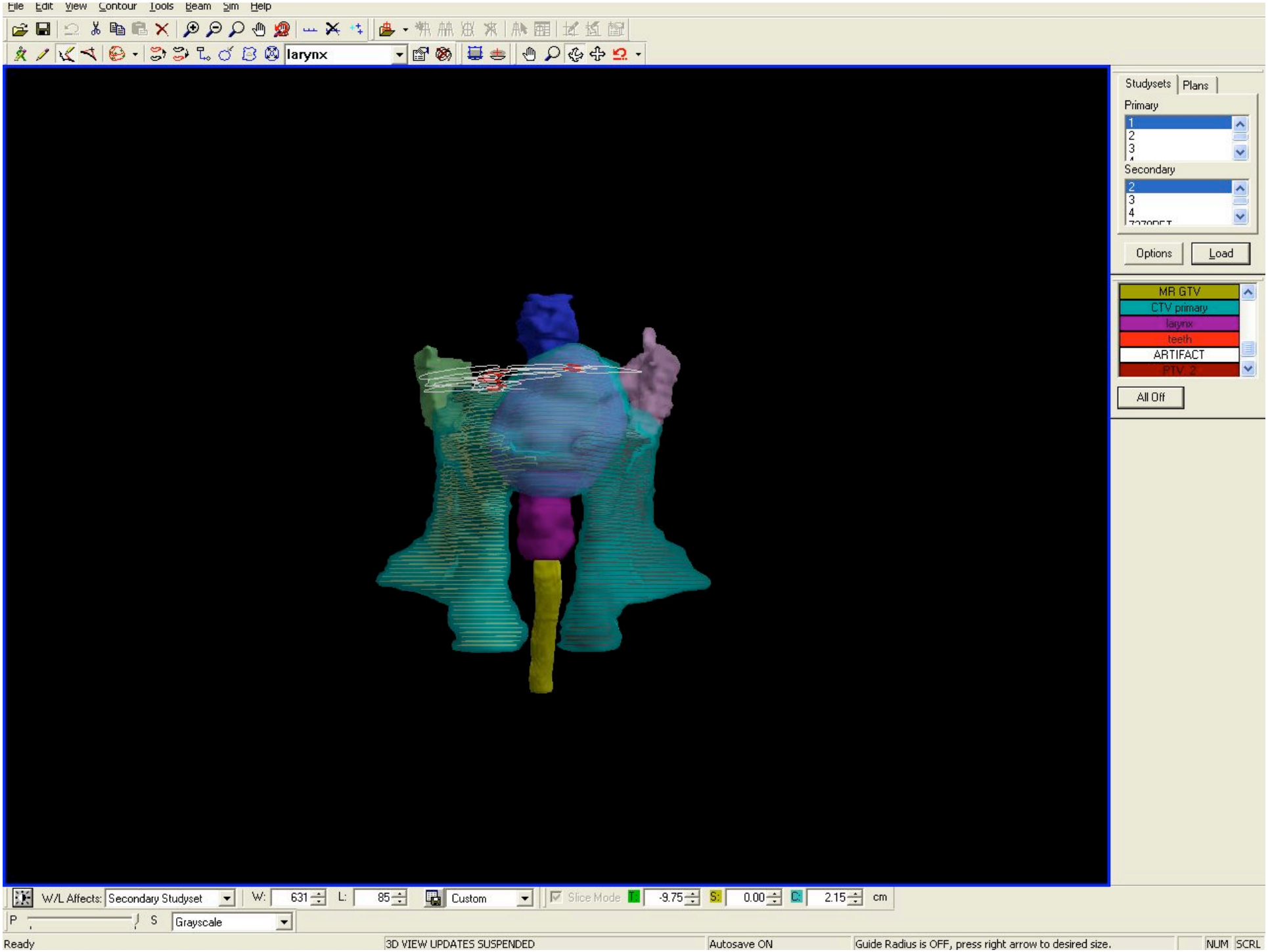
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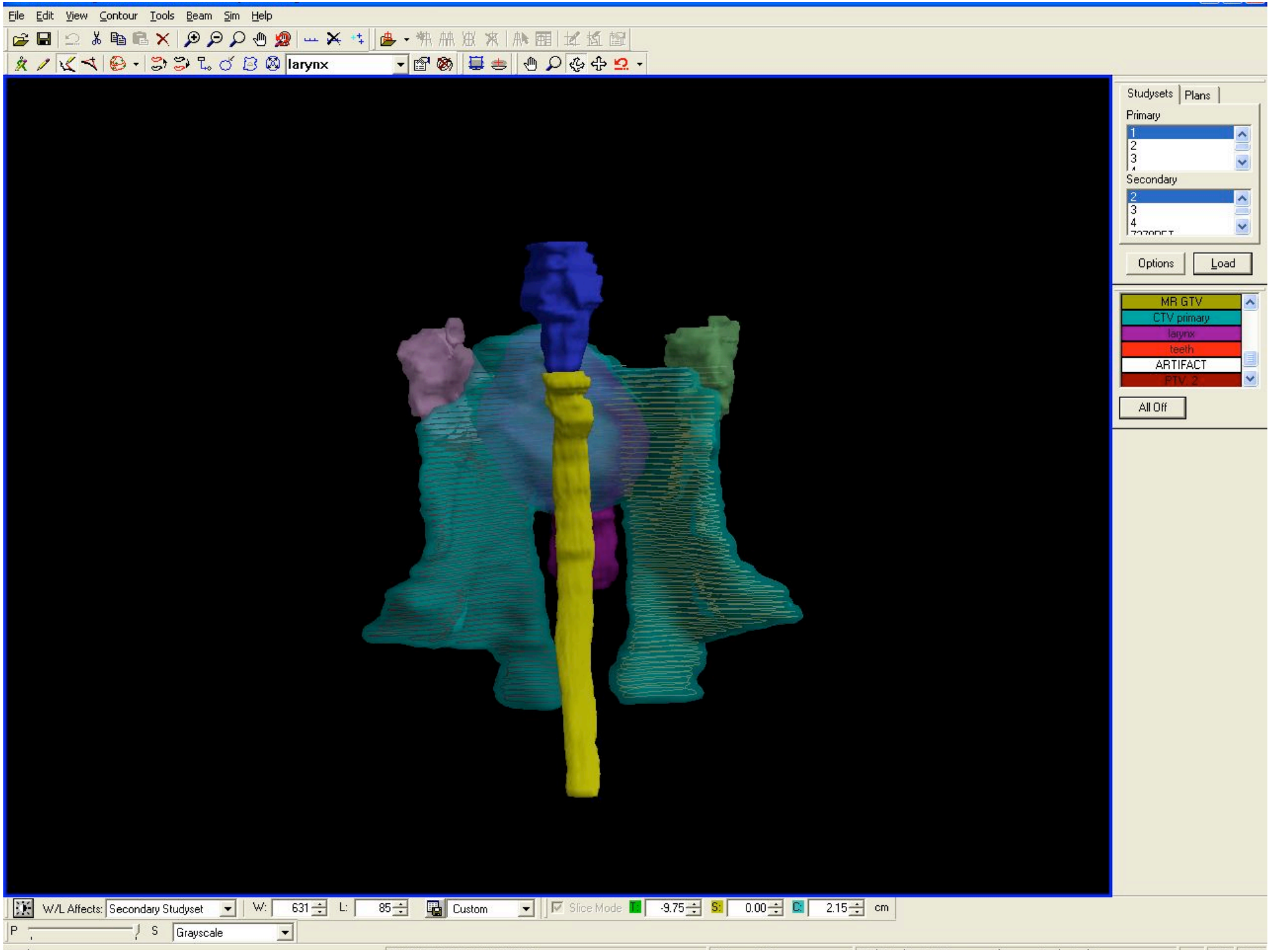
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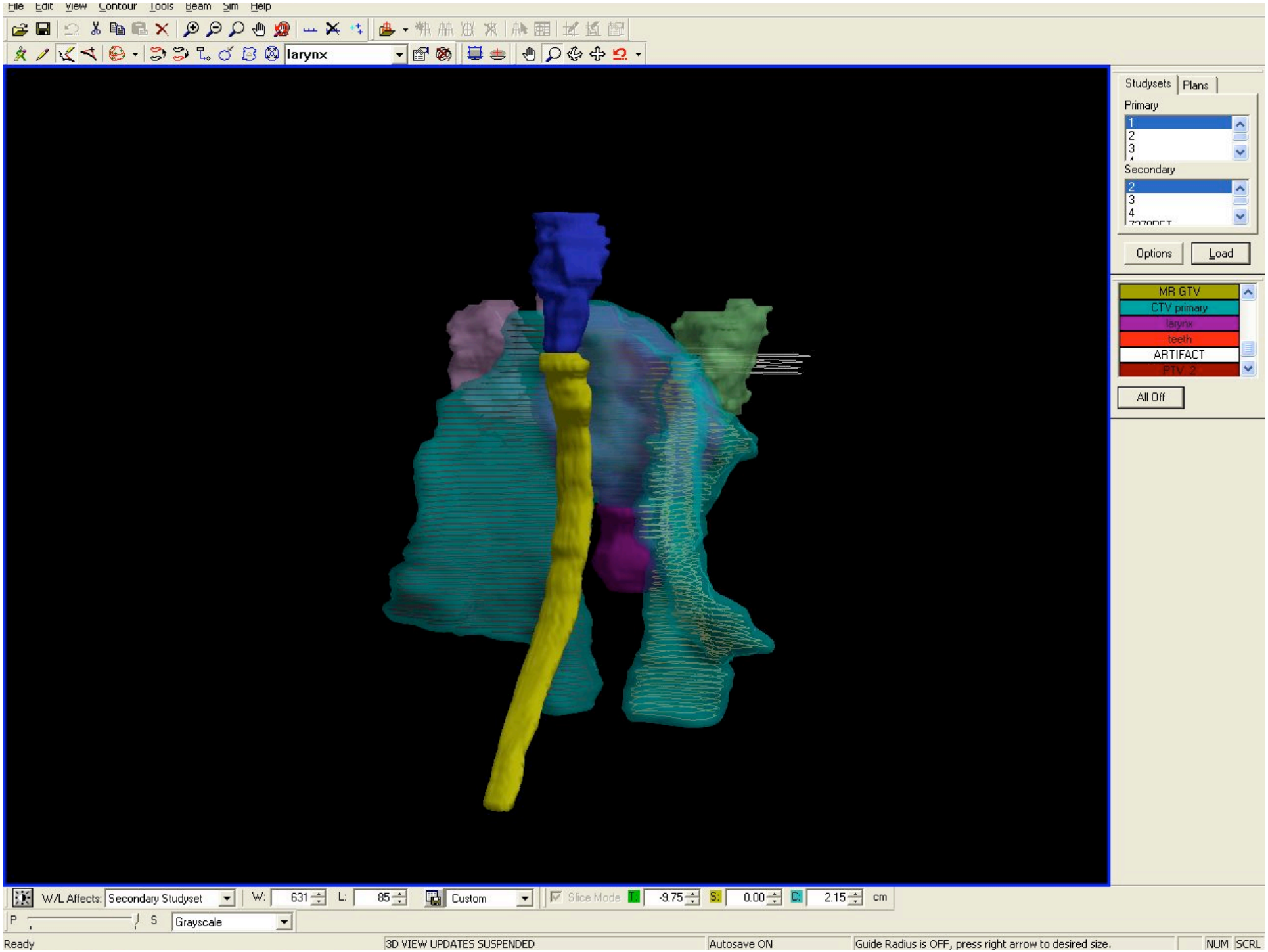
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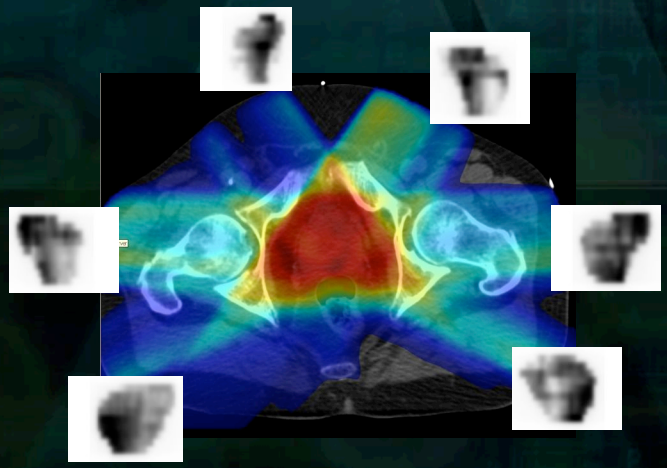
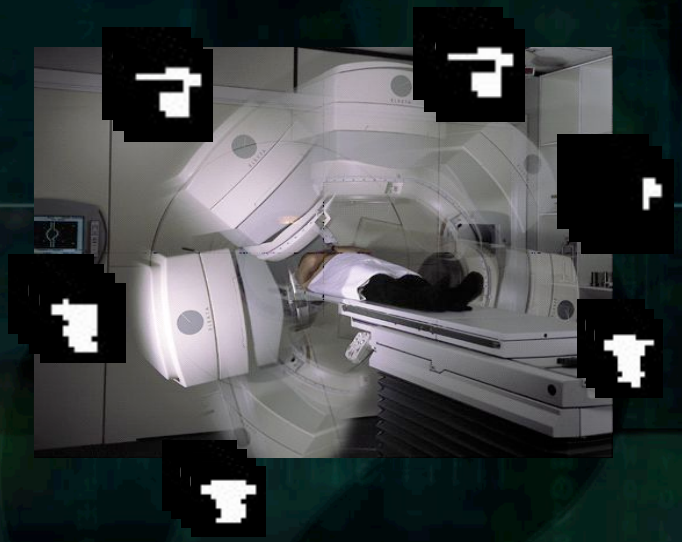
Dose Conformation in Head and Neck - Technological Rationale

