

Dose painting for Medical Oncologists

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Disclosures

- Dr. Jordi Giralt has no disclosures

Radiotherapy Techniques

- **3D-RT**

Homogeneous dose in the whole treatment volume

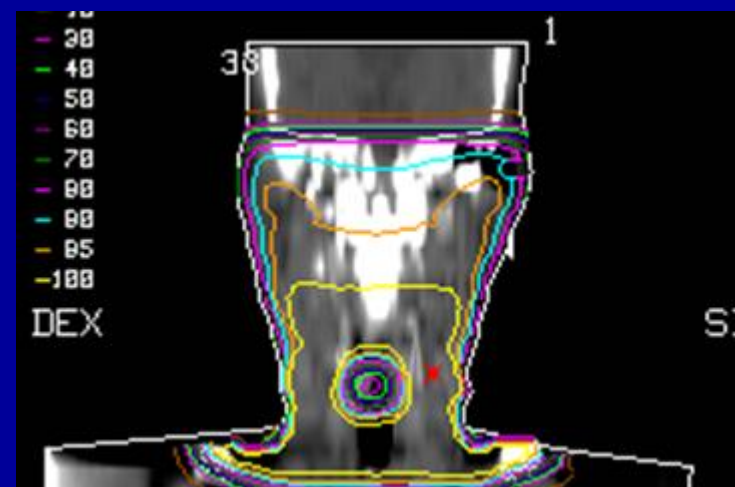
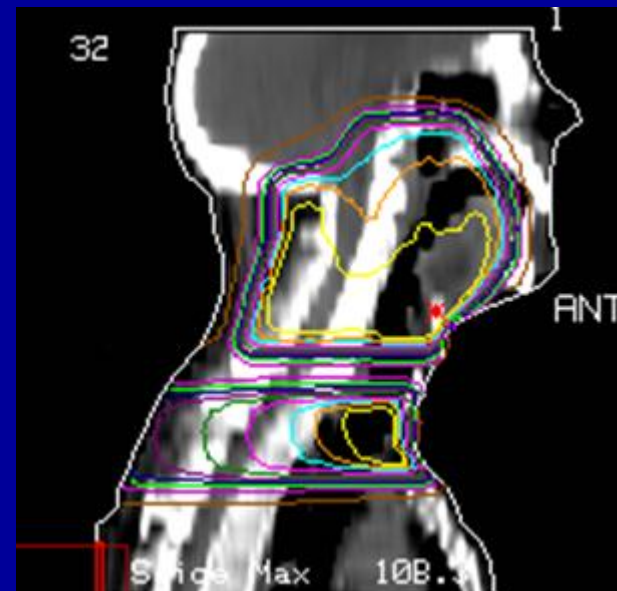
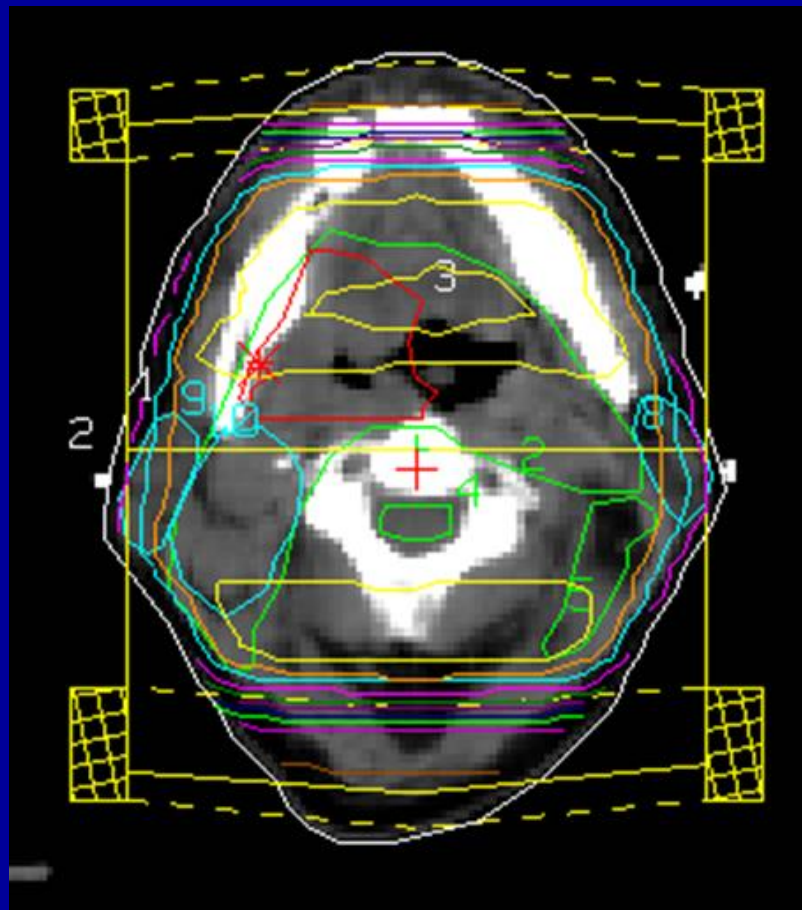
- **IMRT**

Sculpting the dose to the target shape, allows normal tissue protection

- **Dose painting (IMRT Dose intensification)**

The prescription of a nonuniform radiation dose distribution to the target volume based on functional / molecular images

3D-RT



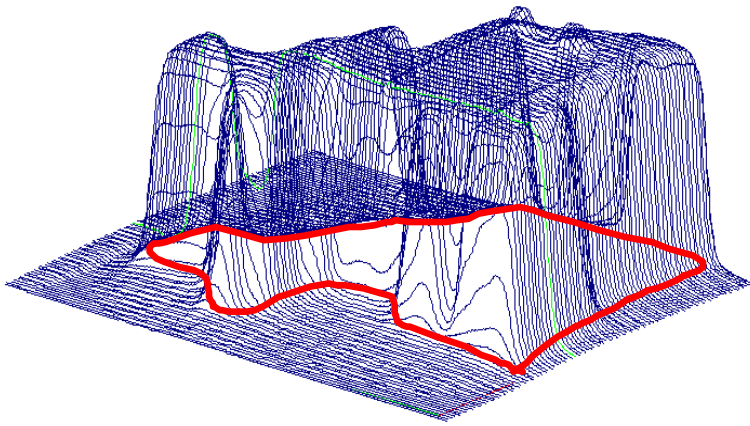
Patterns of relapse

Author	Regimen	Year	TD (Gy)	LocoReg	Distant
Rischin	RT-cisplatin	2010	70	26%	8%
Bourhis	RT-carbo/5FU	2012	70	42%	25%
Bonner	RT- cetuximab	2006	70-77	50%	17%
Vermorken	TPF → RT	2007	70	57%	13%
Posner	TPF → RT-carbo	2007	70-74	30%	5%

IMRT

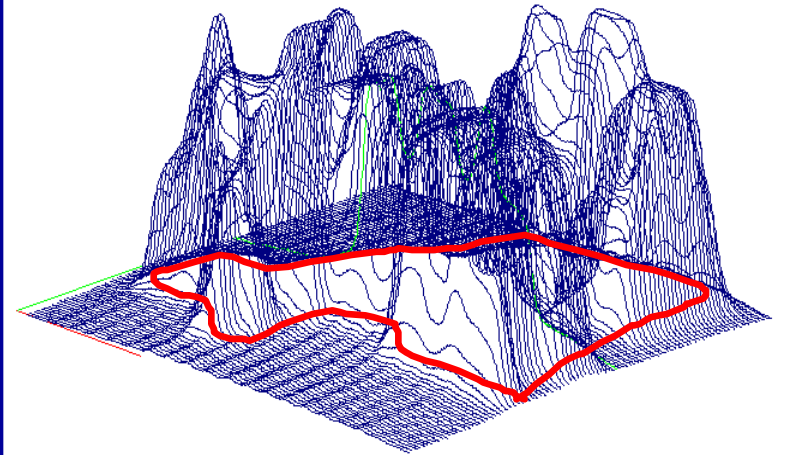
Administration of the radiation dose fields using
NON uniform (\equiv Modulation) fluence (\equiv intensity)

**UNIFORM
Intensity**



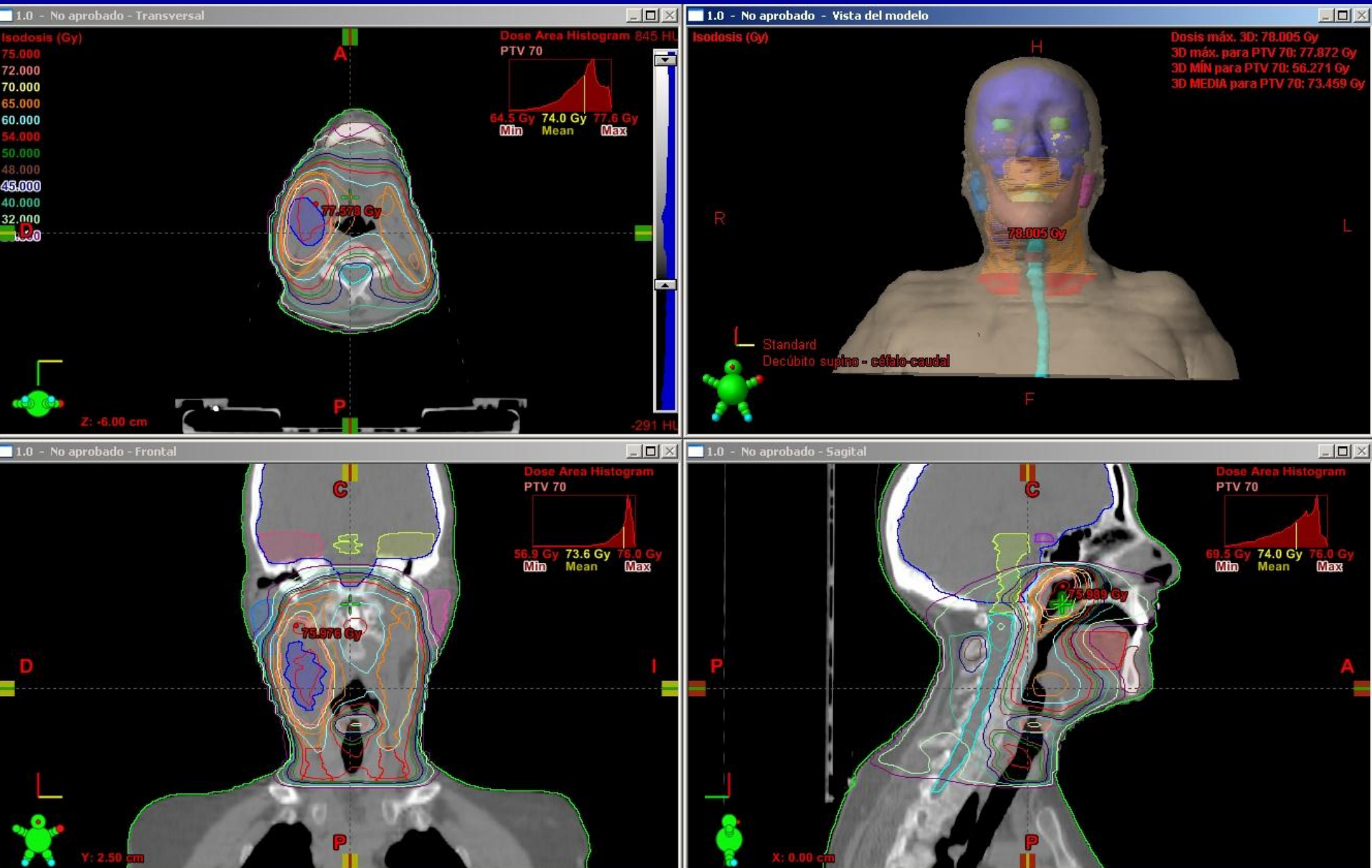
3DCRT

**NON UNIFORM
Intensity**



IMRT

Dose distribution



IMRT reduces toxicity

- Xerostomia in nasopharyngeal carcinoma
 - ❖ Recovery stimulated saliva flow 6% (3DRT) vs. 50% (IMRT)
 - ❖ Better quality of life (QLQ-H&N35 questionnaire)
Pow et al Int J Radiat Onc Biol Phys 2006
- Xerostomia in pharyngeal squamous-cell carcinoma
 - ❖ Salivary flow rates reduction of 90% (3DRT) vs. 40% (IMRT)
 - ❖ Grade ≥ 2 xerostomia 74% (3DRT) vs. 38% (IMRT)
Nutting et al Lancet Onc 2011
- Dysphagia in pharyngeal squamous-cell carcinoma
 - ❖ Pharyngeal constrictor muscles, glottis, esophagus
 - ❖ Worsening liquid swallowing was correlated with dose
Feng et al. Int J Radiat Onc Biol Phys .2007

