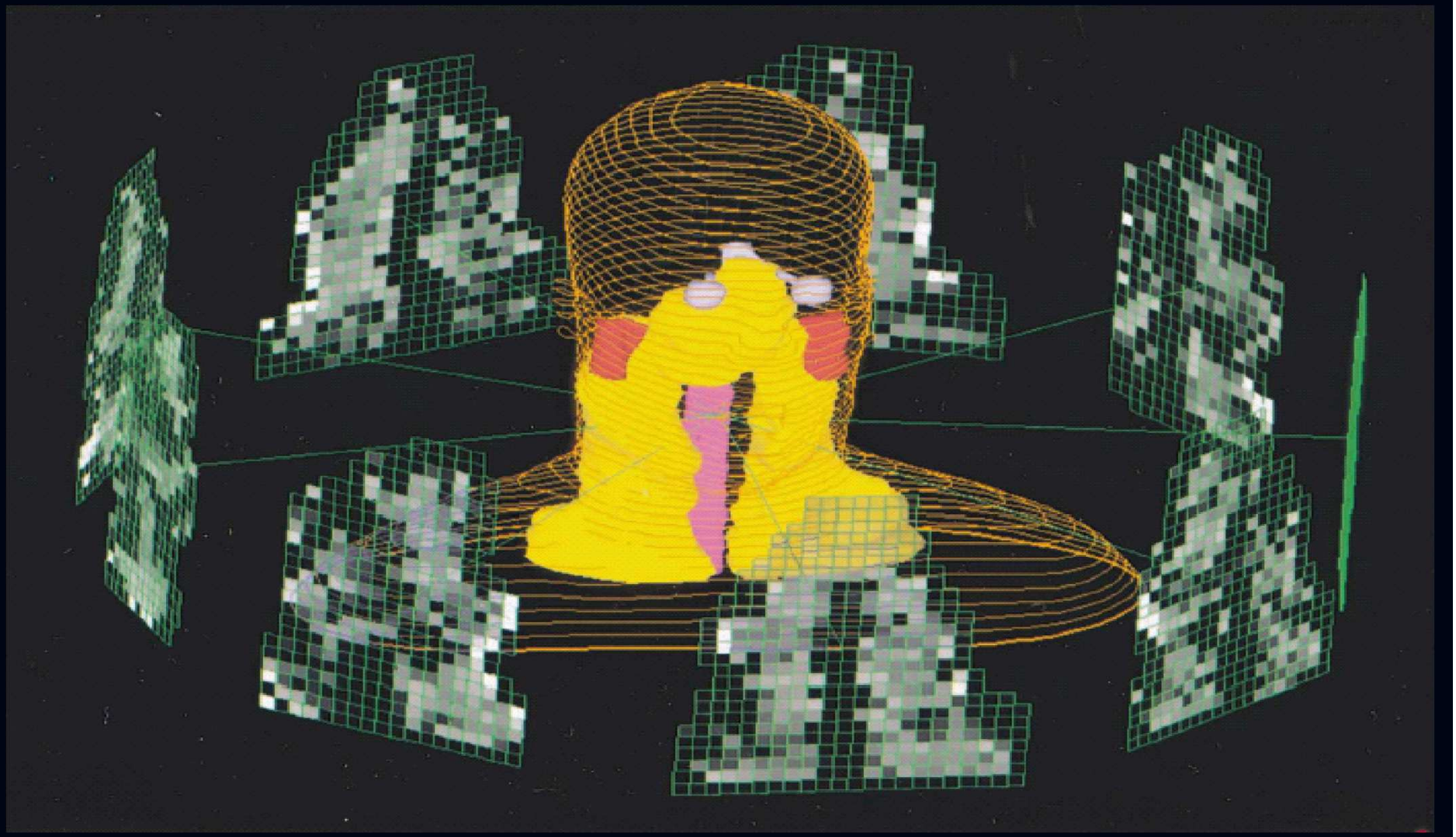
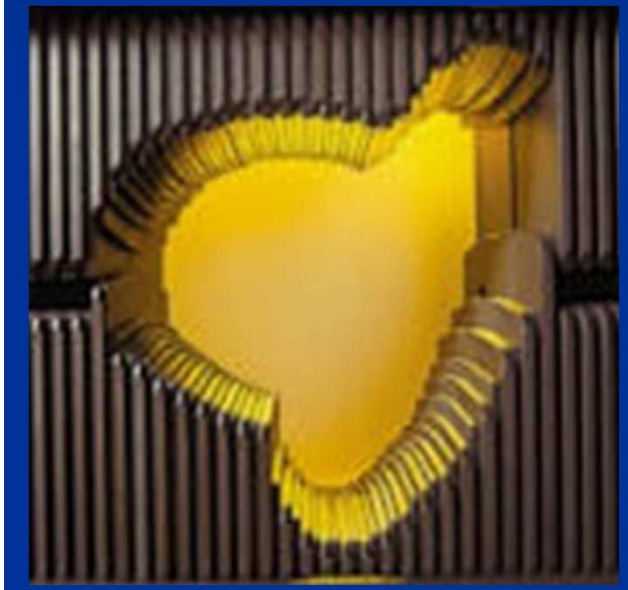
IMRT in Head & Neck Cancer