- Delivery – Linac based – MLC, tomotherapy
- Imaging
  - 3 & 4D (rapid 3D acquisition and binning)
  - CT technology, MR, MRS, PET
- Computing -
  - Dose prediction calculation algorithms
    - Pencil beam, superposition, Monte Carlo
  - Visualization tools – target, plan analysis and verification, QA
- QA tools – incl EPIDs and 3D on board imaging devices





Rationale for dose conformation
- Planning studies

- Planning studies
  - Better target coverage
  - Better sparing of dose limiting structures including parotid glands
  - Possibility of dose escalation

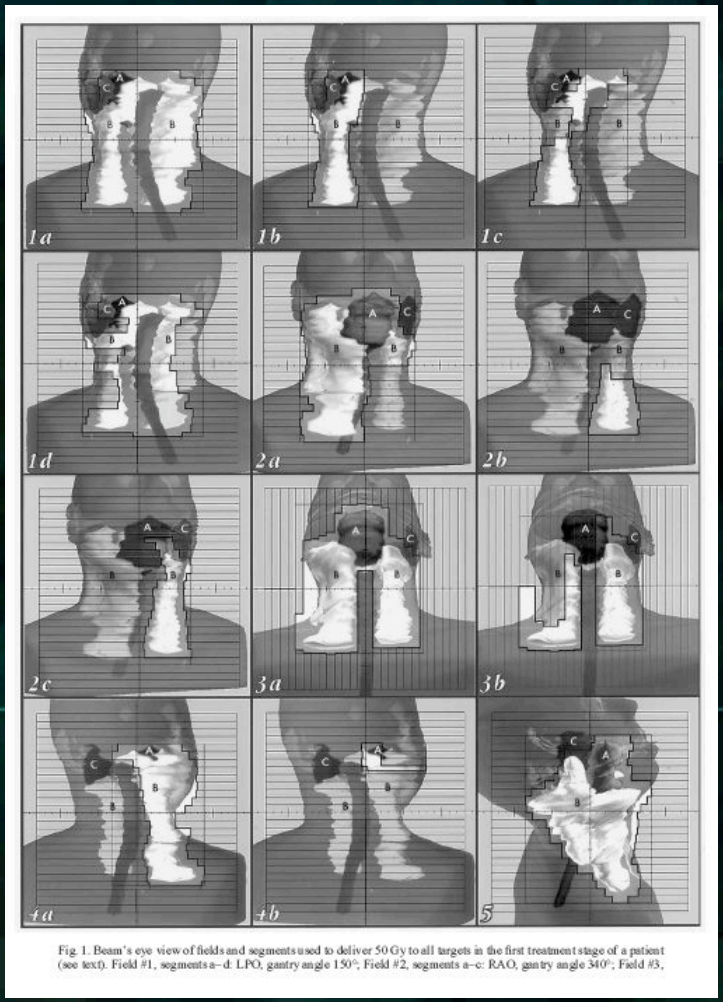


Fig. 1. Beam's eye view of fields and segments used to deliver 50 Gy to all targets in the first treatment stage of a patient (see text). Field #1, segments a–d: LPO, gantry angle 150°; Field #2, segments a–c: RAO, gantry angle 340°; Field #3,

Planning studies

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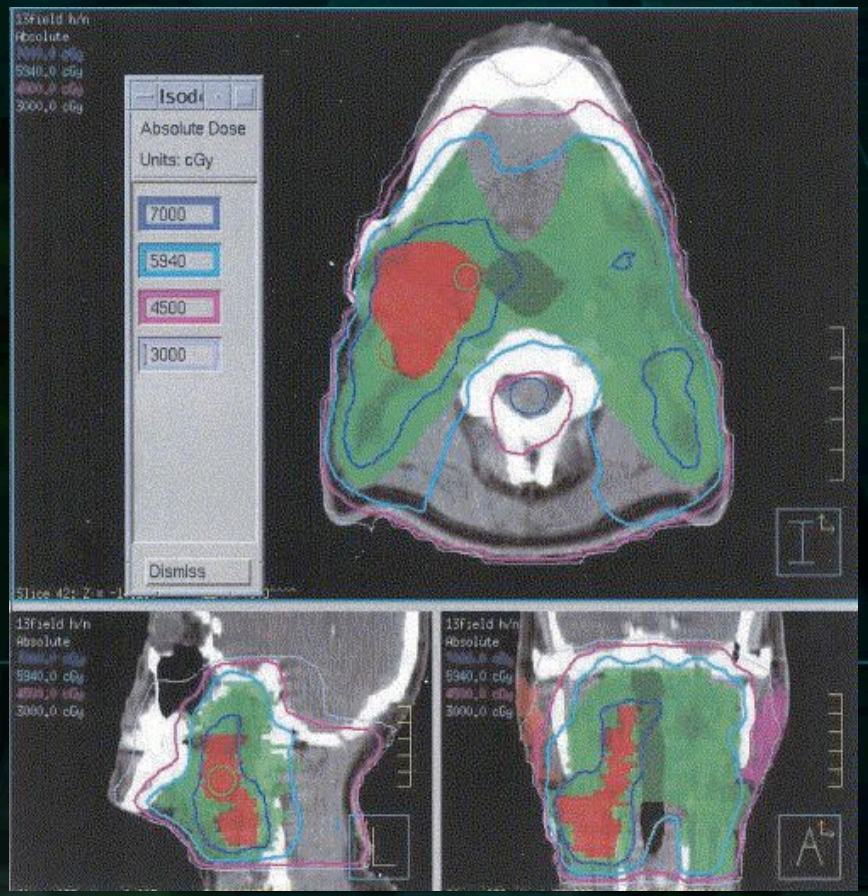
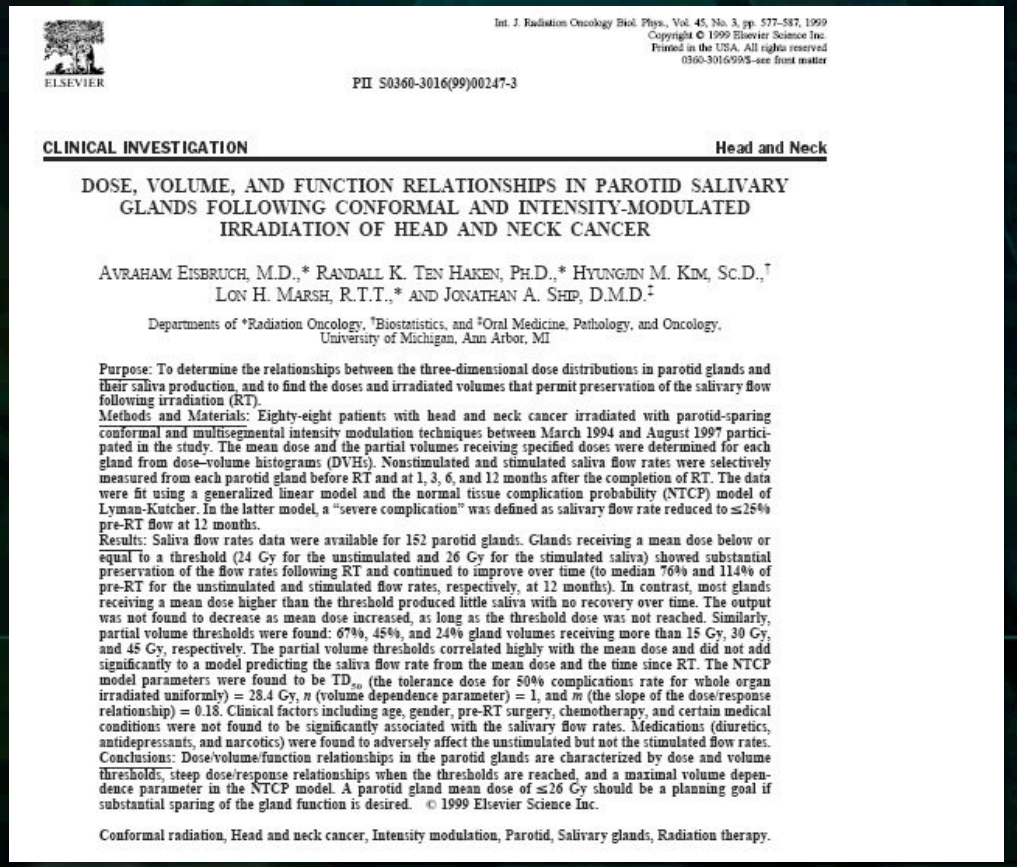


Rationale for dose conformation - Correlative clinical outcome

- Mounting evidence for salivary sparing
- Improvement of QoL with long term follow up



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CLINICAL INVESTIGATION — Head and Neck

DOSE, VOLUME, AND FUNCTION RELATIONSHIPS IN PAROTID SALIVARY GLANDS FOLLOWING CONFORMAL AND INTENSITY-MODULATED IRRADIATION OF HEAD AND NECK CANCER

AVRAHAM EISBRUCH, M.D.,* RANDALL K. TEN HAKEN, PH.D.,* HYUNGJIN M. KIM, SC.D.,† LON H. MARSH, R.T.T.,* AND JONATHAN A. SHIP, D.M.D.‡

Departments of *Radiation Oncology, †Biostatistics, and ‡Oral Medicine, Pathology, and Oncology, University of Michigan, Ann Arbor, MI

Purpose: To determine the relationships between the three-dimensional dose distributions in parotid glands and their saliva production, and to find the doses and irradiated volumes that permit preservation of the salivary flow following irradiation (RT).

Methods and Materials: Eighty-eight patients with head and neck cancer irradiated with parotid-sparing conformal and multisegmental intensity modulation techniques between March 1994 and August 1997 participated in the study. The mean dose and the partial volumes receiving specified doses were determined for each gland from dose–volume histograms (DVHs). Nonstimulated and stimulated saliva flow rates were selectively measured from each parotid gland before RT and at 1, 3, 6, and 12 months after the completion of RT. The data were fit using a generalized linear model and the normal tissue complication probability (NTCP) model of Lyman-Kutcher. In the latter model, a "severe complication" was defined as salivary flow rate reduced to ≤25% pre-RT flow at 12 months.

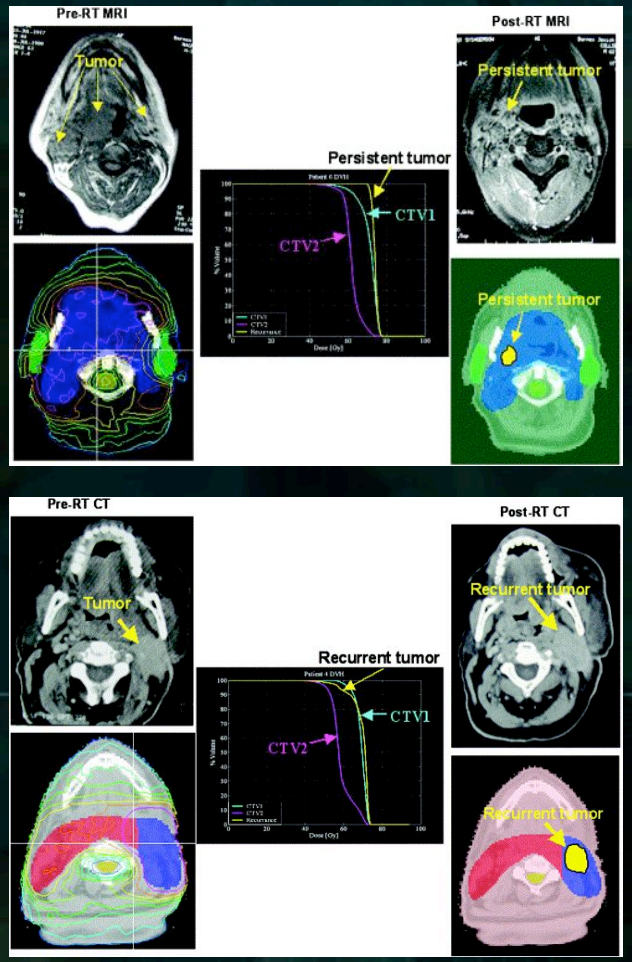
Results: Saliva flow rates data were available for 152 parotid glands. Glands receiving a mean dose below or equal to a threshold (24 Gy for the unstimulated and 26 Gy for the stimulated saliva) showed substantial preservation of the flow rates following RT and continued to improve over time (to median 76% and 114% of pre-RT for the unstimulated and stimulated flow rates, respectively, at 12 months). In contrast, most glands receiving a mean dose higher than the threshold produced little saliva with no recovery over time. The output was not found to decrease as mean dose increased, as long as the threshold dose was not reached. Similarly, partial volume thresholds were found: 67%, 45%, and 24% gland volumes receiving more than 15 Gy, 30 Gy, and 45 Gy, respectively. The partial volume thresholds correlated highly with the mean dose and did not add significantly to a model predicting the saliva flow rate from the mean dose and the time since RT. The NTCP model parameters were found to be TD_{50} (the tolerance dose for 50% complications rate for whole organ irradiated uniformly) = 28.4 Gy, n (volume dependence parameter) = 1, and m (the slope of the dose/response relationship) = 0.18. Clinical factors including age, gender, pre-RT surgery, chemotherapy, and certain medical conditions were not found to be significantly associated with the salivary flow rates. Medications (diuretics, antidepressants, and narcotics) were found to adversely affect the unstimulated but not the stimulated flow rates.

Conclusions: Dose/volume/function relationships in the parotid glands are characterized by dose and volume thresholds, steep dose/response relationships when the thresholds are reached, and a maximal volume dependence parameter in the NTCP model. A parotid gland mean dose of ≤26 Gy should be a planning goal if substantial sparing of the gland function is desired. © 1999 Elsevier Science Inc.

Conformal radiation, Head and neck cancer, Intensity modulation, Parotid, Salivary glands, Radiation therapy.