IMRT Dose intensification

Dose painting

- Definitions / examples
- Biological tumor volume
- Adaptive RT
- Clinical results

General principles

- Local recurrences arise from cells that are resistant at the standard radiation dose
- Functional imaging will allow spatiotemporal mapping of these regions of relative radioresistance
- Advances in radiation therapy facilitate the delivery of a graded dose within the GTV

General principles

- Define subvolumes with higher risk of relapse
“biological target volume” (BTV) → PET
- Define an inhomogeneous distribution of dose
gradients → Complex IMRT
- Consider impact of volume variation during treatment
and its effect on dose → Adaptive RT

Plan Aims

- ❖ Maximize probability of local tumour control
- ❖ Minimize probability of toxicity due to normal tissue damage
- ❖ Physical constraints on dose delivery

Dose painting methods

- Dose painting by volume
- Dose painting by numbers

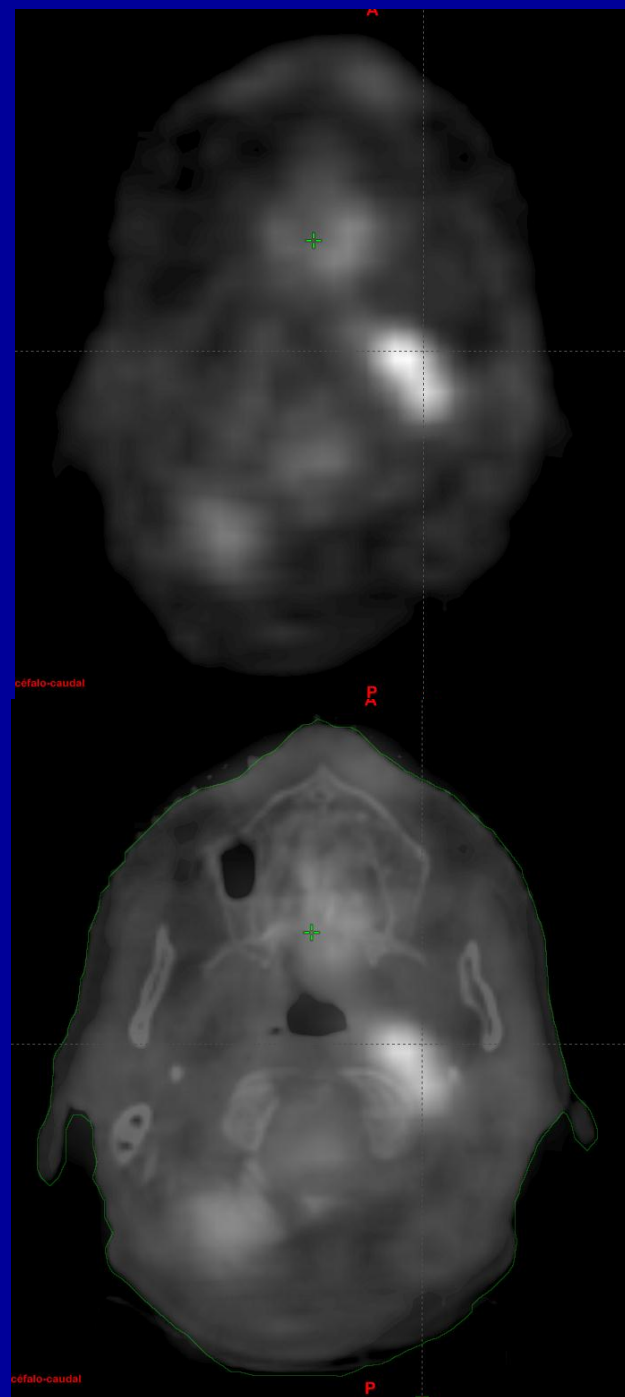
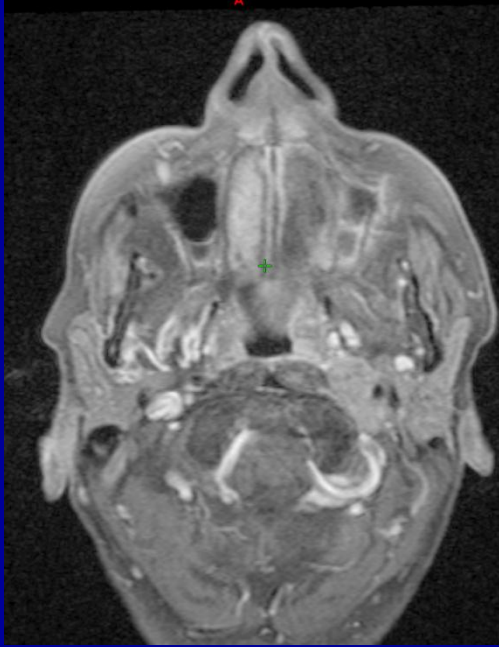
Dose painting by volume

- Define discrete biologically different tumour regions
- Radioresistant region within a tumour
- Prescribe different doses to these volumes
- Threshold to determine extent of “Biological Target Volume”
 - ❖ SUV (PET)
 - ❖ Choline/Citrate Ratio (MRSI)

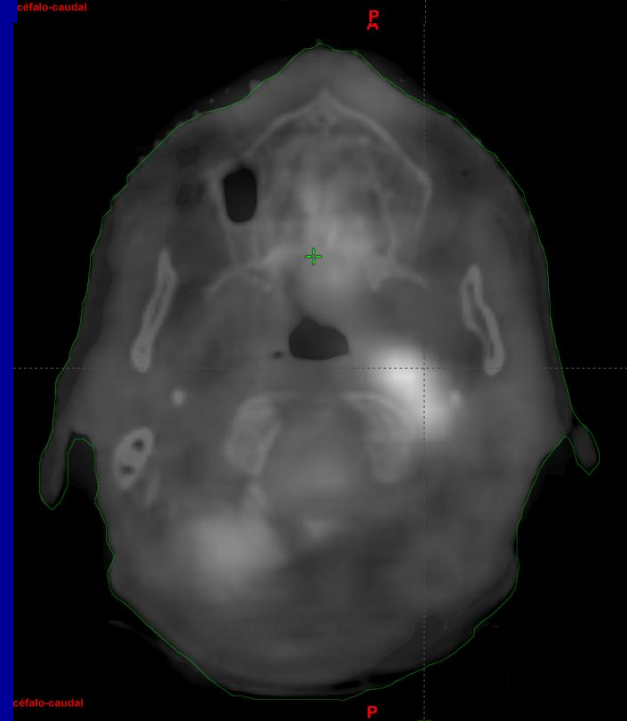
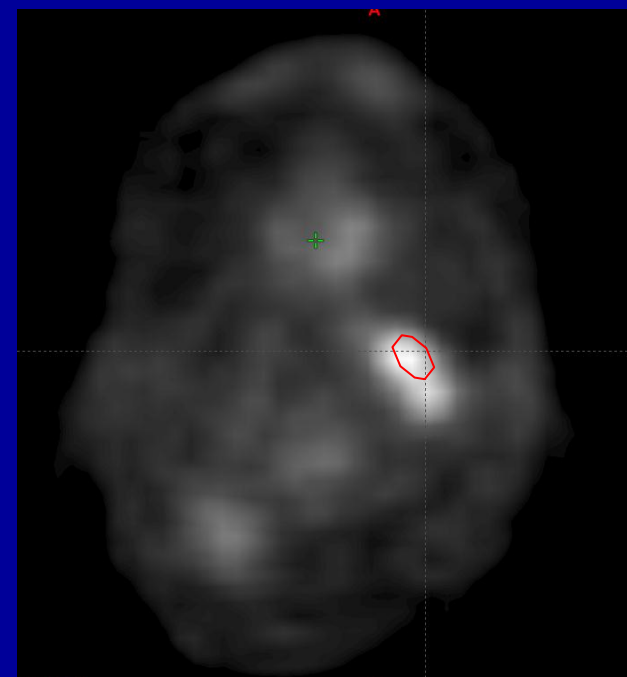
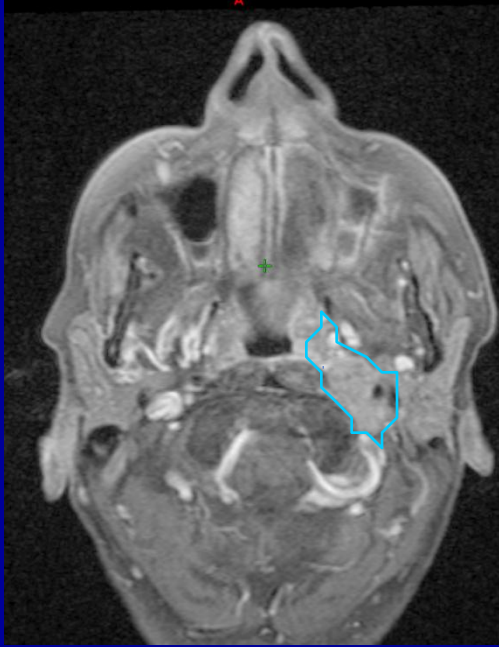
Dose painting by numbers

- Directly link image signal to prescription dose on a voxel-by-voxel basis
- Each voxel receives a different dose based on the intensity of a given image parameter
- The dose is prescribed at the voxel level
- The dose plan optimizer arrives at the best physically deliverable dose distribution