Clinical outcome of dose conformation – pattern of failure studies

- E.g.
  - UCSF – Nasopharynx
  - Michigan – SCC
  - Mallinckrodt – SCC and nasopharynx
  - All suggest excellent local control rates
  - No suggestion of "geographical miss" with dose conformation to carefully delineated target volumes



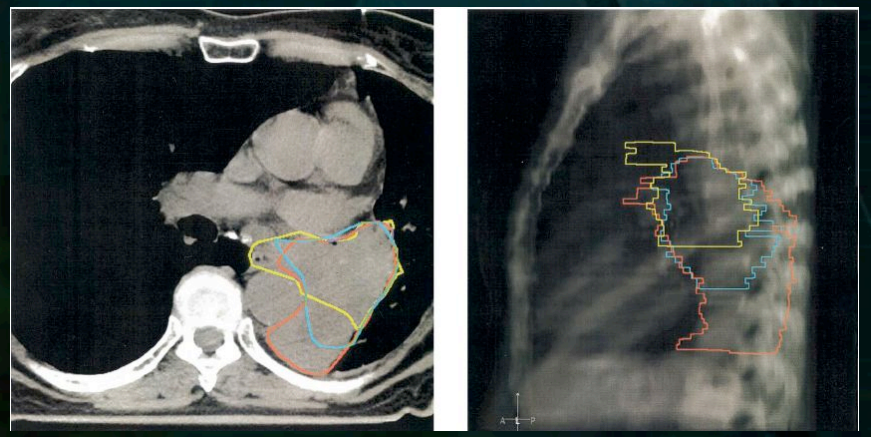
- But.....

Improved dose conformation and its consequences

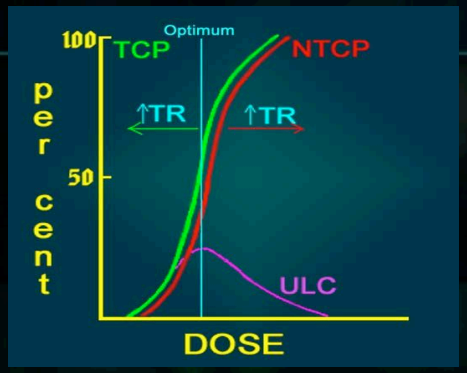
- Three-dimensional conformal radiotherapy and intensity modulated radiotherapy allow accurate dose delivery on target volumes.
- With improved accuracy of treatment delivery, target volume definition, i.e. "*contouring emerges as one of the most questionable steps in treatment planning procedures*"

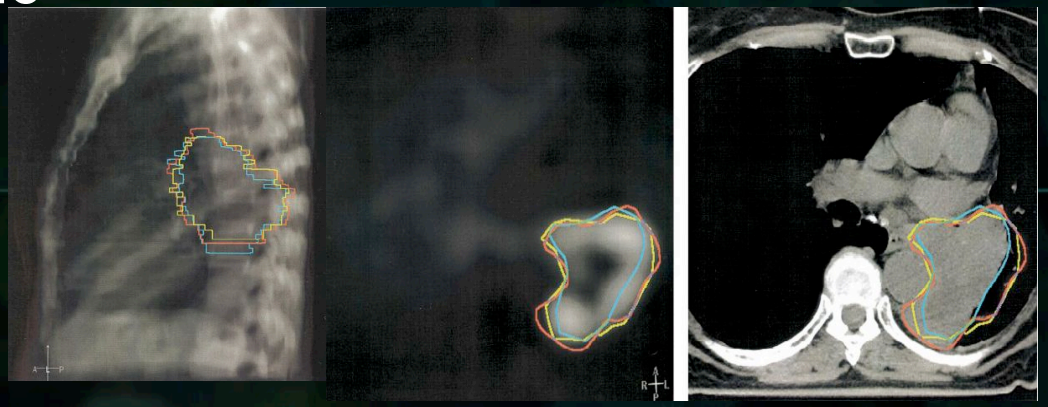
Need for improved target definition process

- Concept of precision delivery and verification to an incorrect target
- Precision mis-hit!!



- Very bad for therapeutic ratio!!





- Rapid acceptance of PET in oncology community (US)

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doi:10.1016/j.ijrobp.2003.10.045

EDITORIAL

FDG-PET IN RADIOTHERAPY TREATMENT PLANNING: PANDORA'S BOX?

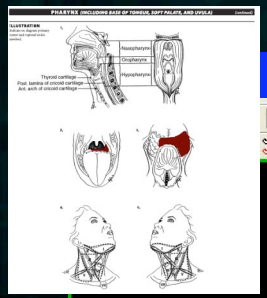
ARNOLD C. PAULINO, M.D., AND PETER A. S. JOHNSTONE, M.D.

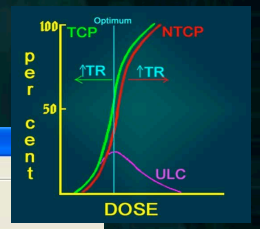
Department of Radiation Oncology, Emory University, Atlanta, GA

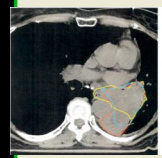
In the meantime, PET-CT fusion in radiotherapy treatment planning is here to stay. As pointed out (3), over 200 PET-CT scanners were installed in the last *2 years alone*! Although the mythical box of PET-CT is clearly attractive from a theoretical standpoint, it carries many unknowns awaiting answers. Data are accumulating; we await their presentation.

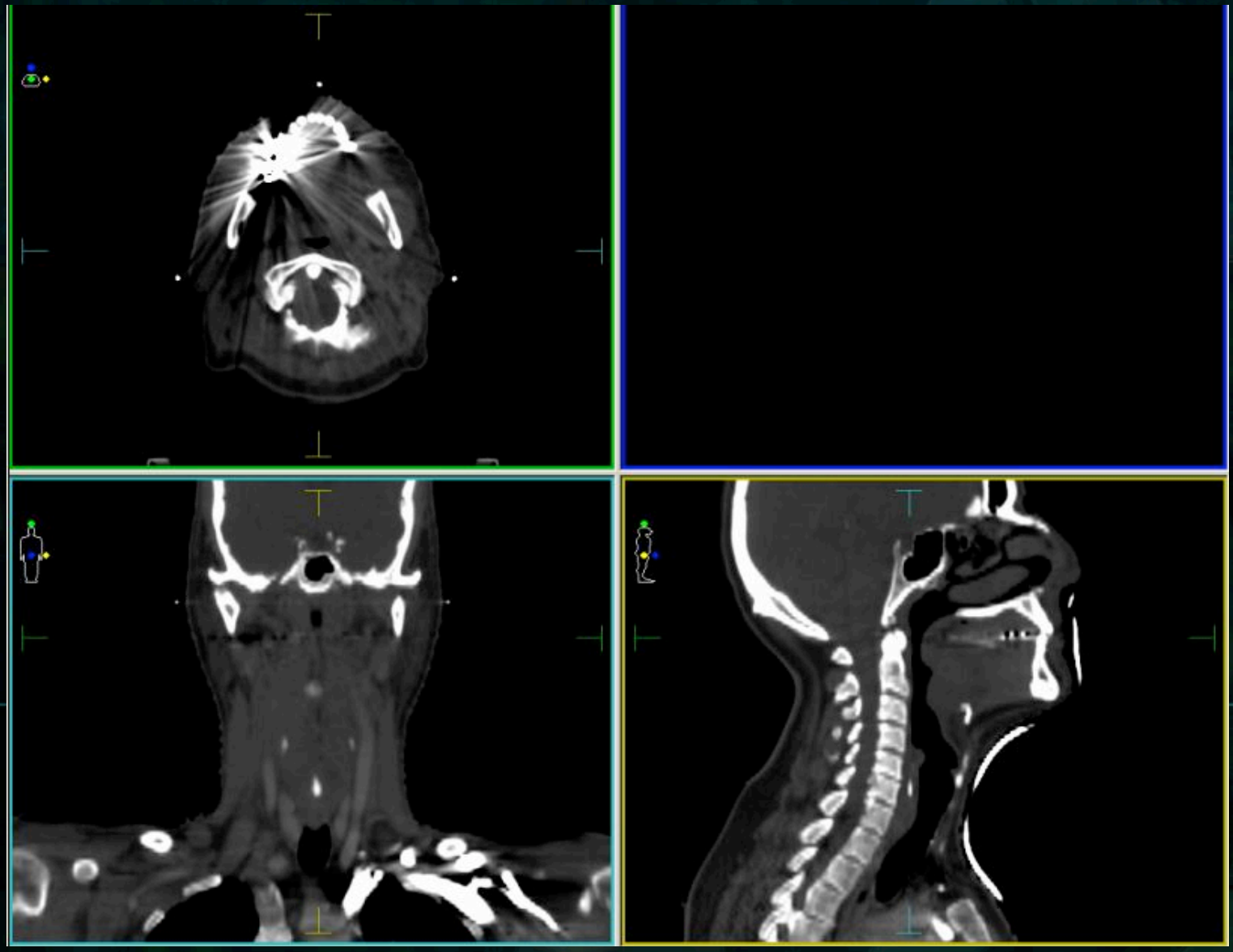
- So…..

Back to Mr. K.C.





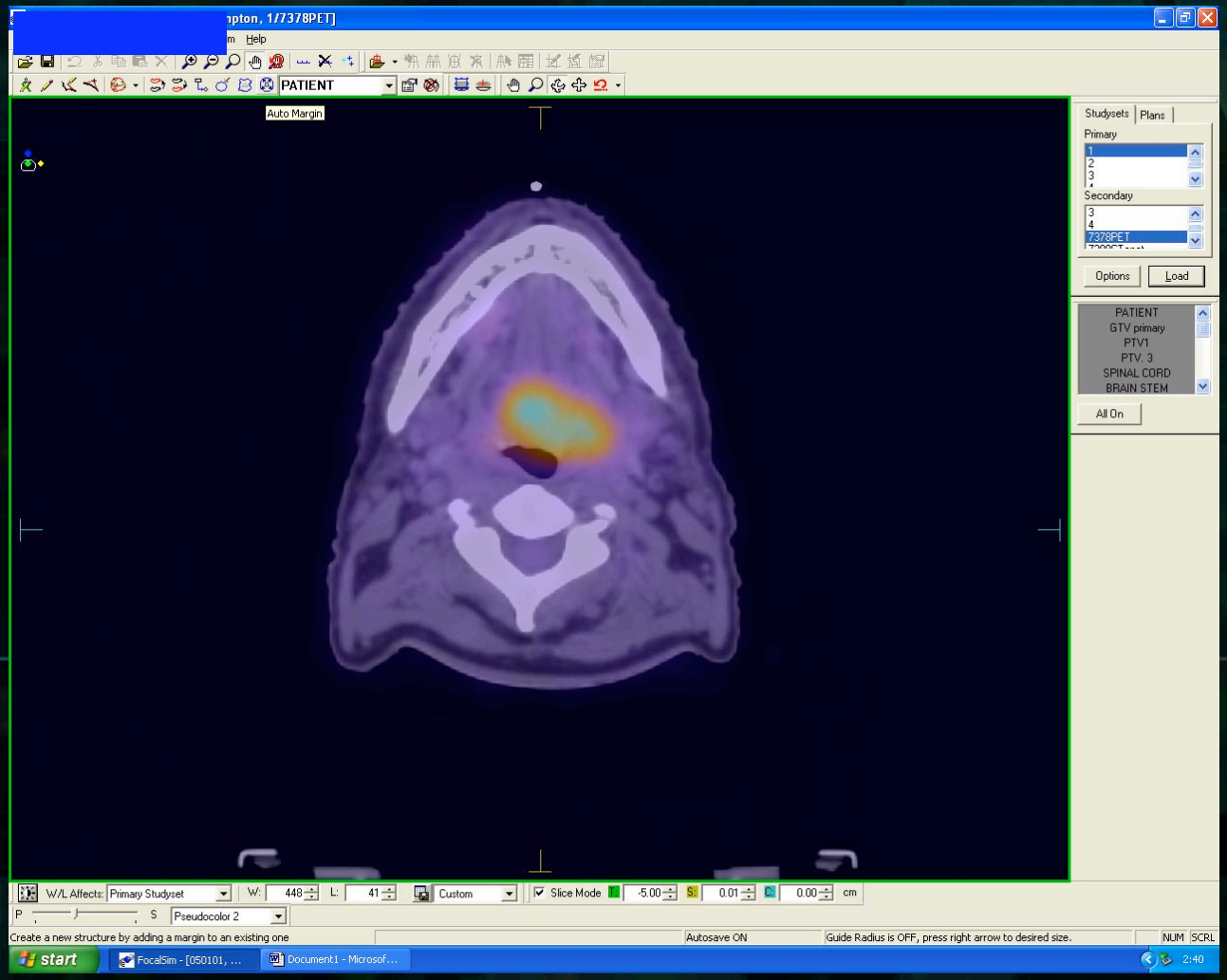




PET – Literature – does this help Mr K.C.

- Suggestion in the head and neck literature
  - All hypothesis generating, small studies only
  - Reduction in apparent inter and intra expert / observer error
  - CT / MR / FDG-PET GTV – different
    - Various methodologies of PET contouring
      - Qantitative vs qualiative, automated delineation
  - But what is the gold standard?
    - Phantom studies using various thresholding strategies
    - Primary SCC not spherical, varied uptake within lesion, gradual density of clonogens from centre of tumor
    - Approximates histological GTV than MRI and CT – Gregoire
  - BTV dose escalation – IMRT planning studies and clinical implementation in some centres!!
  - “Dose painting”

Mr. K.C. – use the PET data??



At Austin Health ROC

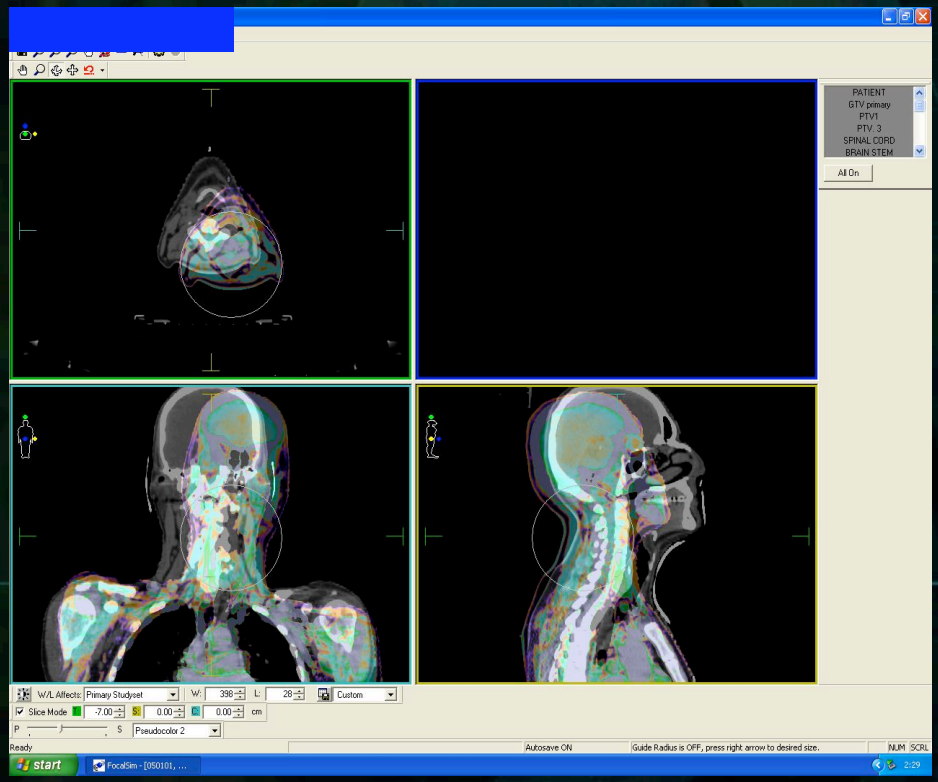
- Conformal XRT and careful contouring of target volume routine in appropriate cases
  - FPIMRT / parotid sparing clinical
  - IPIMRT – final 3D QA stage
- PET/CT on site / collaboration
- Routine use in mucosal SCC H&N staging / re -staging
  - Specificity for nodal disease cf CT/MR
  - 10-15% metastatic upstaging
  - Second primary
  - Occult primary
  - Response assessment
- PET is here to stay!!
- *Cautious optimism re: its role in RTP*

At Austin Health ROC

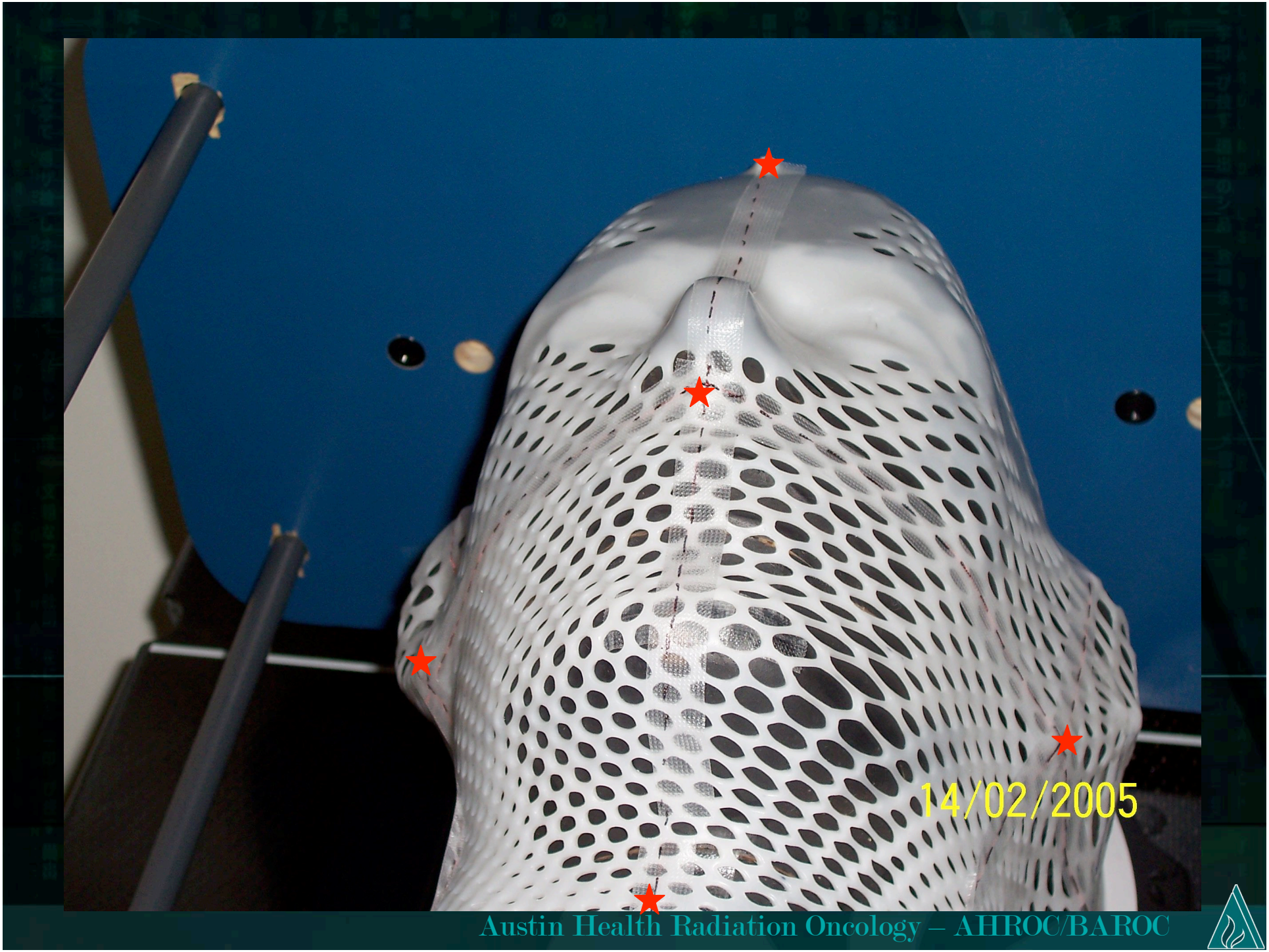
- PET QA/protocol in head and neck
  - Early draft and Austin Health ethics approval - Dr Khaw in 2002
  - Long lead time
    - DICOM NM/PET vs. CMS focus
    - Late 2004
    - Protocol amendment, logistic / technical details - 2004
  - All eligible radical cases mucosal H&N SCC
  - Learning curve

Target definition protocol - ROC

- CT simulation
  - Immobilization
  - Bite block
- Mutimodality image acquisition
  - CT – contrast and non contrast – 2.5mm cuts
  - MRI – T2 and GdT1
  - FDG PET – in cast
  - F MISO - protocol
- Image co-registration
  - PET vs. planning CT
  - Fiducial – PET
  - Vs. MI