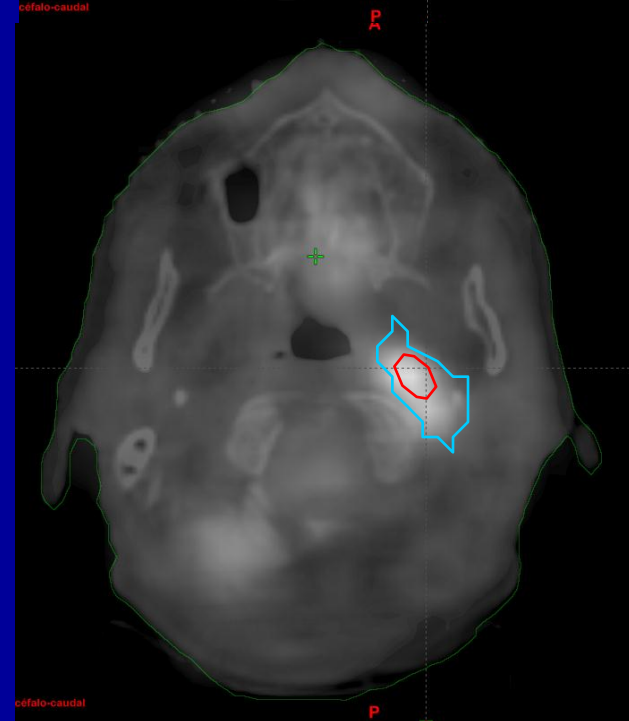
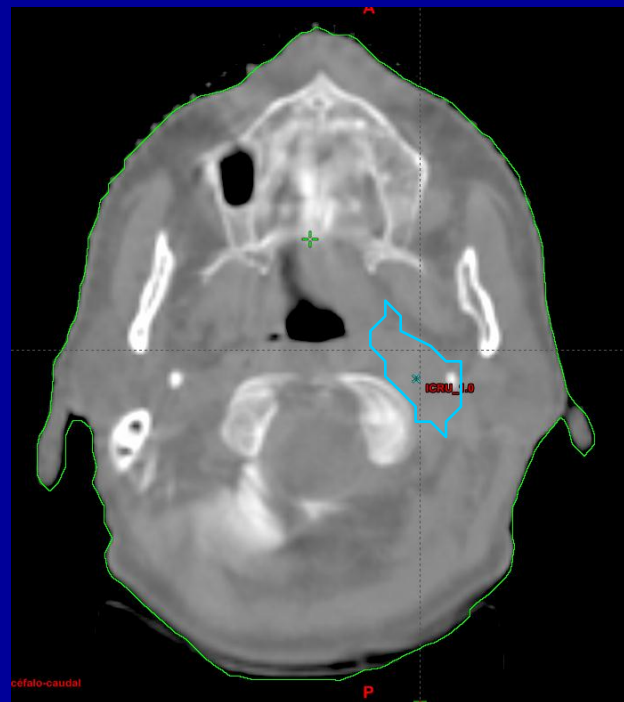
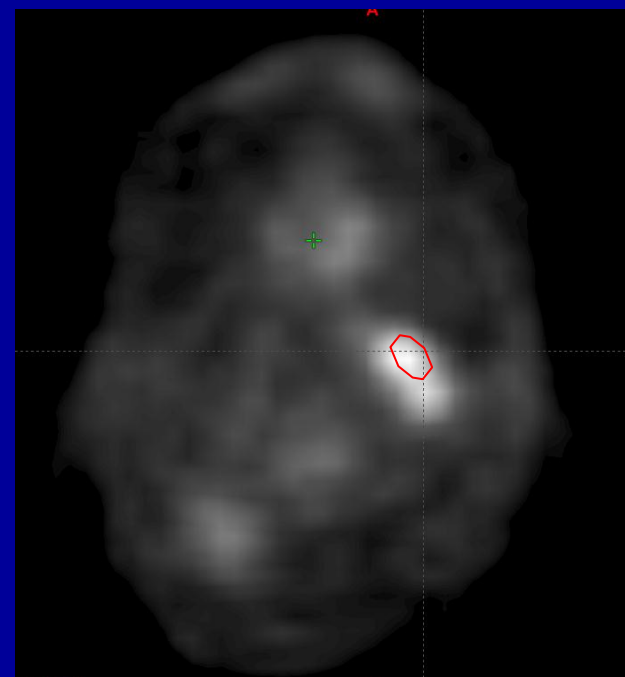
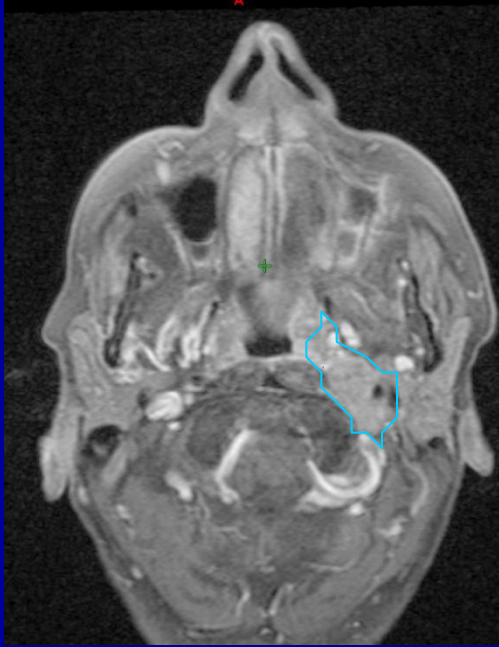
Procedure