Our protocol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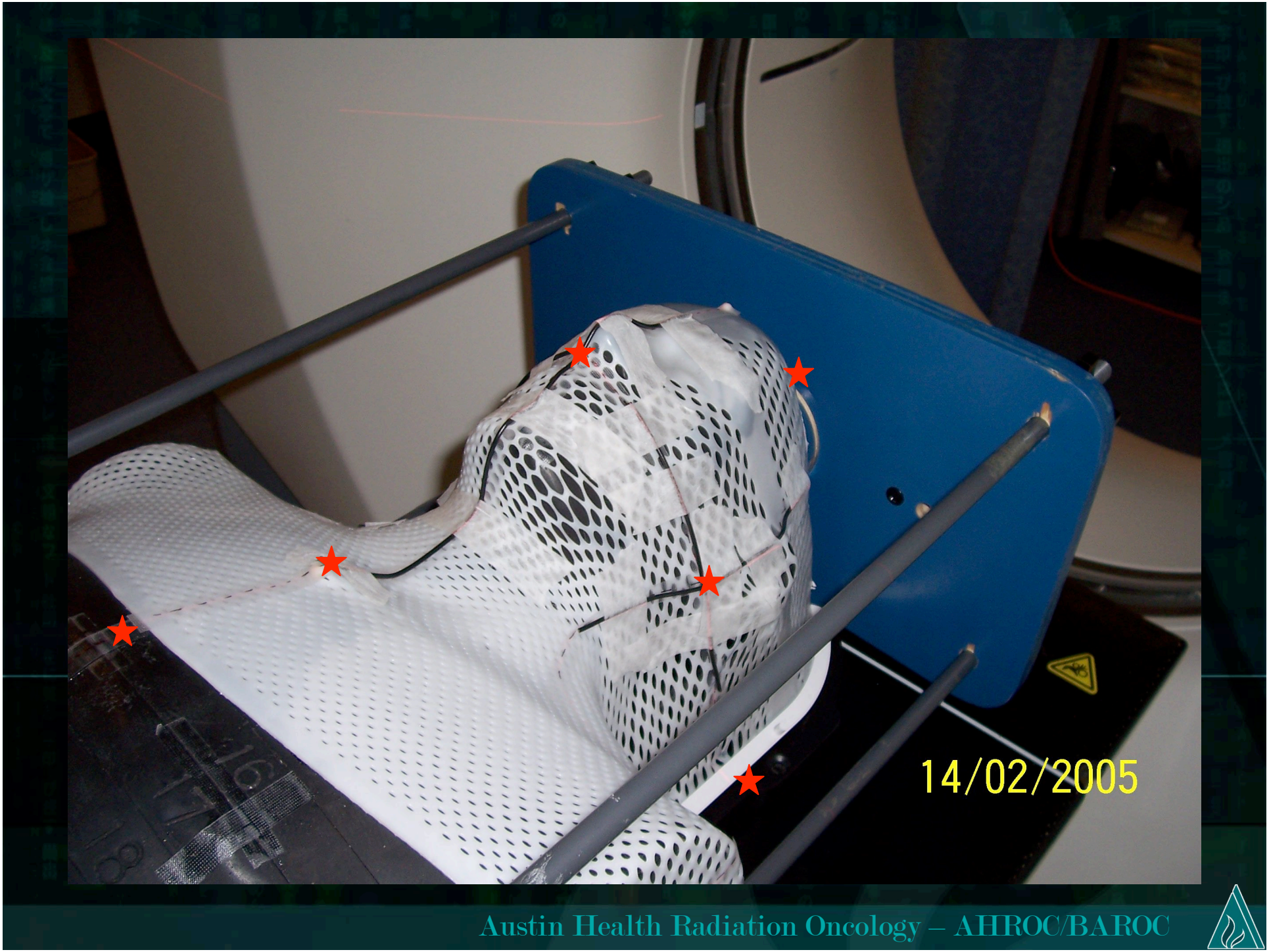
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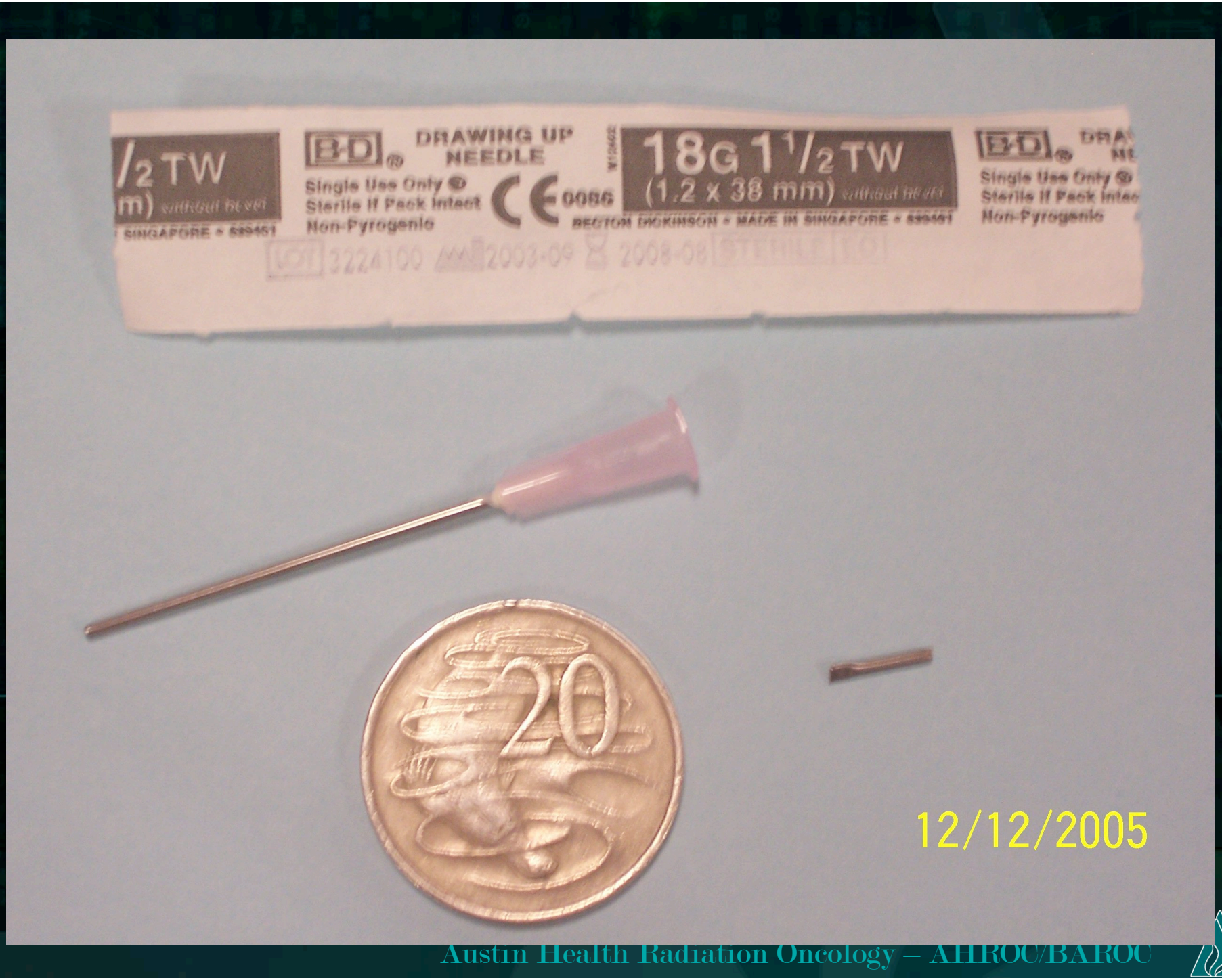
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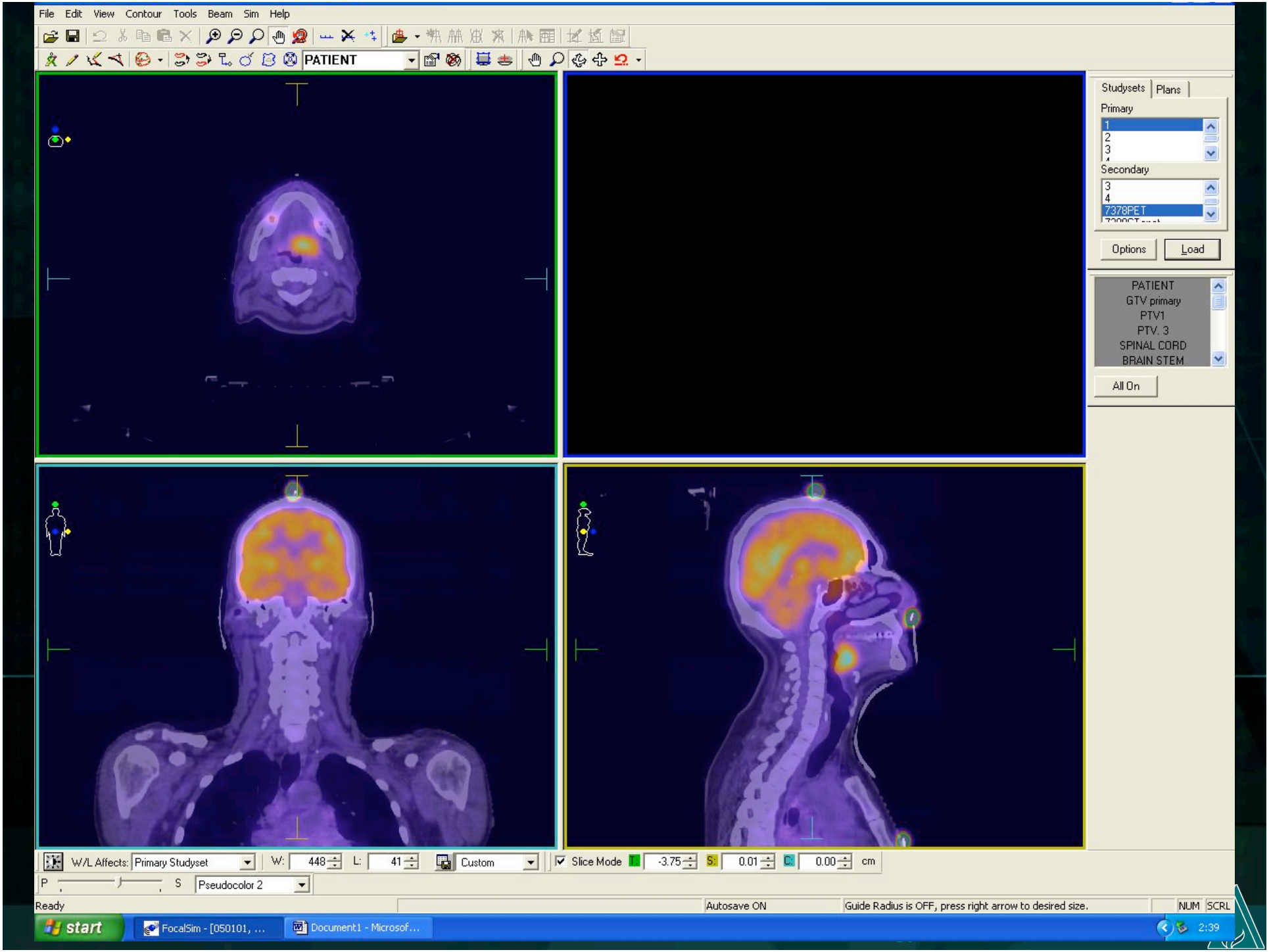
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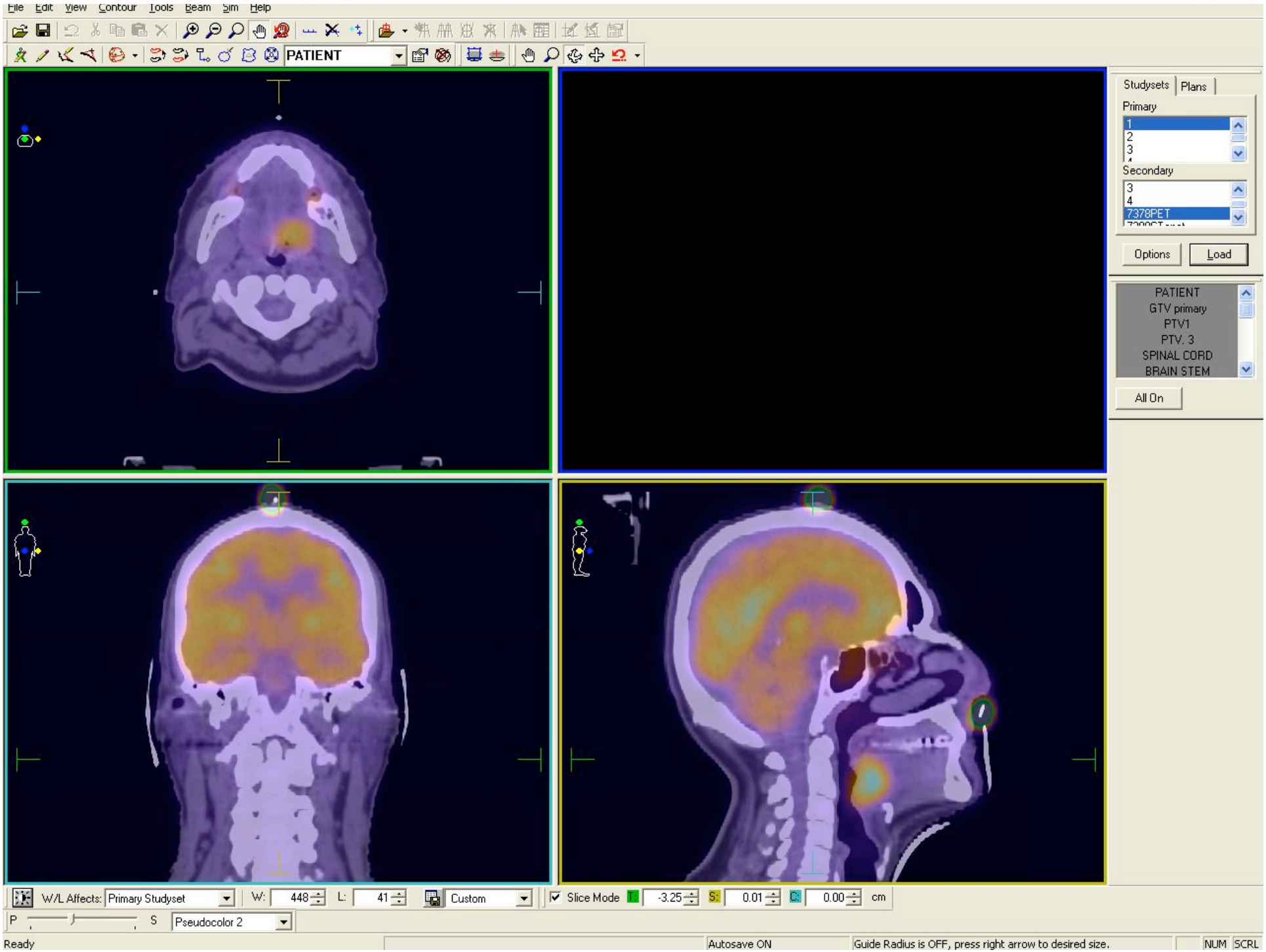
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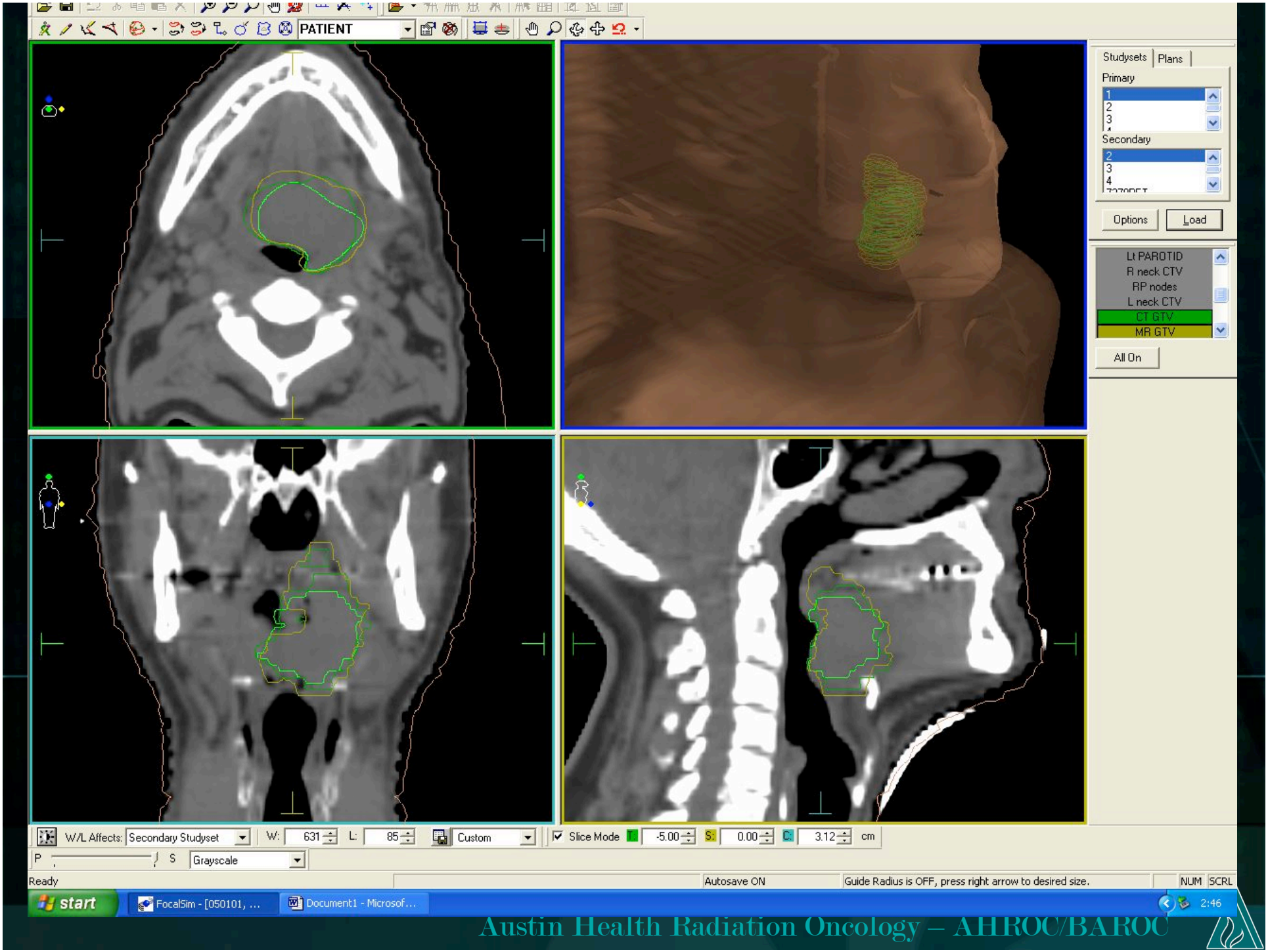
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R neck CTV
RP nodes
L neck CTV
CT GTV
MR GTV
All On
W/L Affects:
Secondary Studyset
W:
631
L:
85
Custom
Slice Mode
T:
-5.00
S:
0.00
C:
3.12
cm
P
S
Grayscale
Ready
Autosave ON
Guide Radius is OFF, press right arrow to desired size.
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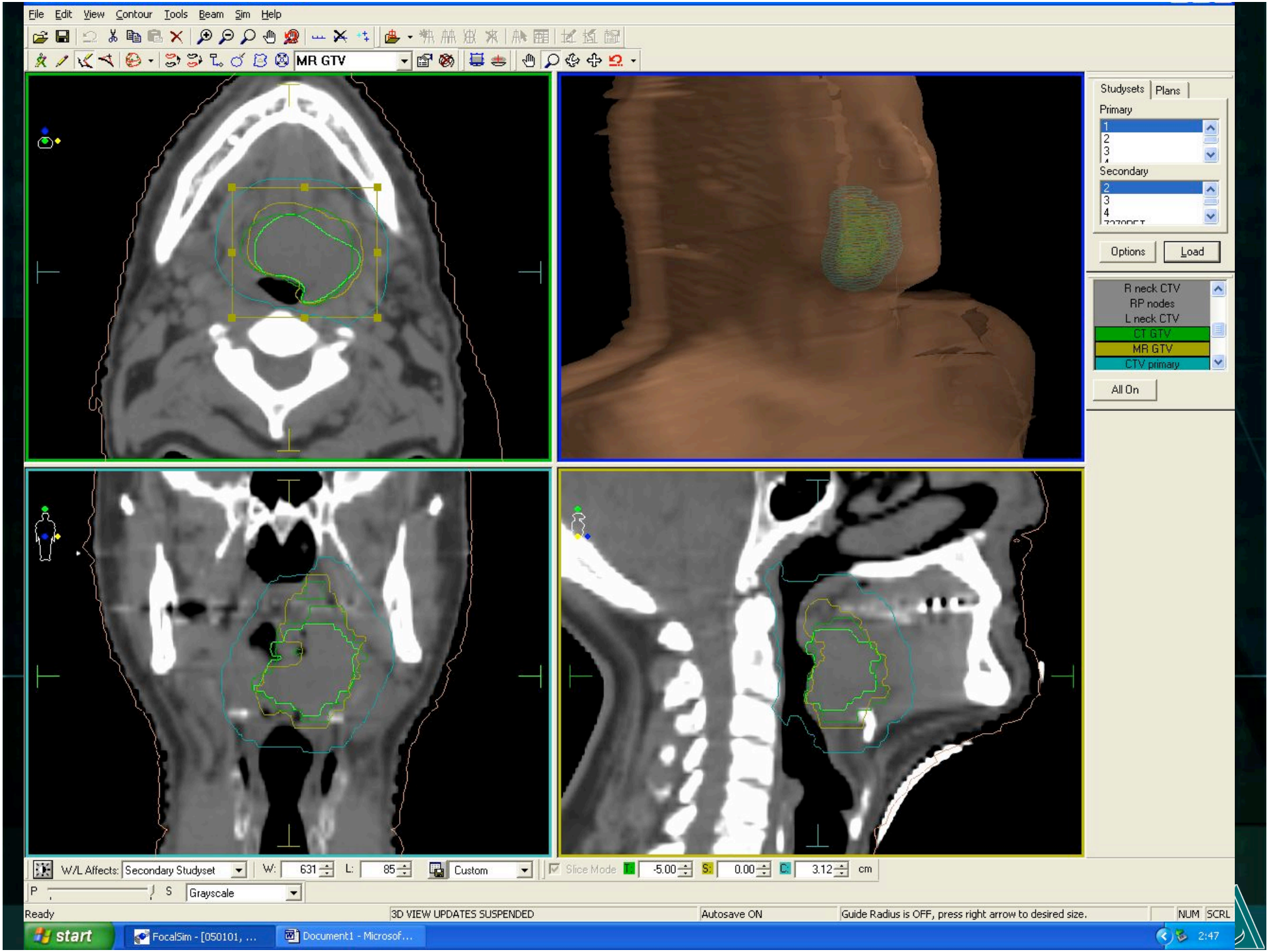
SCRL
start
FocalSim - [050101, ...
Document1 - Microsof...
2:46


File Edit View Contour Tools Beam Sim Help
MR GTV
Studysets Plans
Primary
1
2
3
Secondary
2
3
4
Options
Load
R neck CTV
RP nodes
L neck CTV
CT GTV
MR GTV
CTV primary
All On
W/L Affects: Secondary Studyset
W: 631
L: 85
Custom
Slice Mode
T: -5.00
S: 0.00
C: 3.12
cm
P
S
Grayscale
Ready
3D VIEW UPDATES SUSPENDED
Autosave ON
Guide Radius is OFF, press right arrow to desired size.
NUM
SCRL
start
FocalSim - [050101, ...
Document1 - Microsof...
2:47

Management of the neck

- CT MR clinical exam
- Documented patterns of spread
- Predictable and well documented
- Neck in radical setting is irradiated to equivalent of 5000cGy for occult microscopic nodal deposits
- PET help this, but false negative rate high
- Negative predictive value still in order of 70-80% not microscopic examination, as still has finite resolution 3-4mm

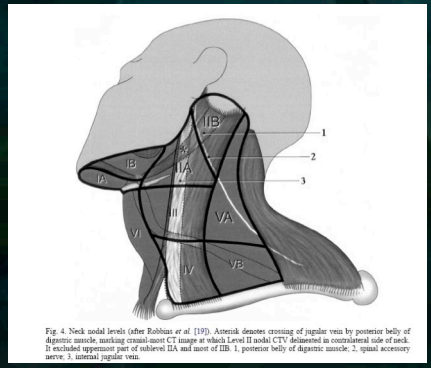
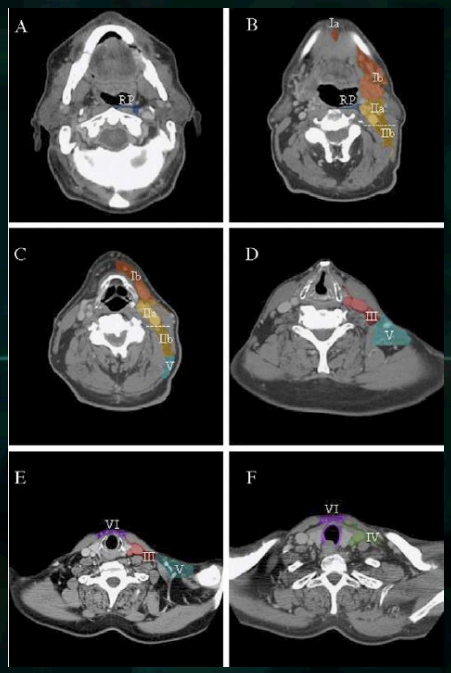
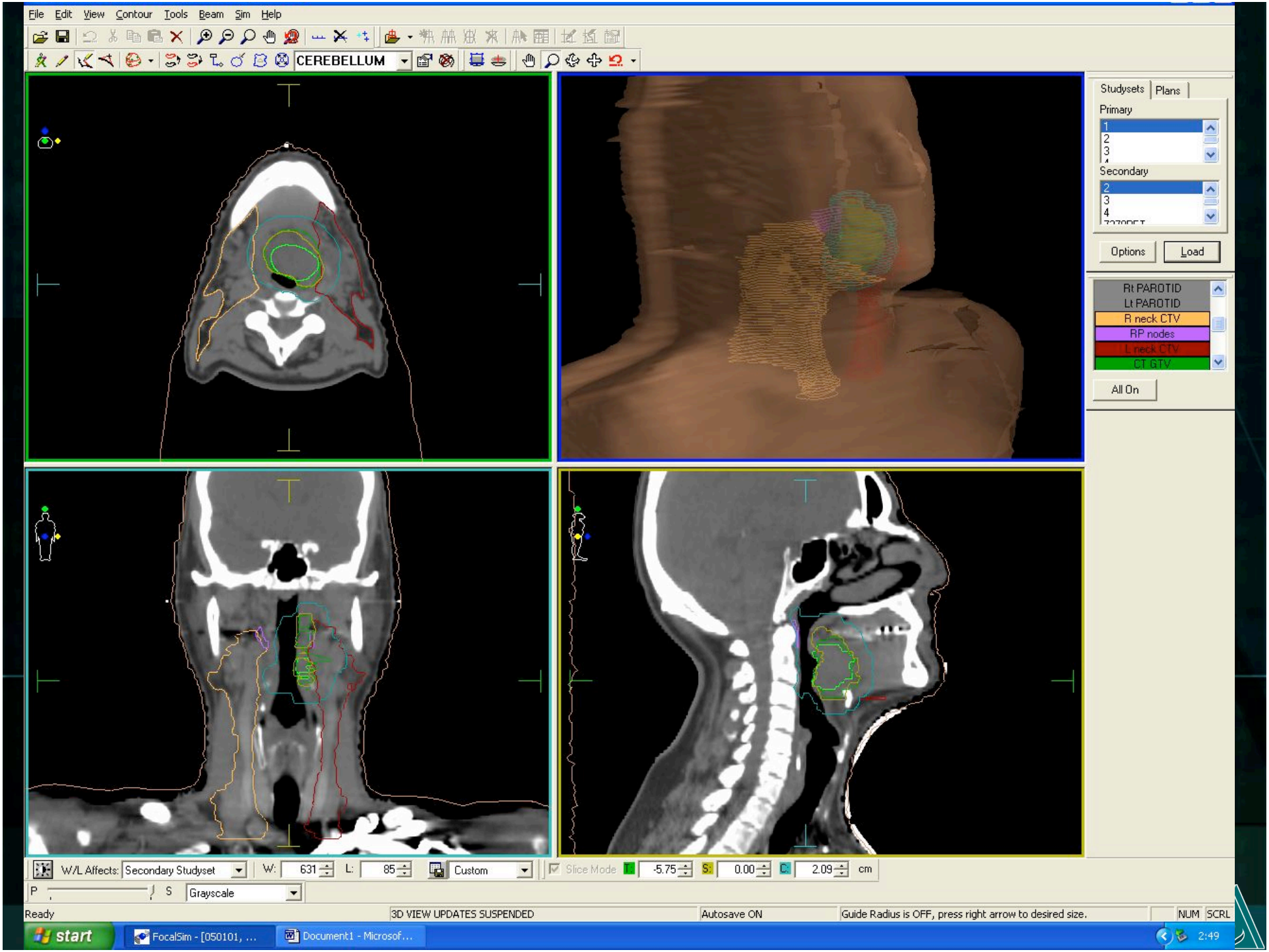
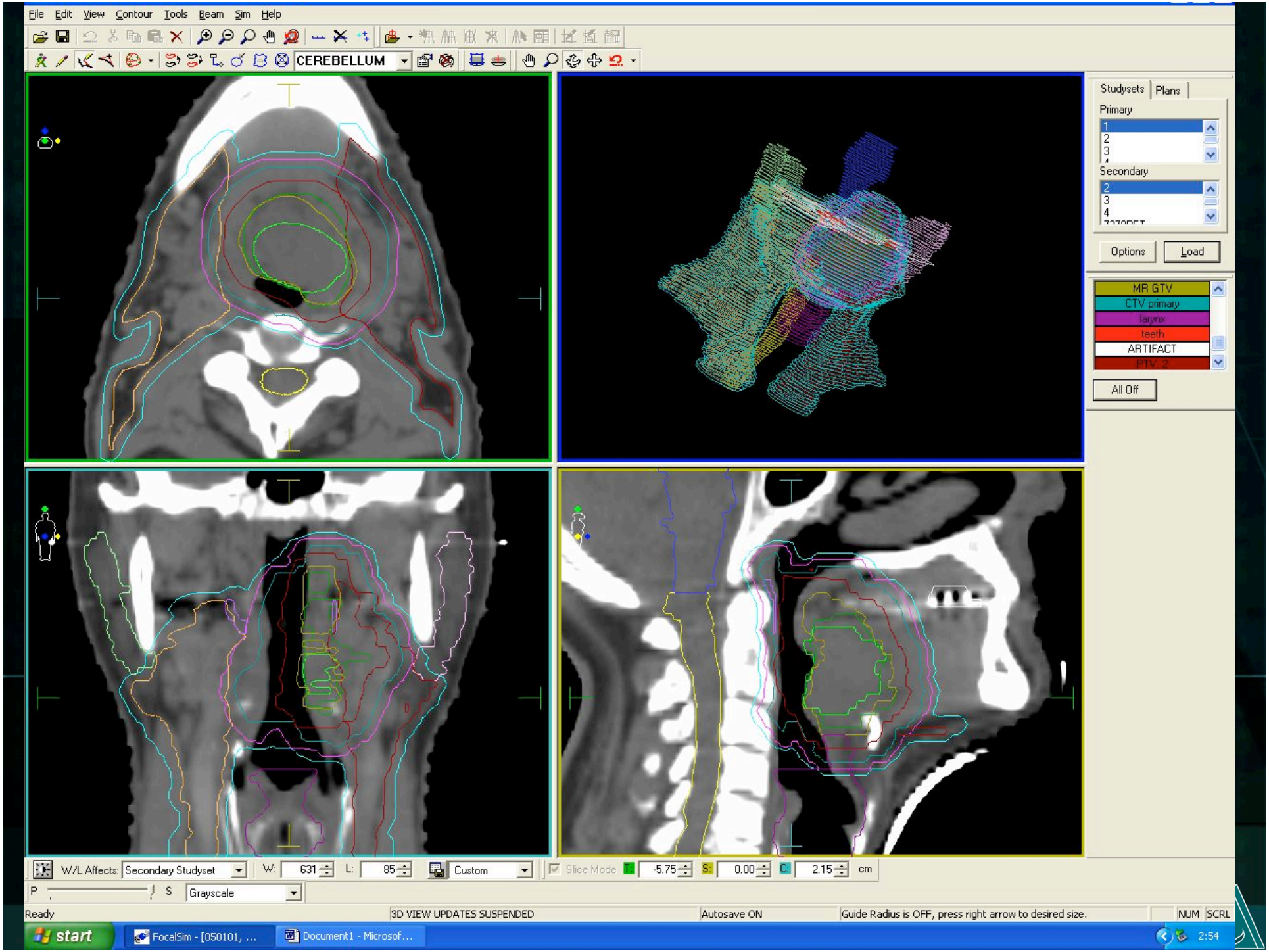


Fig. 4. Neck nodal levels (after Robbins *et al.* [19]). Asterisk denotes crossing of jugular vein by posterior belly of digastric muscle, marking cranial-most CT image at which Level II nodal CTV delineated in contralateral side of neck. It excluded uppermost part of sublevel IIA and most of IIB. 1, posterior belly of digastric muscle; 2, spinal accessory nerve; 3, internal jugular vein.