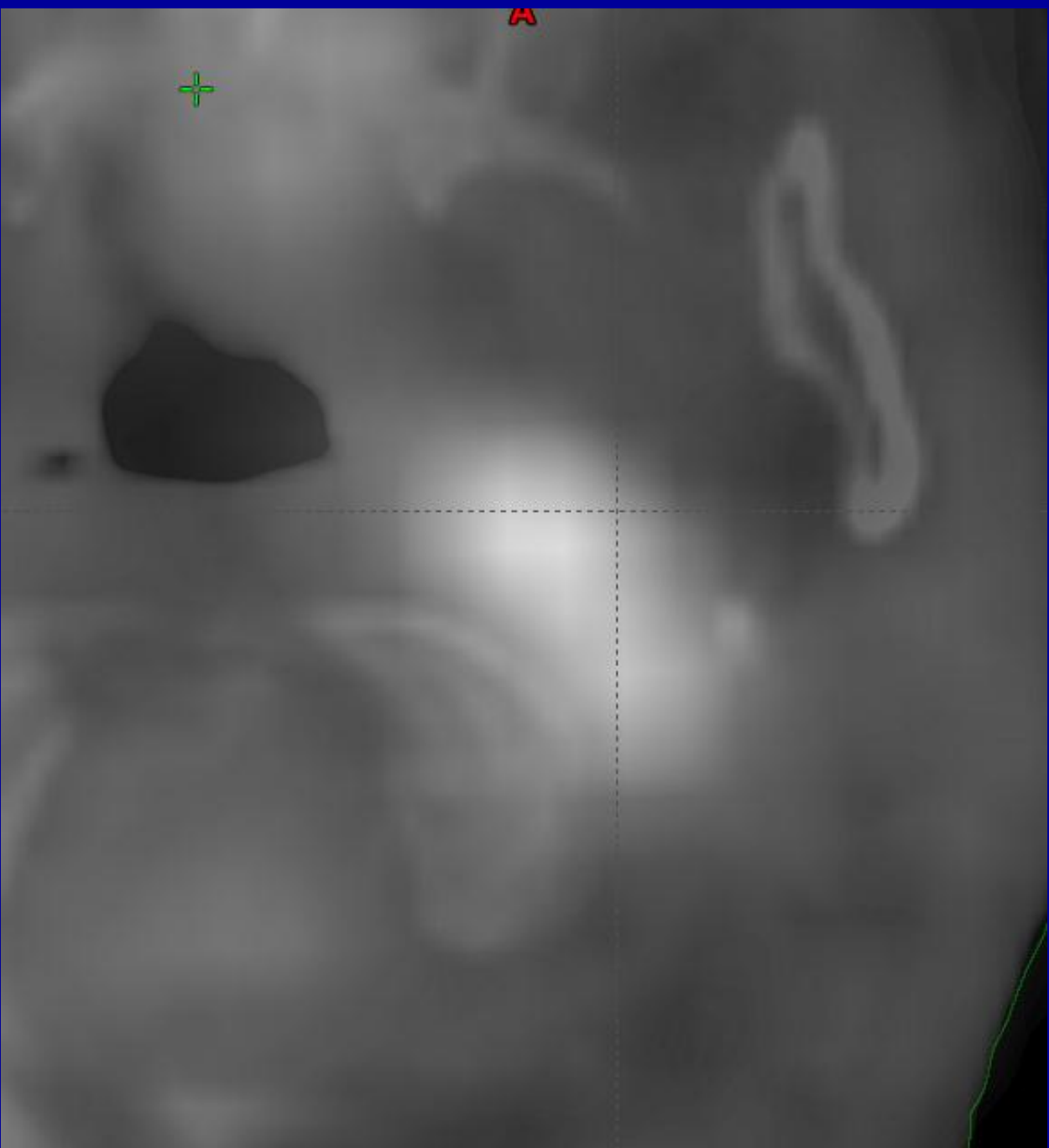


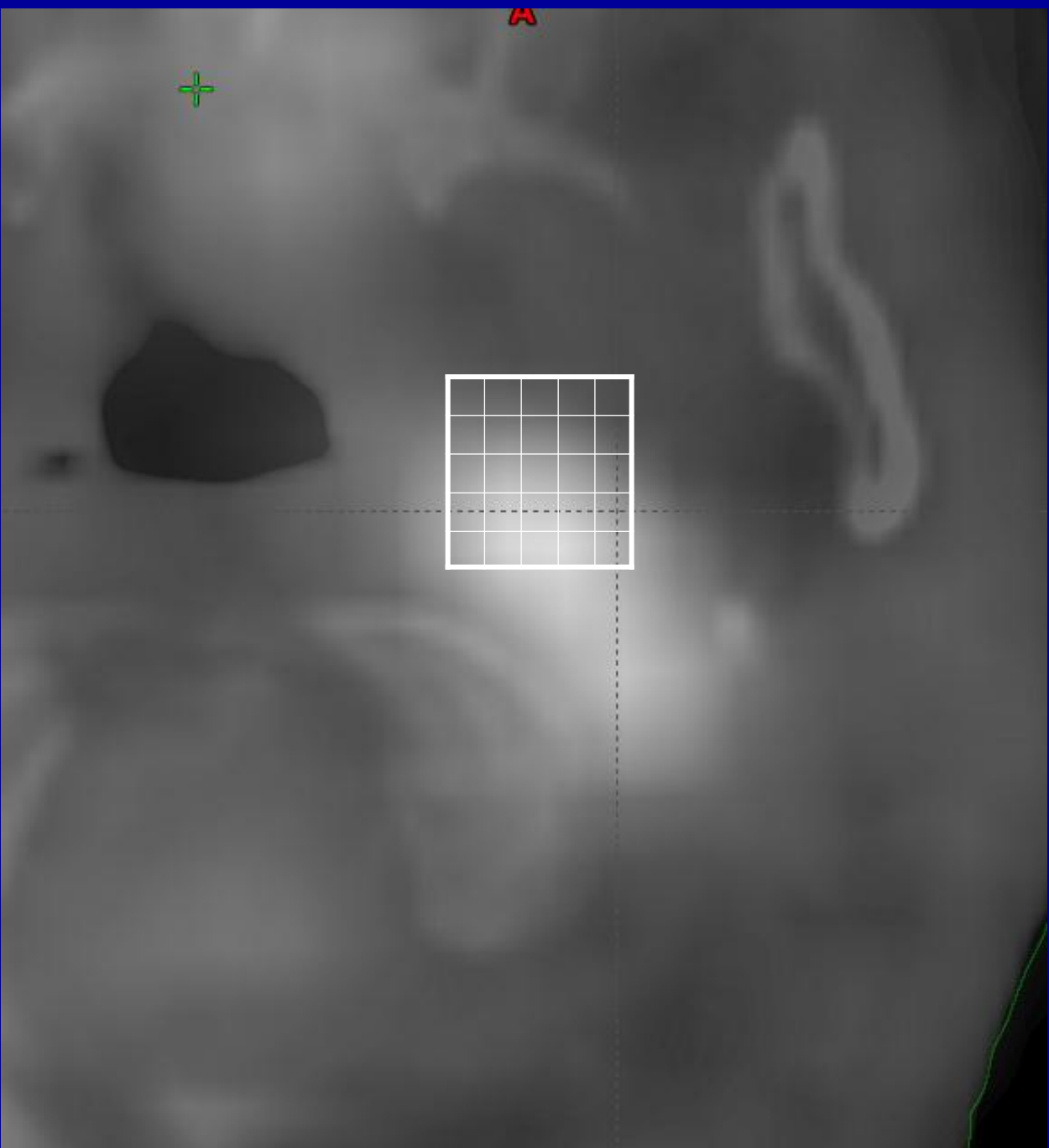
Procedure

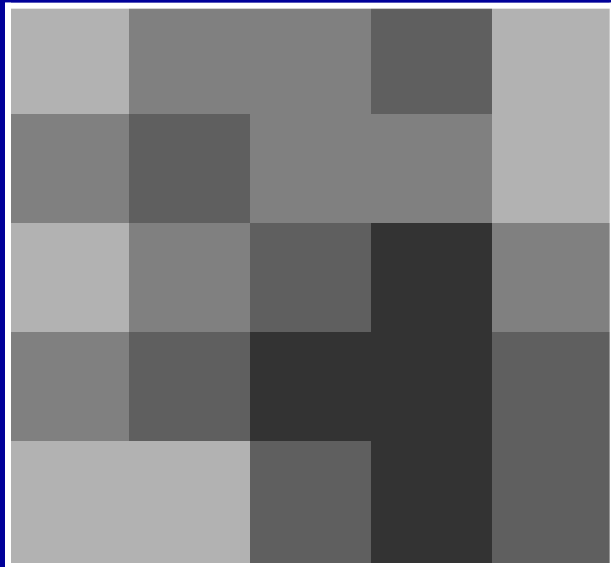
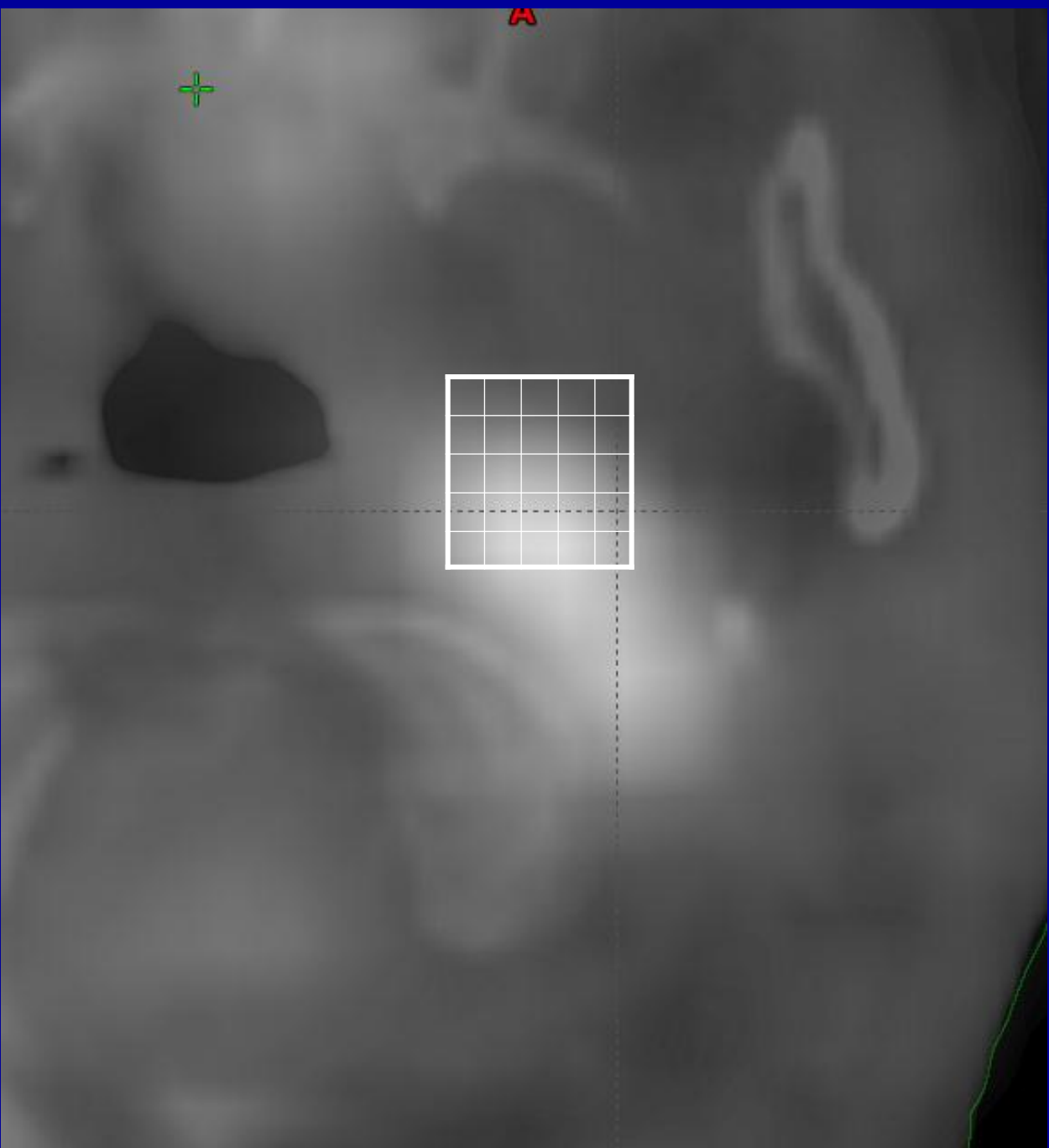


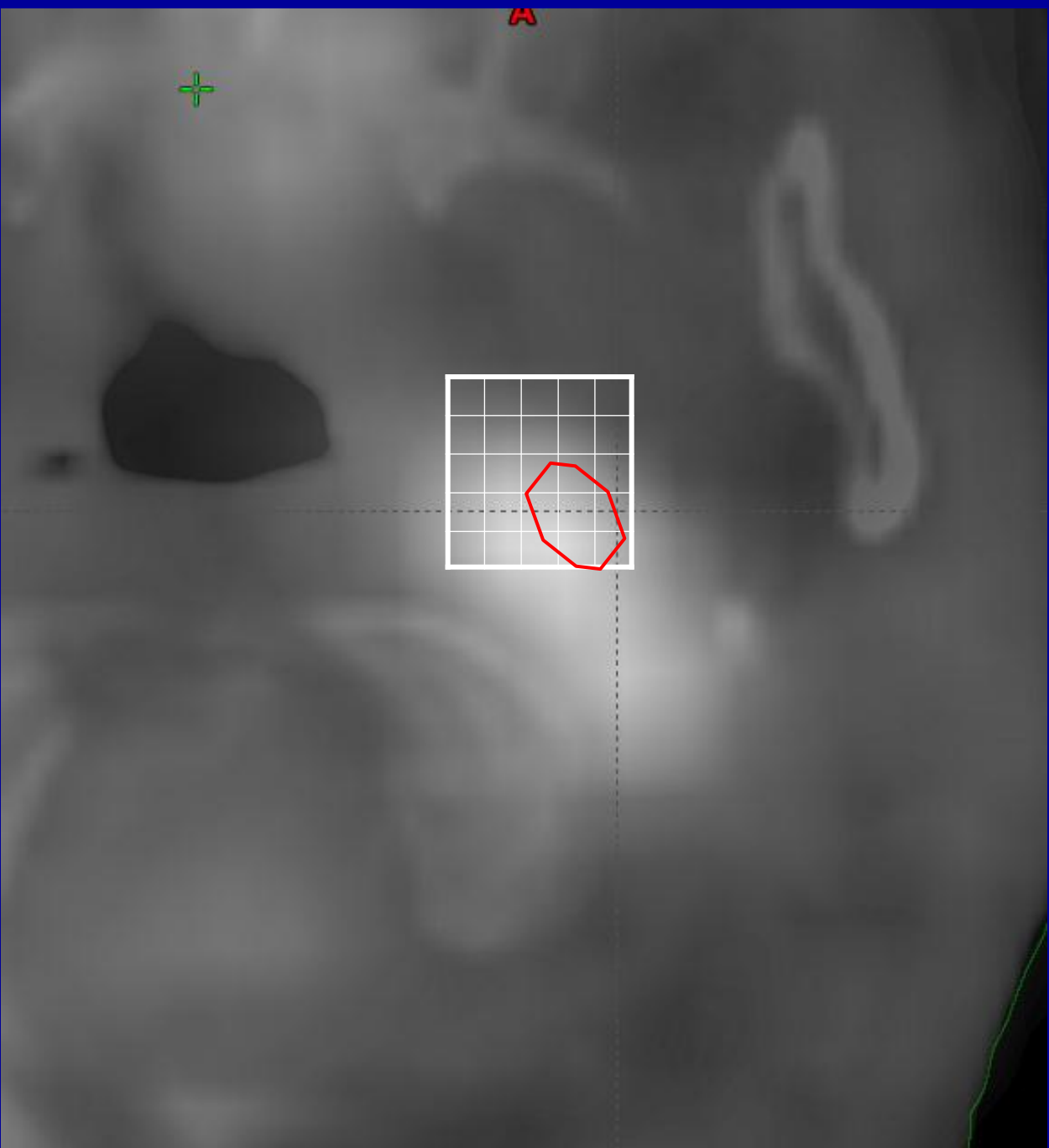
Procedure







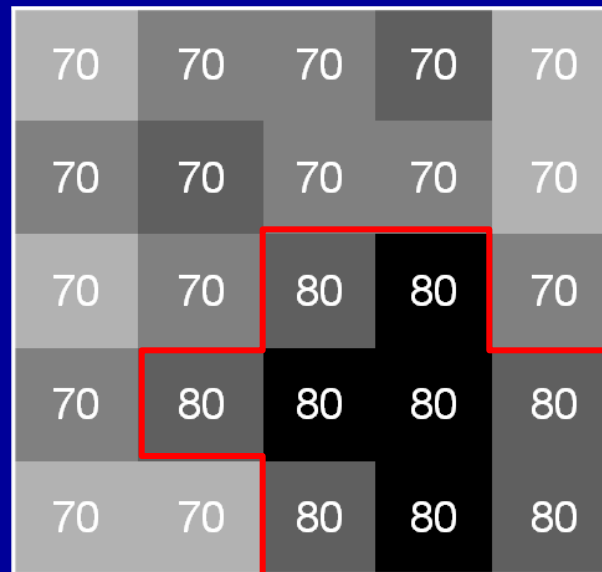




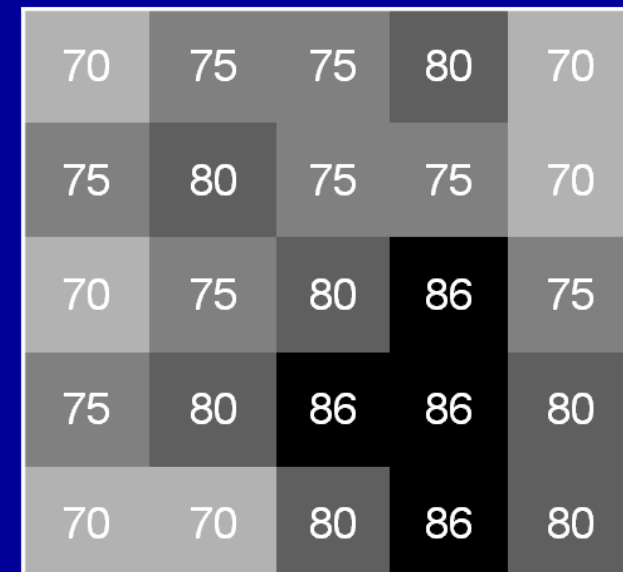
Homogeneously delivered



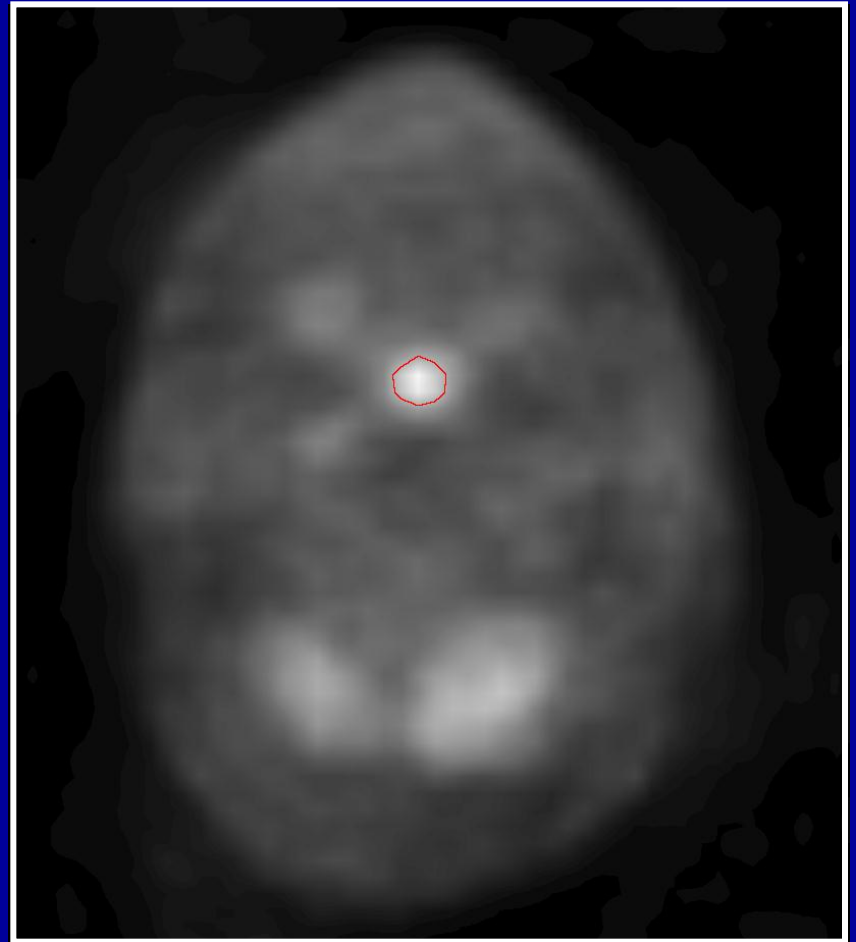
Dose painting by volume



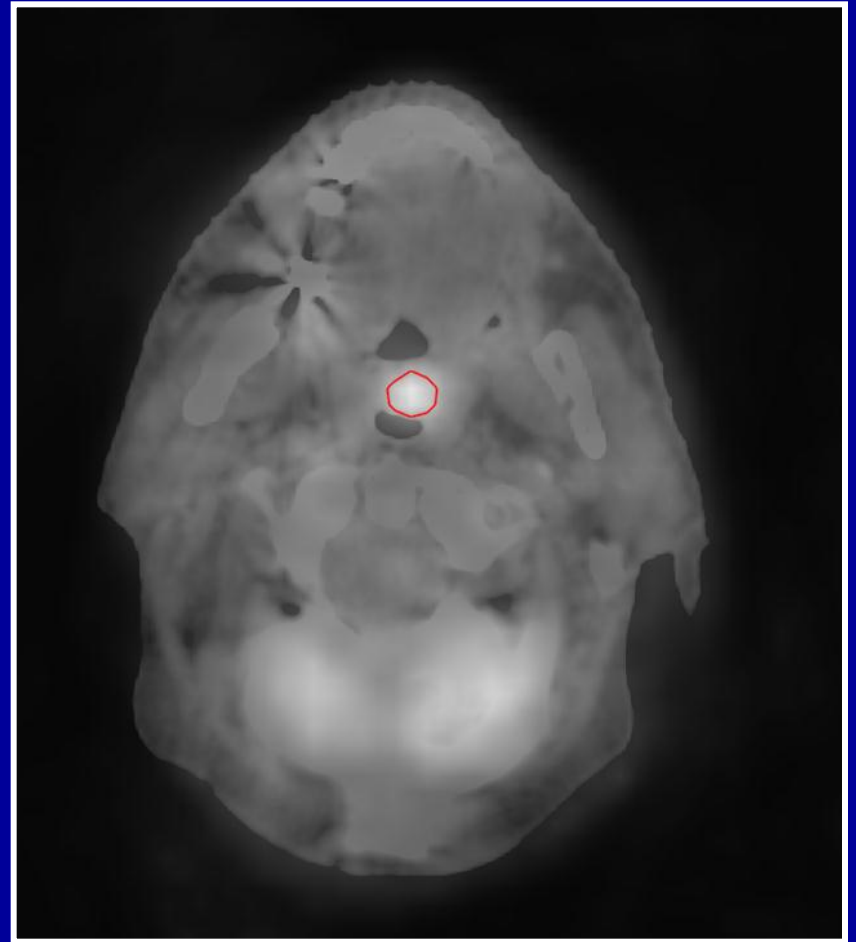
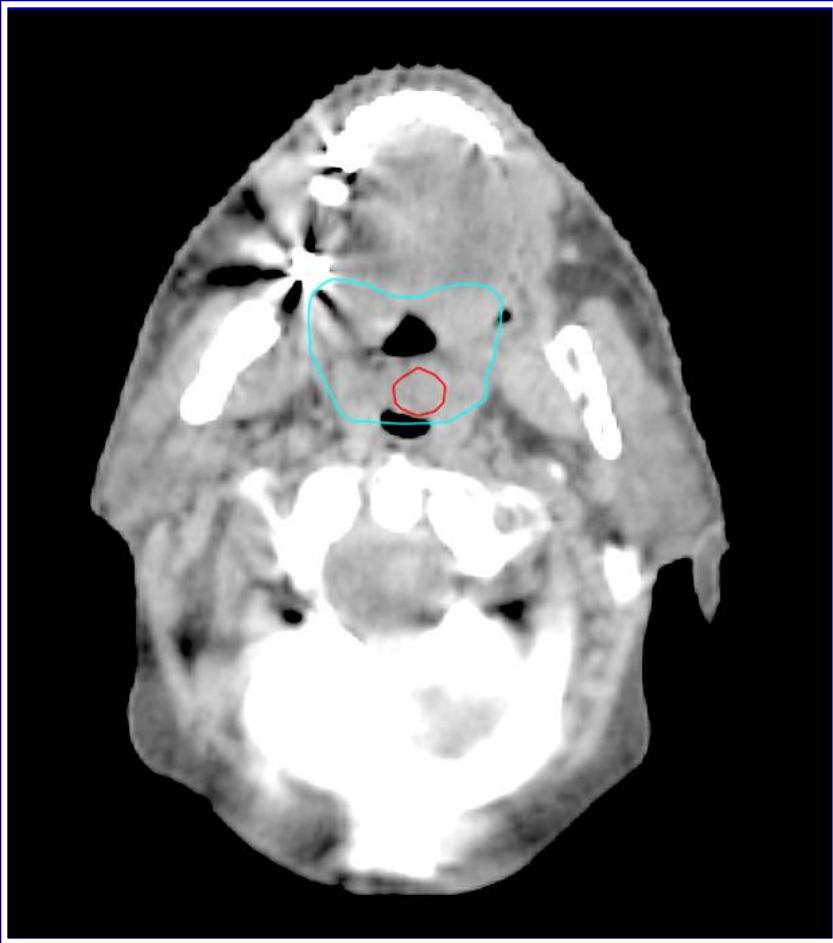
Dose painting by numbers



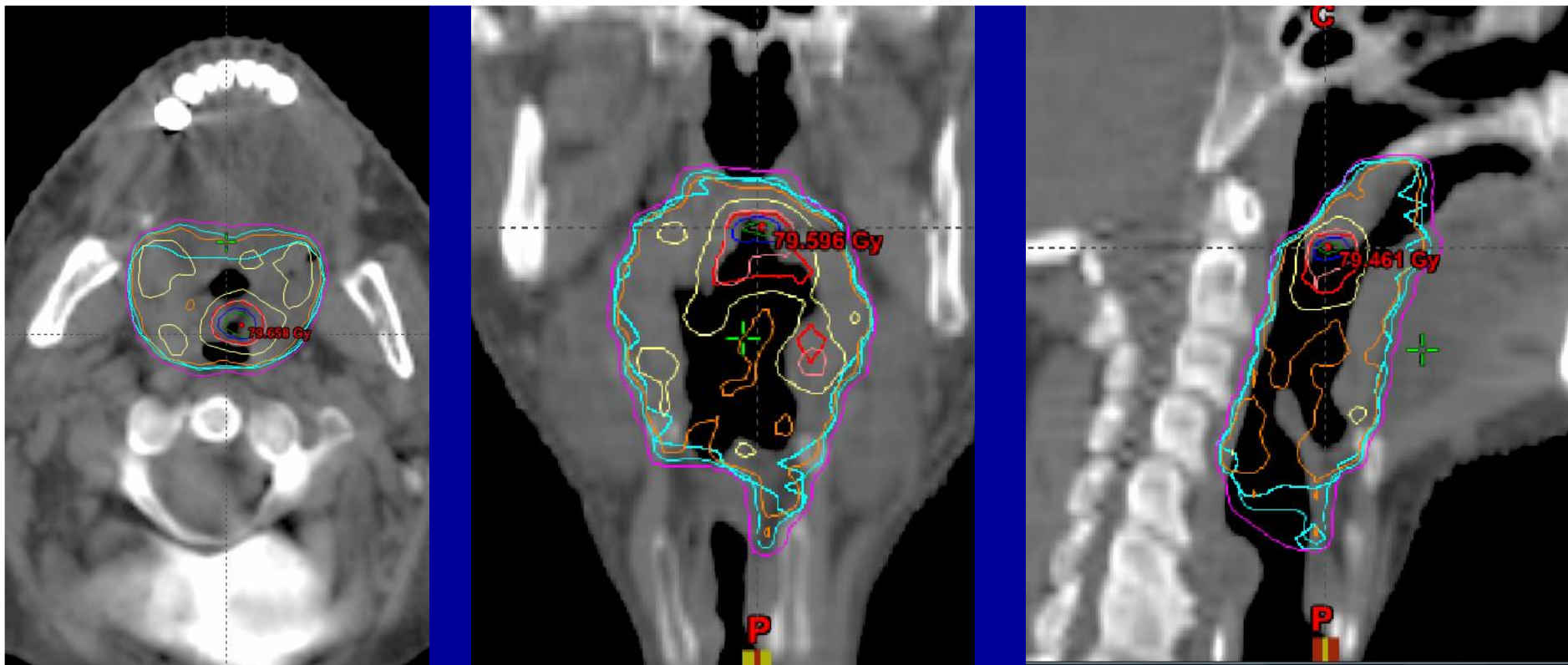
Dose painting by volume



Dose painting by volume



Dose painting by volume



— 68 Gy

— 70 Gy

— 73 Gy

— 76 Gy

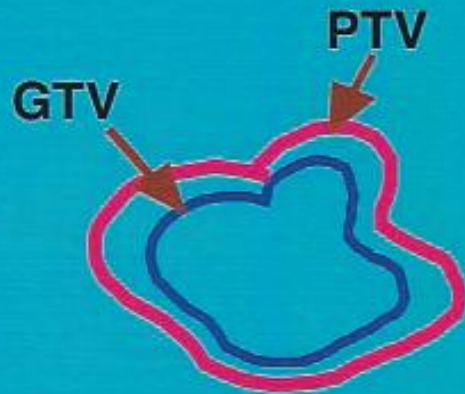
— 79 Gy

IMRT Dose intensification

Dose painting

- Definitions / examples
- Biological tumor volume
- Adaptive RT
- Clinical results