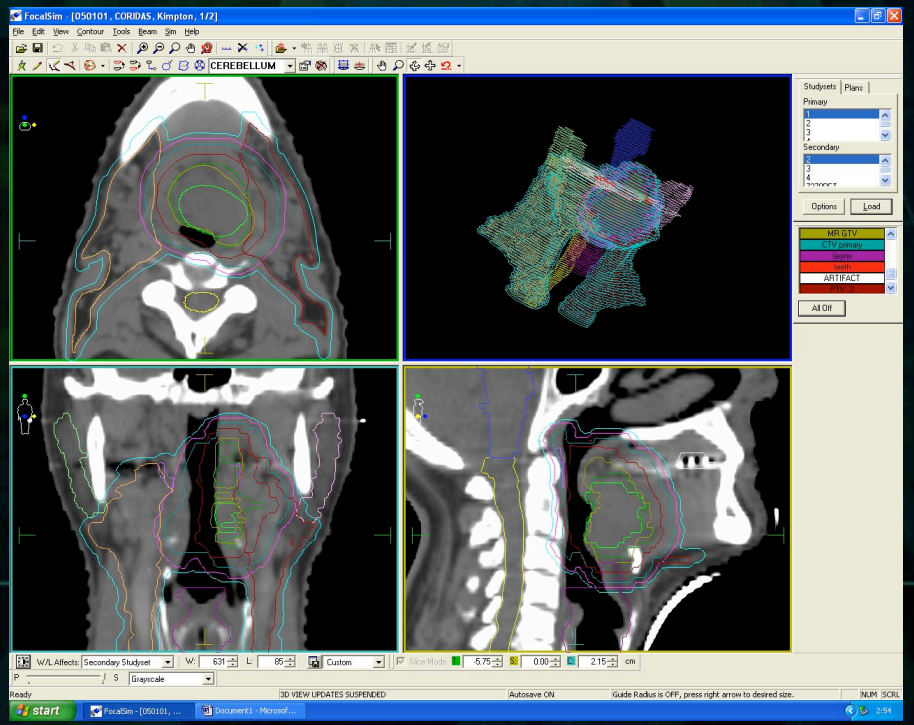


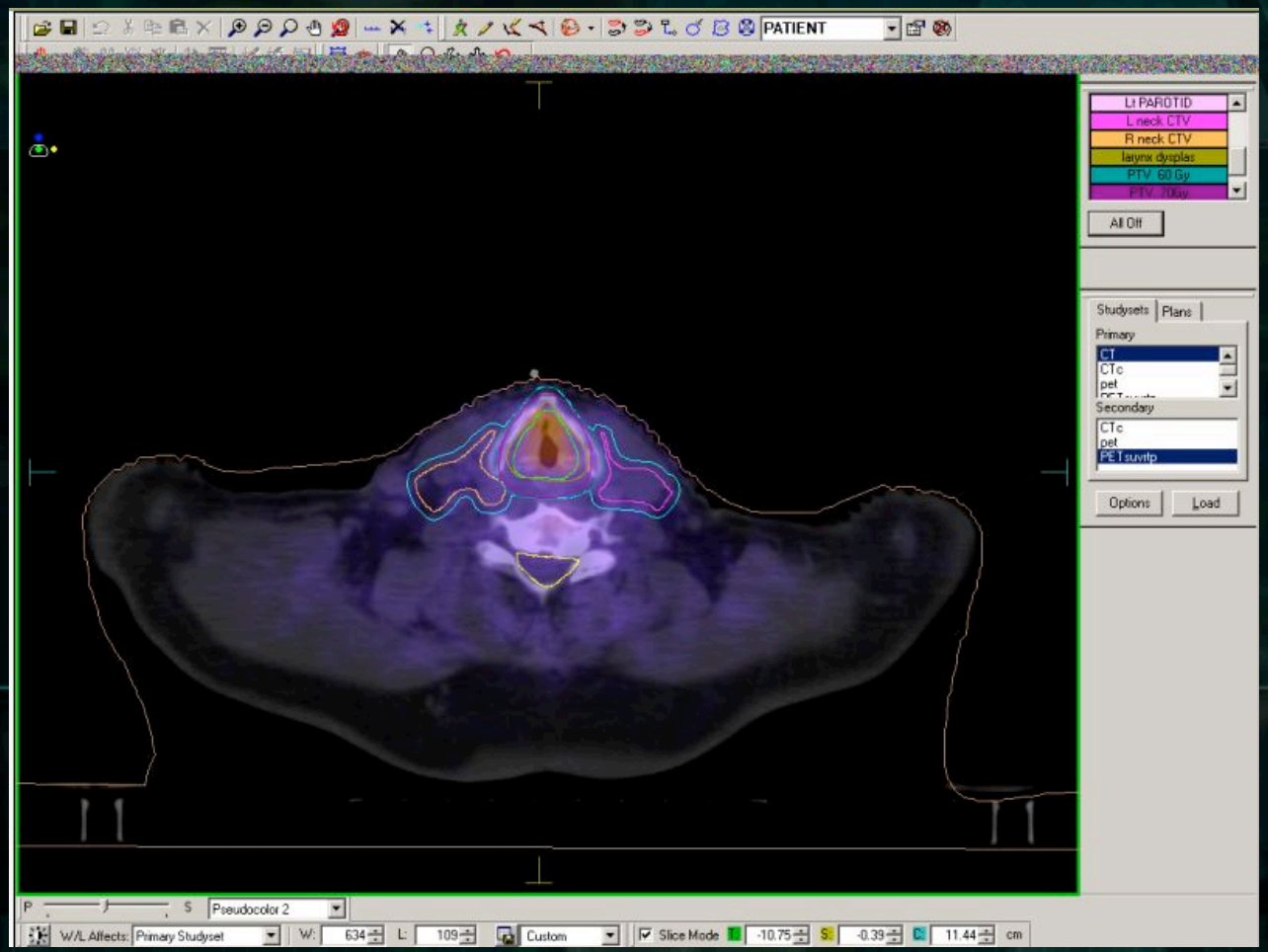

File Edit View Contour Tools Beam Sim Help
CEREBELLUM
Studysets Plans
Primary
1
2
3
Secondary
2
3
4
Options
Load
Rt PAROTID
Lt PAROTID
R neck CTV
RP nodes
L neck CTV
CT GTV
All On
W/L Affects: Secondary Studyset
W: 631
L: 85
Custom
Slice Mode
T: -5.75
S: 0.00
C: 2.09
cm
P
S
Grayscale
Ready
3D VIEW UPDATES SUSPENDED
Autosave ON
Guide Radius is OFF, press right arrow to desired size.
NUM
SCRL
start
FocalSim - [050101, ...
Document1 - Microsof...
2:49

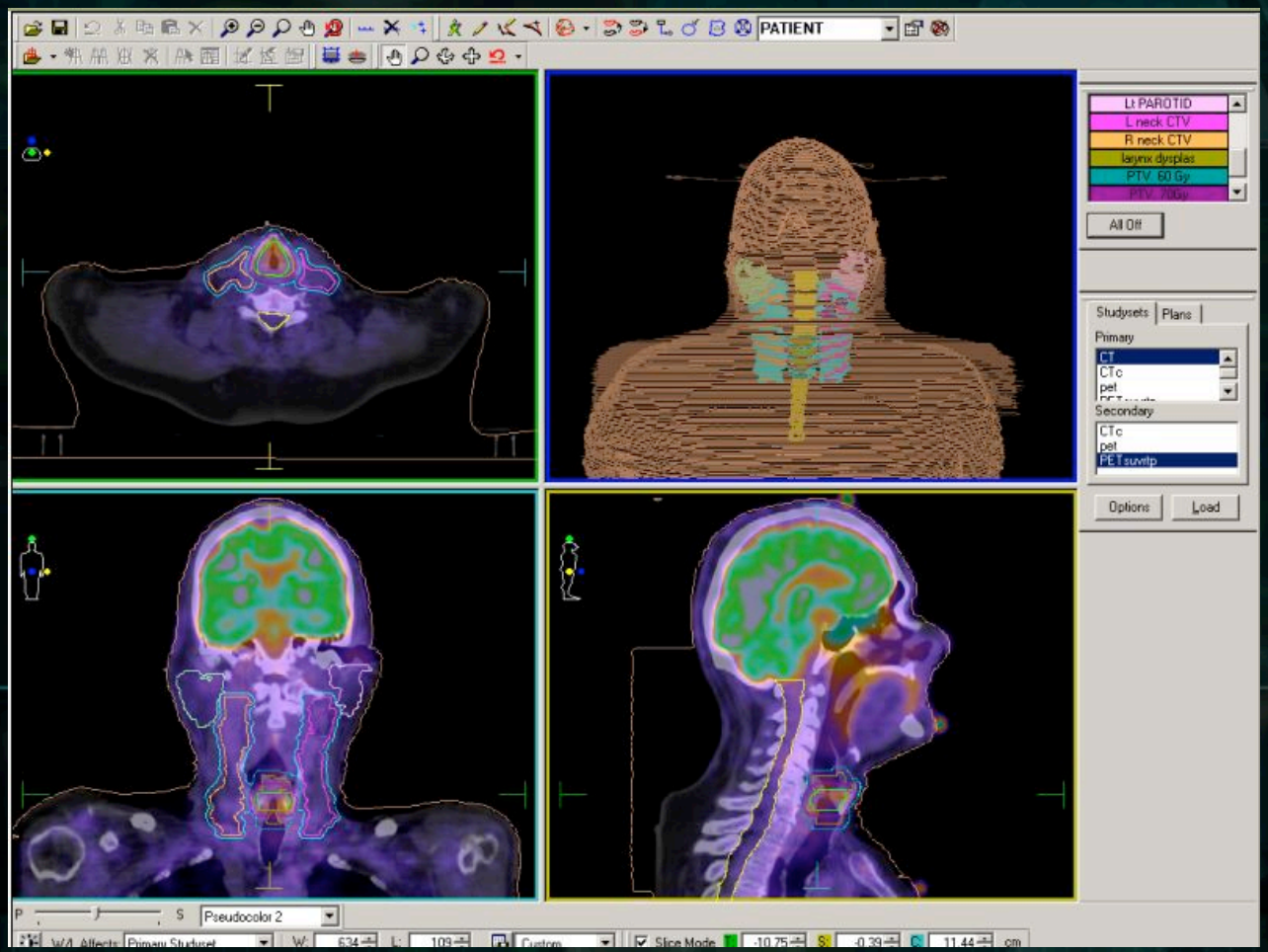

File Edit View Contour Tools Beam Sim Help
CEREBELLUM
Studysets Plans
Primary
1
2
3
Secondary
2
3
4
Options
Load
MR GTV
CTV primary
larynx
teeth
ARTIFACT
PTV 2
All Off
W/L Affects: Secondary Studyset
W: 631
L: 85
Custom
Slice Mode
T: -5.75
S: 0.00
C: 2.15
cm
P
S
Grayscale
Ready
3D VIEW UPDATES SUSPENDED
Autosave ON
Guide Radius is OFF, press right arrow to desired size.
NUM
SCRL
start
FocalSim - [050101, ...
Document1 - Microsof...
2:54

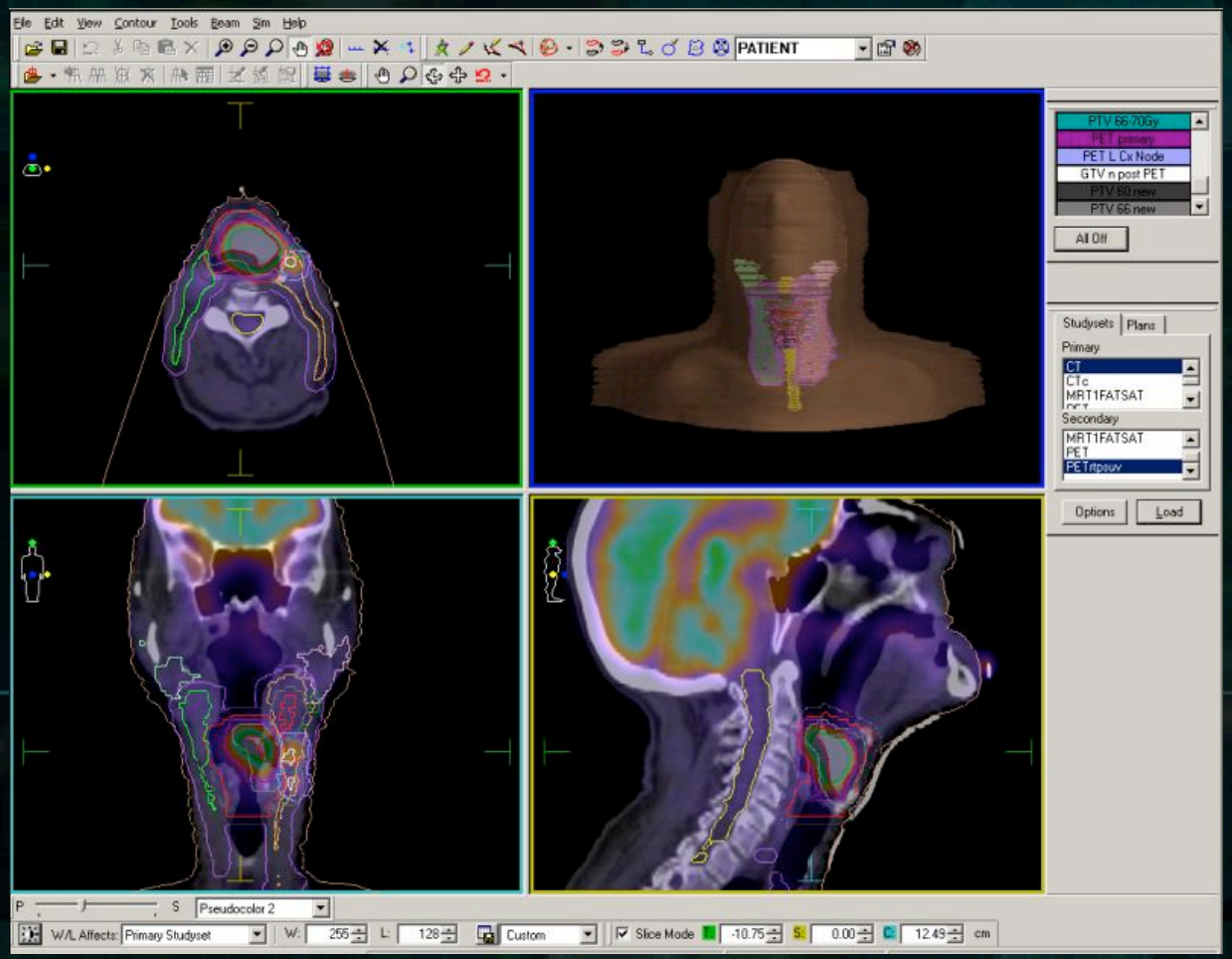
Back to Mr. K.C.

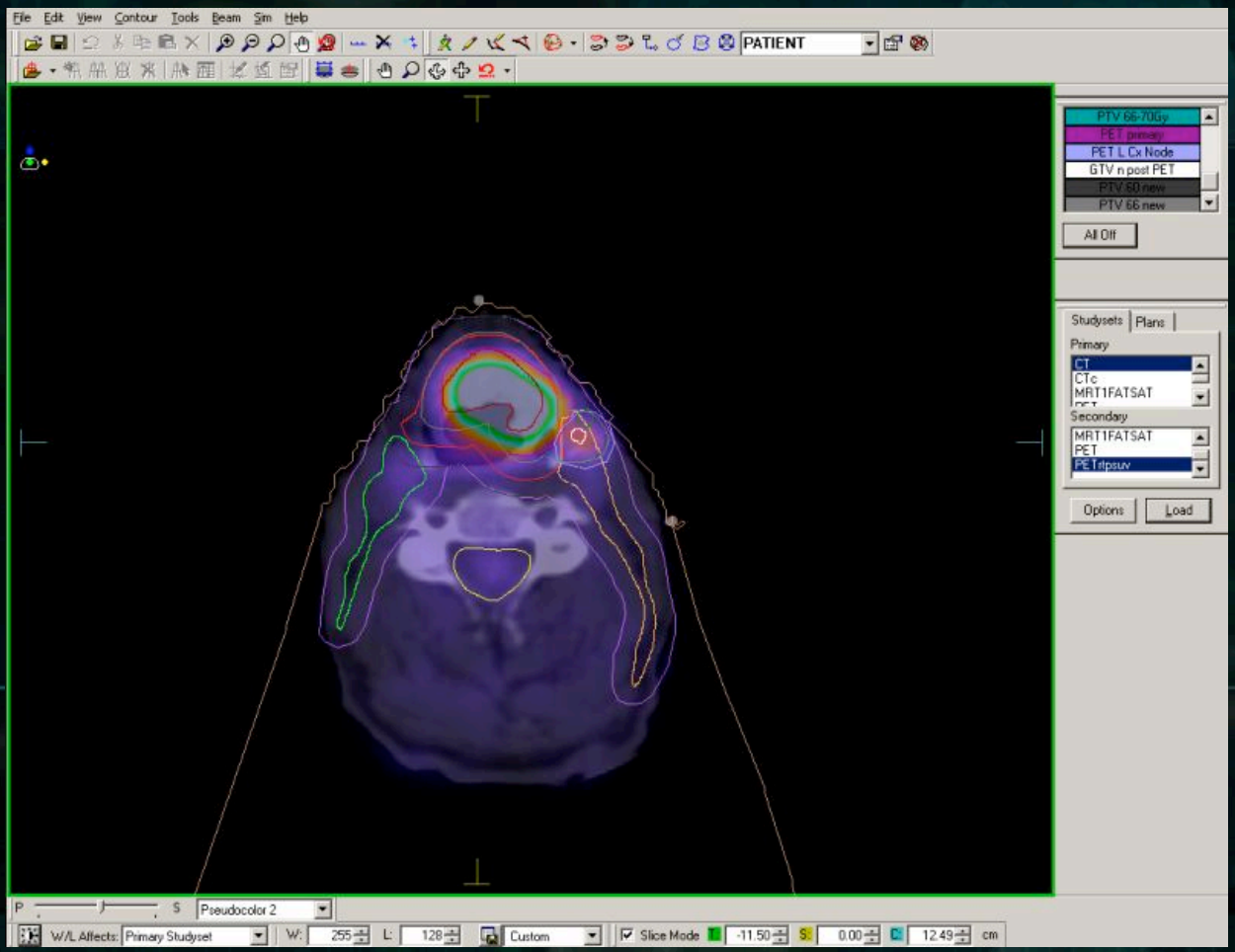
- Completed chemoradiotherapy under combined modality trial
- CR – CT / PET – at 3months post Rx
- Slow swallowing recovery – PEG out after 4 months….
- Trismus
  - Dental, faciomax, ENT review
  - CT / MR / PET – NED
  - Resolved promptly with antibiotics
- Currently well at 9 months…
- Stimulated salivary flow but dry…

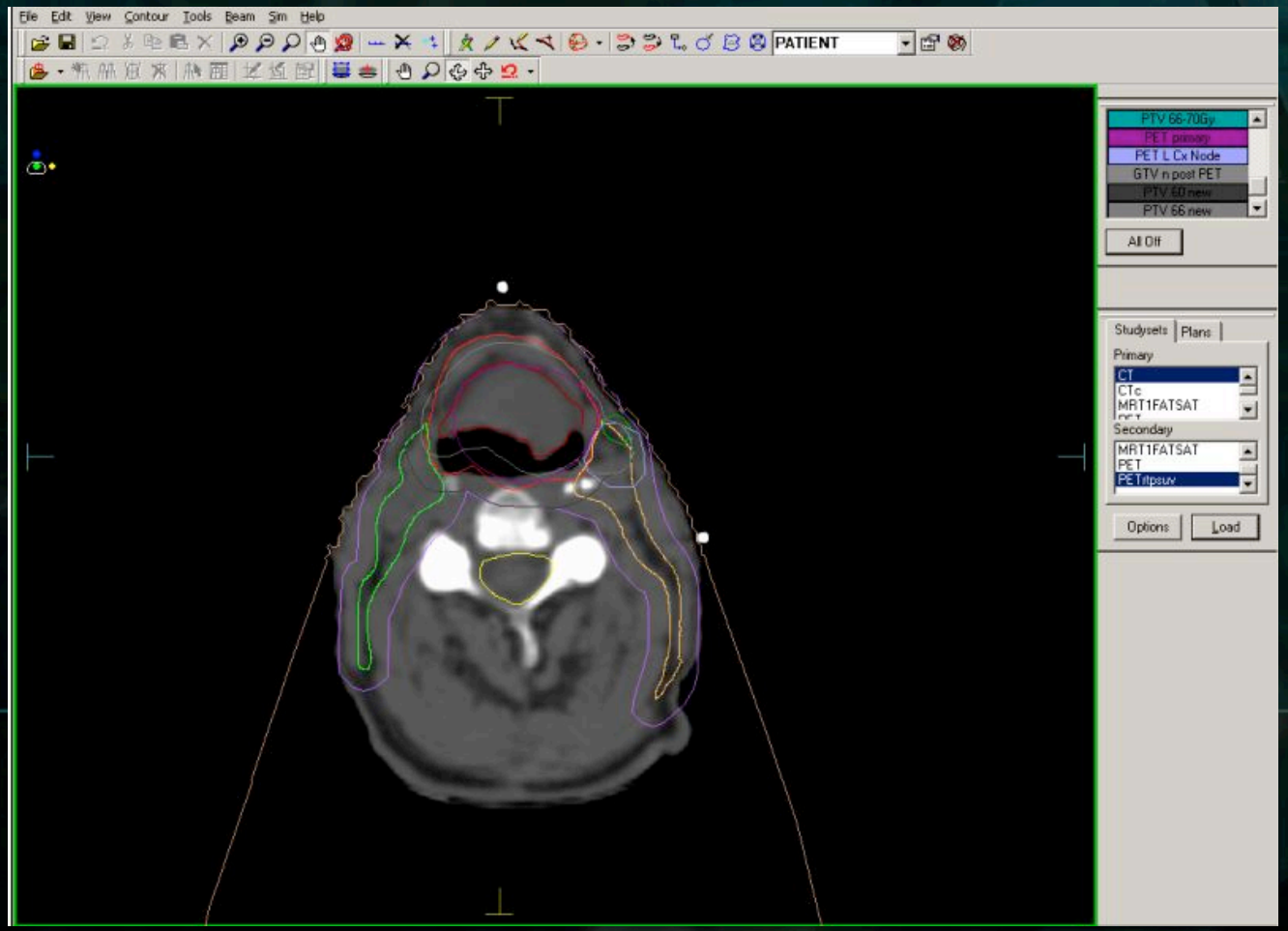



PATIENT
Lt PAROTID
L neck CTV
R neck CTV
larynx dysplas
PTV 60 Gy
PTV 70Gy
All Off
Studysets
Plans
Primary
CT
CTc
pet
Secondary
CTc
pet
PET suvrtp
Options
Load
Pseudocolor 2
W/L Affects:
Primary Studyset
W:
634
L:
109
Custom
Slice Mode
-10.75
-0.39
11.44
cm


PATIENT
Lt PAROTID
L neck CTV
R neck CTV
larynx dysplas
PTV 60 Gy
All Off
Studysets
Plans
Primary
CT
CTc
pet
Secondary
CTc
pet
PETsuvltp
Options
Load
Pseudocolor 2


File Edit View Contour Tools Beam Sim Help
PATIENT
PTV 66-70Gy
PET primary
PET L Cx Node
GTV n post PET
PTV 60 new
PTV 66 new
All Off
Studysets Plans
Primary
CT
CTc
MRT1FATSAT
Secondary
MRT1FATSAT
PET
PETrtpsuv
Options
Load
Pseudocolor 2
W/L Affects: Primary Studyset
W: 255
L: 128
Custom
Slice Mode
-10.75
0.00
12.49
cm


File Edit View Contour Tools Beam Sim Help
PATIENT
PTV 66-70Gy
PET primary
PET L Cx Node
GTV n post PET
PTV 60 new
PTV 66 new
All Off
Studysets Plans
Primary
CT
CTc
MRT1FATSAT
Secondary
MRT1FATSAT
PET
PETdpsuv
Options Load
Pseudocolor 2
W/L Affects: Primary Studyset
W: 255 L: 128
Custom
Slice Mode -11.50 0.00 12.49 cm


File Edit View Contour Tools Beam Sm Help
PATIENT
PTV 66-70Gy
PET primary
PET L Cx Node
GTV n post PET
PTV 60 new
PTV 66 new
All Off
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Plans
Primary
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Secondary
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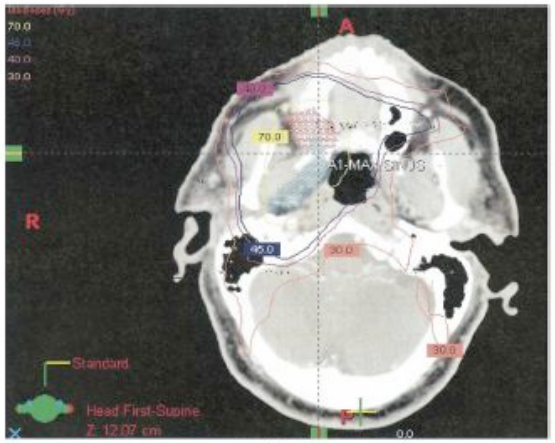
Options
Load



(a)

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0360-3016/05/$–see front matter

doi:10.1016/j.ijrobp.2004.08.037

CLINICAL INVESTIGATION **Head and Neck**

COMPARISON OF CT- AND FDG-PET–DEFINED GROSS TUMOR VOLUME IN INTENSITY-MODULATED RADIOTHERAPY FOR HEAD-AND-NECK CANCER

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David Schuster, M.D.,† and Lawrence W. Davis, M.D.*

Departments of *Radiation Oncology and †Radiology, Division of Nuclear Medicine and Molecular Imaging, Emory Clinic and Emory University, Atlanta, GA

Purpose: To compare the gross tumor volume (GTV) identified on CT to that obtained from fluorodeoxyglucose (FDG) positron emission tomography (PET) and determine the differences in volume and dose coverage of the PET-GTV when the CT-GTV is used for radiotherapy planning.

Methods and Materials: A total of 40 patients with intact squamous cell carcinoma arising in the head-and-neck region underwent intensity-modulated radiotherapy (IMRT) at one department. All patients underwent CT simulation for treatment planning followed by PET-CT in the treatment position. CT simulation images were fused to the CT component of the PET-CT images. The GTV using the CT simulation images was contoured (CT-GTV), as was the GTV based on the PET scan (PET-GTV). The IMRT plans were obtained using the CT-GTV.

Results: The PET-GTV was smaller, the same size, and larger than the CT-GTV in 30 (75%), 3 (8%), and 7 (18%) cases respectively. The median PET-GTV and CT-GTV volume was 20.3 cm^3 (range, 0.2–294) and 37.2 cm^3 (range, 2–456), respectively. The volume of PET-GTV receiving at least 95% of the prescribed dose was 100% in 20 (50%), 95–99% in 10 (25%), 90–94% in 3 (8%), 85–89% in 1 (3%), 80–84% in 2 (5%), 75–79% in 1 (3%), and <75% in 3 (8%) cases. The minimal dose received by 95% of the PET-GTV was ≥100% in 19 (48%), 95–99% in 11 (28%), 90–94% in 5 (13%), 85–89% in 2 (5%), and <75% in 3 (8%) cases.

Conclusion: The PET-GTV was larger than the CT-GTV in 18% of cases. In approximately 25% of patients with intact head-and-neck cancer treated using IMRT, the volume of PET-GTV receiving at least 95% of the prescribed dose and minimal dose received by 95% of the PET-GTV were less than optimal. © 2005 Elsevier Inc.

Gross tumor volume, Intensity-modulated radiotherapy, Radiotherapy planning, PET-CT, Head-and-neck cancer.

- Currently accruing patients into our PET RTP protocol for H&N SCC
- Target 30 patients
  - Difference in CT/MR/PET volumes
  - DVH analysis
  - Refining the process – acquisition, co-registration, thresholding
  - Patterns of failure vs. PET uptake – FDG, FMISO
- For treatment delivery
  - Clinical judgement for reconciling volumetric conflict – therapeutic ratio
  - Collaboration with radiation oncologist, head and neck radiologist and nuclear physician