Biological Target Volume



- PET
- F-miso
- Hypoxia**



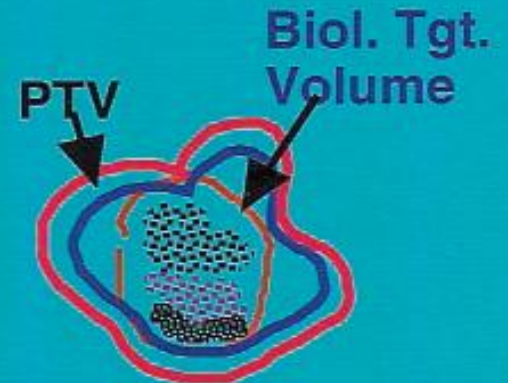
- MRI/MRS
- choline/citrate
- Tumor burden**



- PET
- IUDR
- Tumor growth**



**Biological
Eye View**



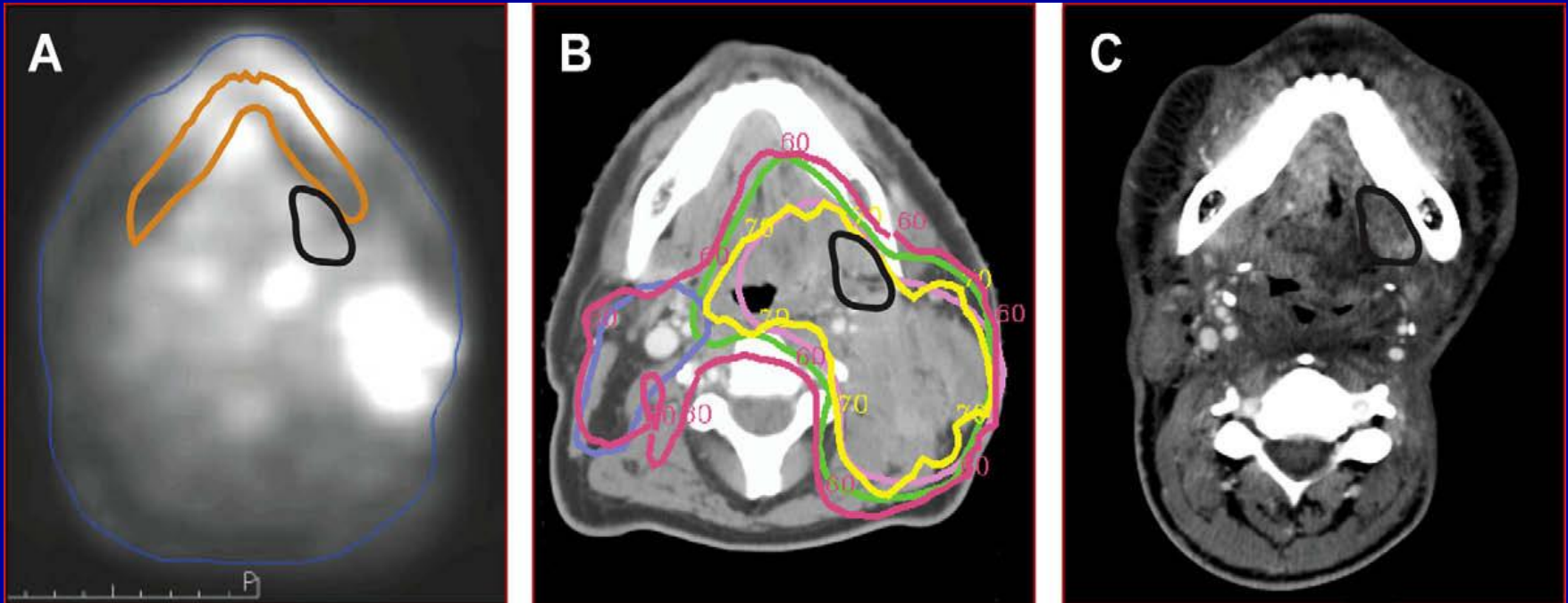
Biologic targets

- Tumor burden
 - FDG uptake is a good surrogate for tumor cell burden
 - In a imaging study FDG-PET leads to better estimate of true tumor volume
- Proliferation
 - [18F] fluorothymidine-PET correlates with Ki-67 index
 - Signal changes in FLT PET may precede tumor response
- Hypoxia
 - FMISO-PET imaging is associated with a high risk of LRF
 - Interval for the administration and spatiotemporal stability

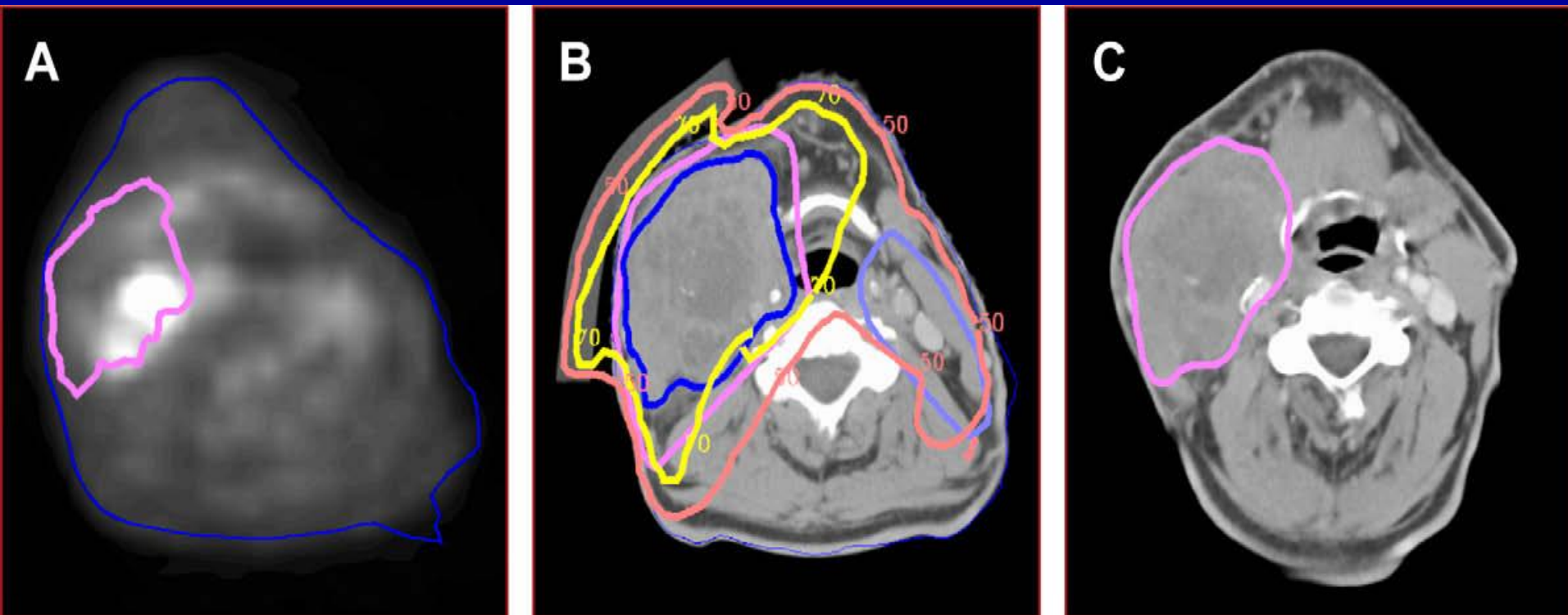
Pretreatment PET and failure

- Correlation between pretreatment PET-BTV with anatomical sites of loco-regional failure
- Retrospective study of 61 patients treated definitively with either 3-D CRT or IMRT who had a pre-therapy PET/CT
- A recurrence volume (V_r) was identified and was mapped to the pretreatment planning CT and pretreatment PET scan
- LRF 9/61; 100% (9/9) of failures were inside the GTV
- Only 1/9 (11%) had V_r outside pretreatment PET-BTV, while 8/9 patients had V_r within the PET-BTV

Pretreatment PET and failure



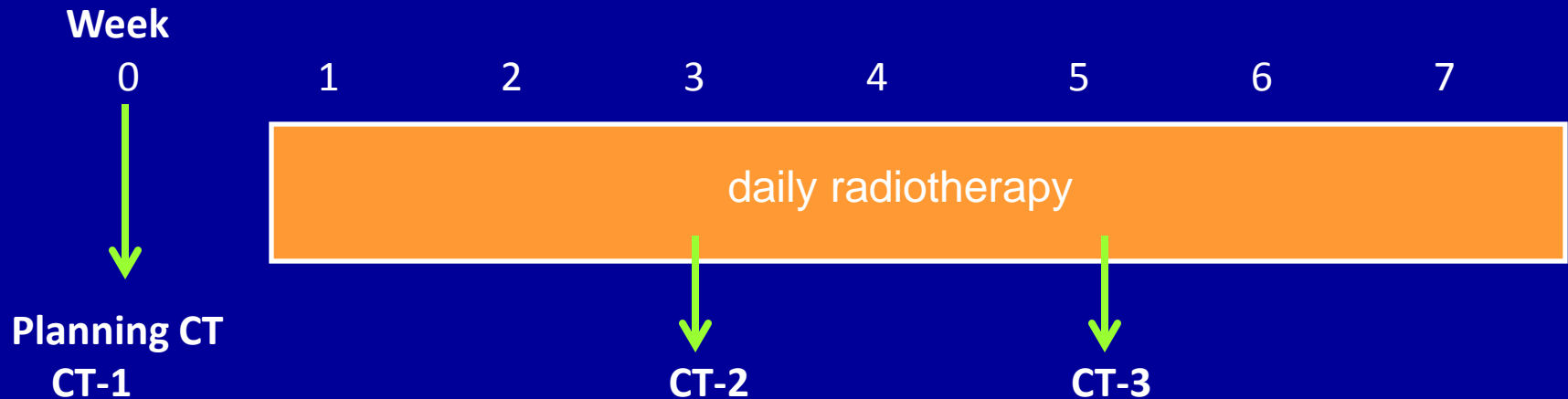
Pretreatment PET and failure



Adaptive RT

- Involves changes to the radiotherapy plan during treatment on the basis of patients specific changes
 - ✓ Patients weight
 - ✓ Tumor volume
 - ✓ Position
- Tumor assessed by repeated CT shrink by 1-2% daily
- Progressive increase in dose

Study design



TARGETS: GTV, CTV, PTV1 & PTV2

OAR: Parotids, Spinal cord, Oral cavity & Mandible

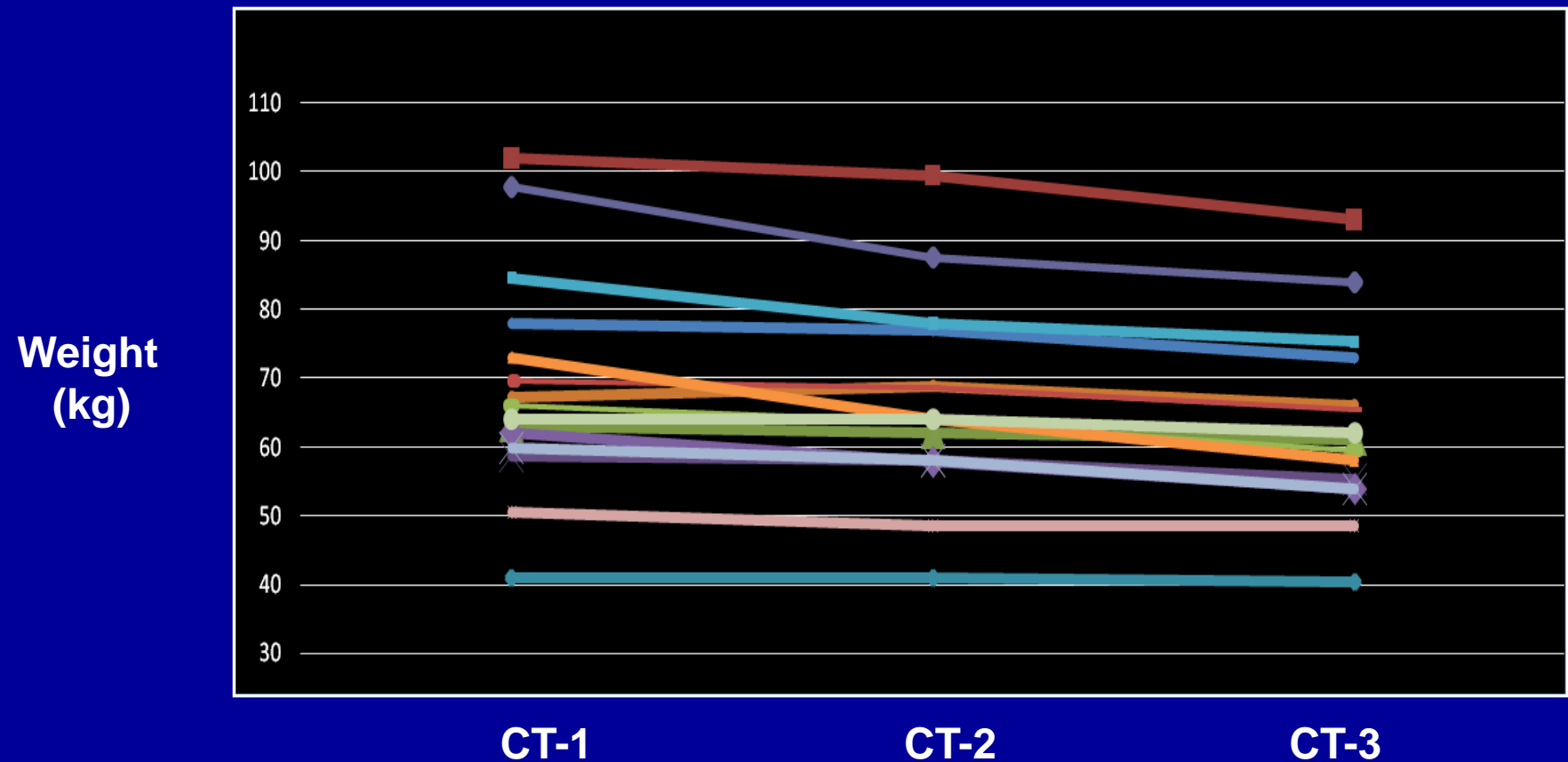
} On CT-1, CT-2
and CT-3

CLINICAL WEEKLY ASSESSMENT:

- Weight control
- Acute toxicity control

Weight loss

	CT-1	CT-2	CT-3	Variation (CT-1/CT2)	Variation (CT1/CT3)	Range
Mean weight (kg)	69.1	66.4	63.3	- 3.91 %	- 7.89 %	1.46% / 20.54%



Mean dose variation

	CT- 1	CT-2	CT-3	Variation CT-1/CT-3	Range
Mean V100% GTV	72.1	79.3	83.5	11.44 %	- 10.6 % / + 41.46 %
Mean V95% GTV	99.1	99.0	99.2	0.08 %	- 5.4 % / +3.8 %
Mean V100% PTV50	50.1	55.8	57.7	7.57 %	-3.4 % / +29.6 %
Mean V95% PTV50	82.3	82.4	84.6	2.3 %	-8.5 % / +3.8 %
Mean D parotid	39.32	43.58	45.01	16.11 %	(- 1.8 % / + 63 %)
Mean V26 parotid (%)	78.75%	80.06	85	9.18 %	(-7.8% / +35.6%)
D max spinal cord	42.6	44.13	44.21	3.9 %	(-4.8 % / +14.57%)
Mean D oral cavity (Gy)	46.46	47.26	47.26	1.47 %	(-8.6% / +9.07%)

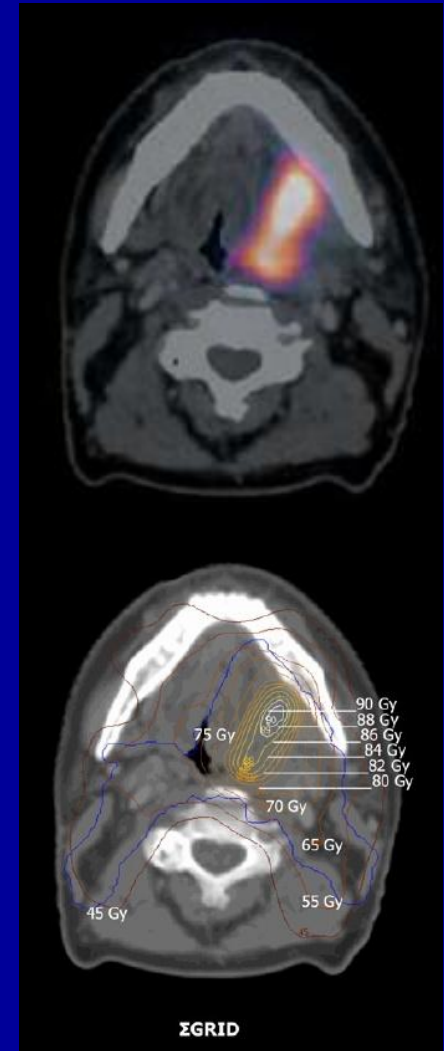
Adaptive biological image-guided IMRT

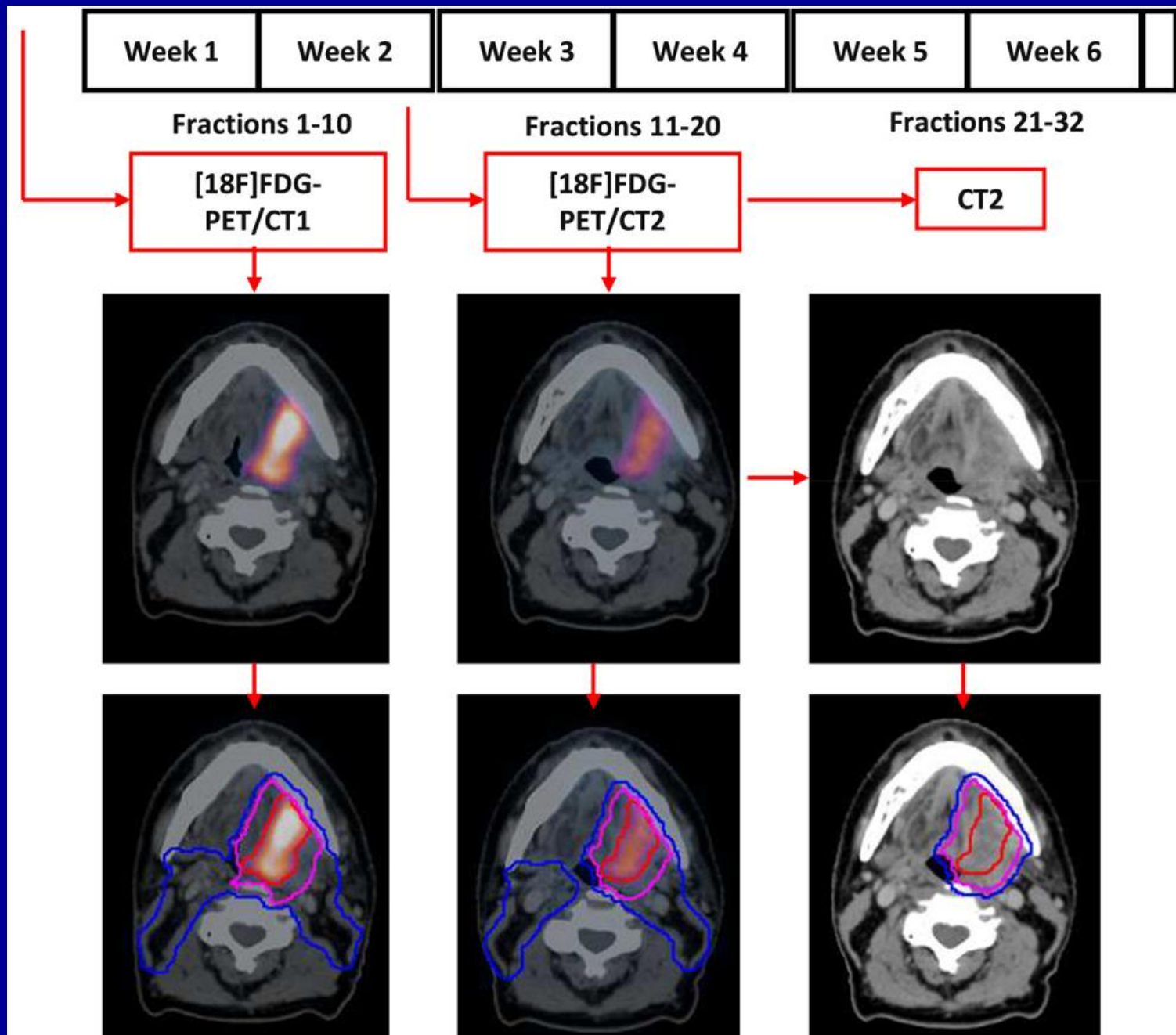
- To assess the impact of anatomical/functional imaging modalities acquired prior to and during RT on the target delineation
- 10 patients treated with RT_QT (70 Gy + carbo/FU) in 7 weeks
- CT, T2-MRI, fat suppressed T2-MRI, and static and dynamic FDG-PET were acquired, basal and after doses of 14, 25, 35 and 45 Gy
- GTVs significantly decreased for all imaging modalities ($p < 0.001$)
- PET-based GTVs significantly smaller compared to anatomical imaging modalities
- Adaptive PET IMRT has a significant impact on the delineation of target volumes

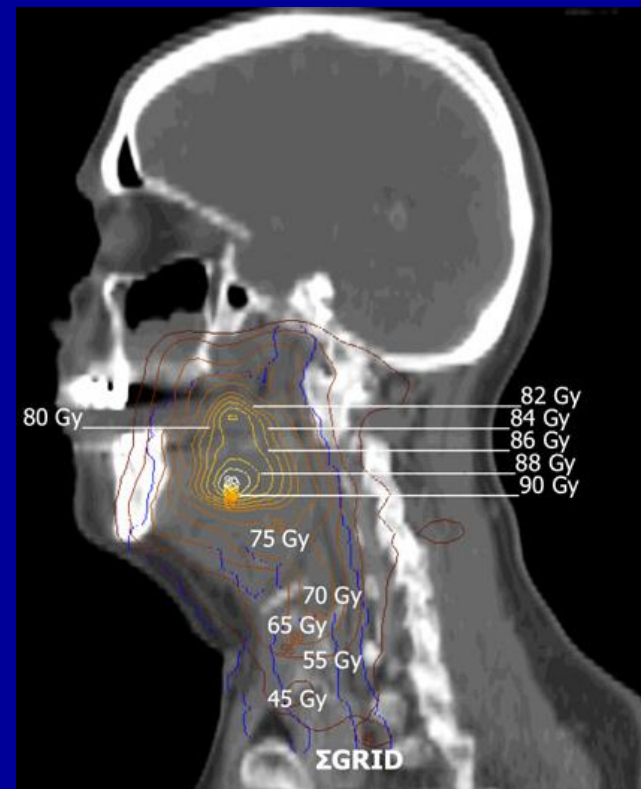
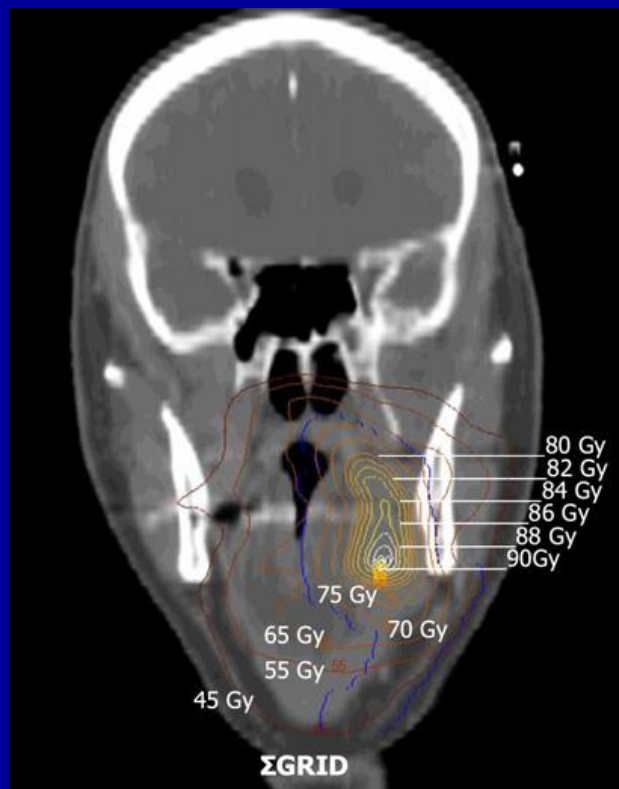
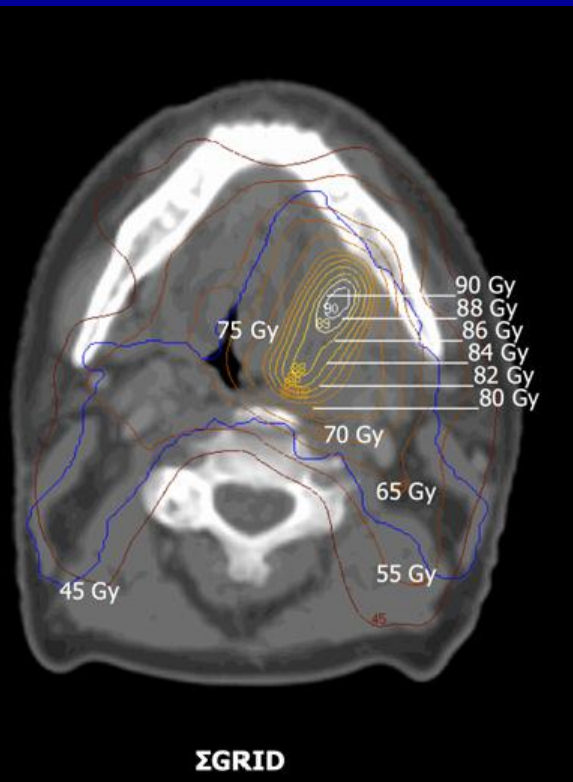
Dose escalation

- Simultaneous treatment of PTV's with several levels of dose fractionation
- Median dose of 80.9 – 85.9Gy to the high-dose clinical target volume (GTV_{high_dose})
- 21 patients (7pt. 81 Gy / 14 pt. 86 Gy)
- No Grade 4 acute toxicity

Toxicity	Dose level I	Dose level II
Dysphagia	5 (71%)	5 (36%)
Mucositis	3 (43%)	5 (36%)
Pain due to radiotherapy	—	—
Dermatitis	1 (14%)	3 (21%)
Weight loss	1 (14%)	—

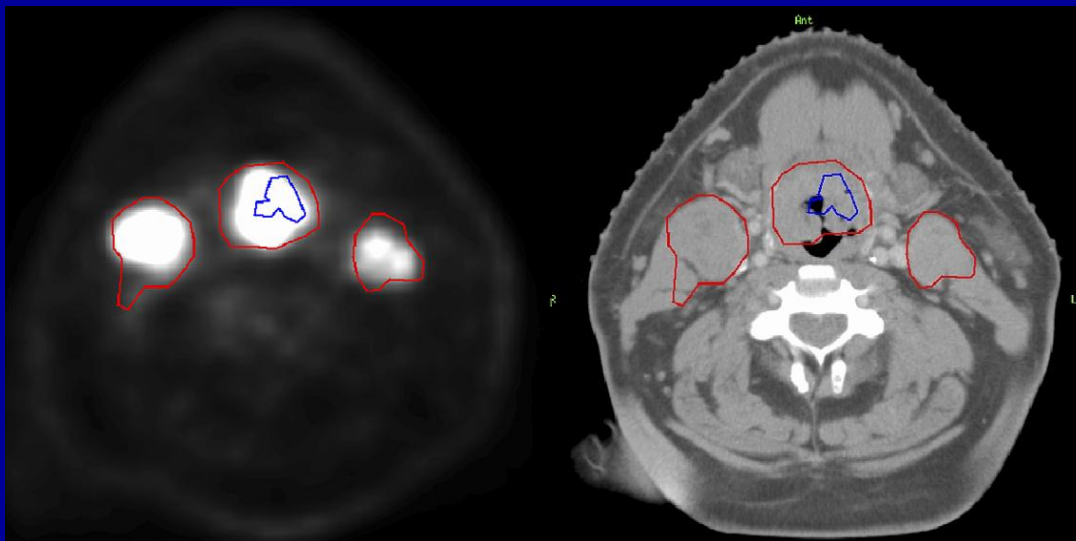






Dose escalation

- ^{18}F -FMISO was administered intravenously for PET imaging.
- 10 HNC patients achieved 84 Gy to the GTVh and 70 Gy to the GTV, without exceeding the normal tissue tolerance.



Levels in cGy.

8400.0

7000.0

ANT

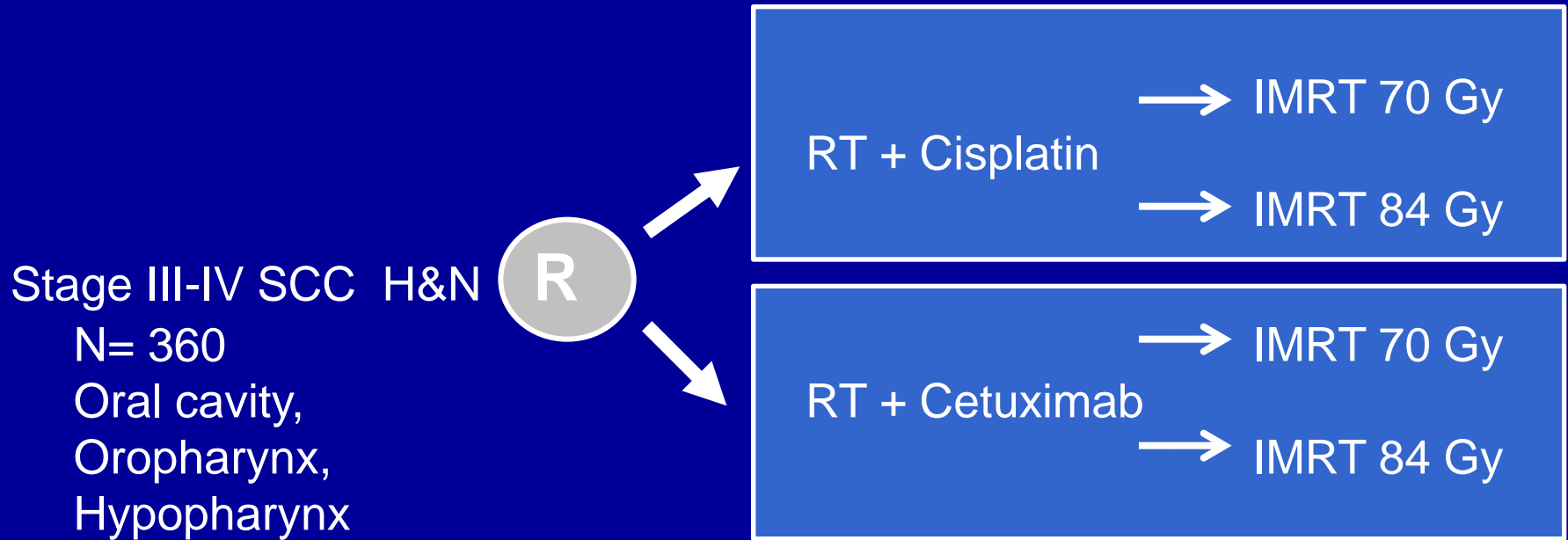
5940.0

5400.0



Lee F. IJROBP, 2008

Adaptive and innovative Radiation Treatment **FOR** improving Cancer treatment outcome (ARTFORCE)



CT scan in RT position is performed week 2 with replanning in week 3
in adaptive radiotherapy fashion

Summary

- Technological development enables more precise RT
- Dose painting is a new strategy for optimal dose intensification
- Biological target volume means high-risk for relapse
- Controlled trials have shown dose painting it is feasible
- Clinical trials are required to validate this strategy