Dr P Vijay Anand Reddy

- Introduction
- How does IMRT work?
- Delivery techniques
- Planning steps, Tumor vol delineation
- Advantages, Pit falls
- Clinical studies
- Conclusions

3D-Conformal Radiation Therapy



3D-CRT

- Radiation intensity is uniform within each beam
- Modulation conferred only by wedges.

Intensity Modulated Radio Therapy

Conformal Radiation Therapy with Non-uniform intensity distributions generated by a computer optimization process.

"Intensity of Radiation is modulated"

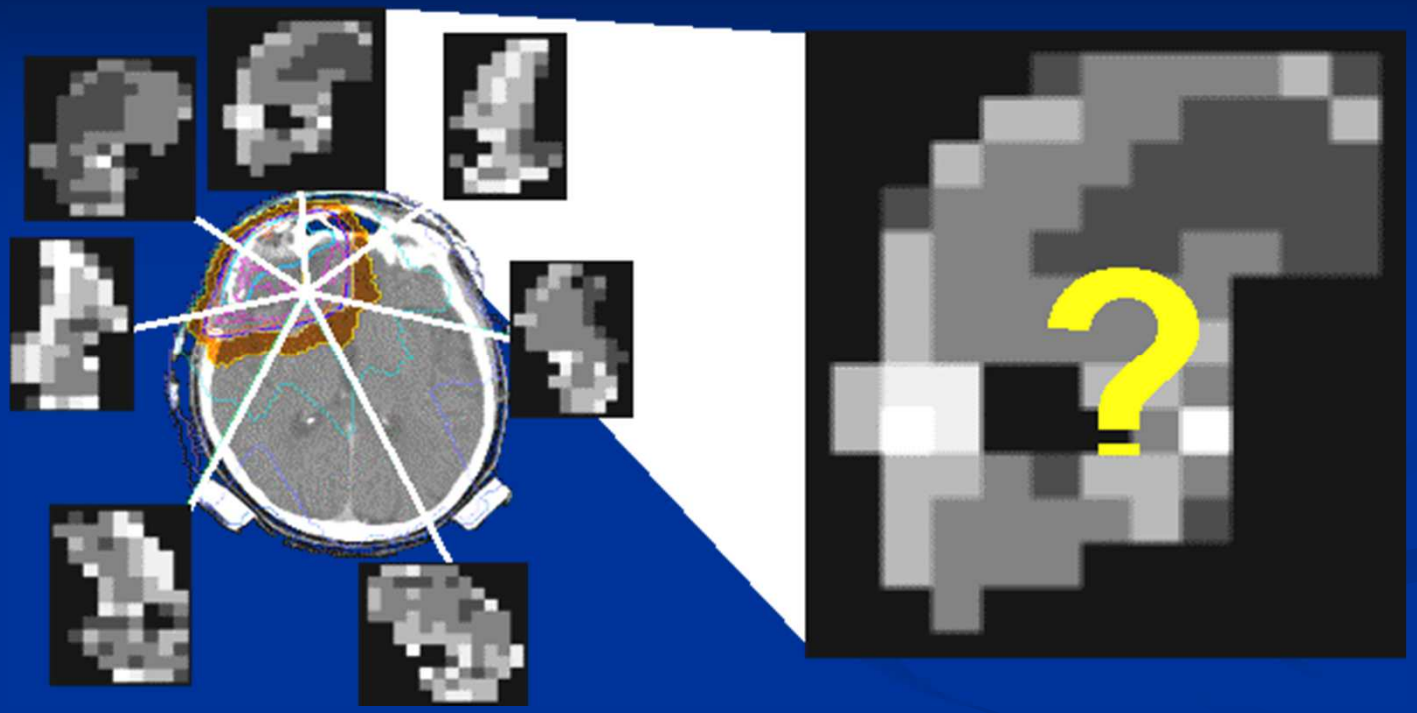
How does I M R T works

Each field is subdivided into numerous "beamlets"

whose intensities are individually modulated

to achieve a nonuniform dose contribution from each field.

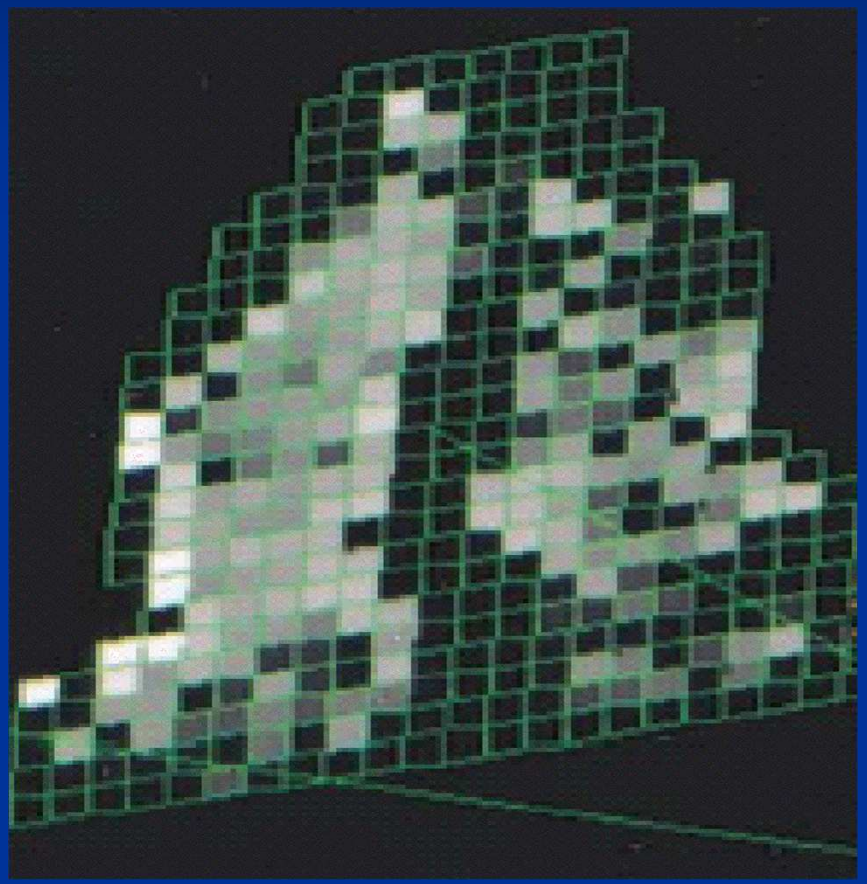
How to modulate RT fields?



Beamlet modulation is accomplished by actively moving multiple leaves during radiation treatment

thus achieving the desired dose distribution throughout the tissue volume.

How does I M R T work

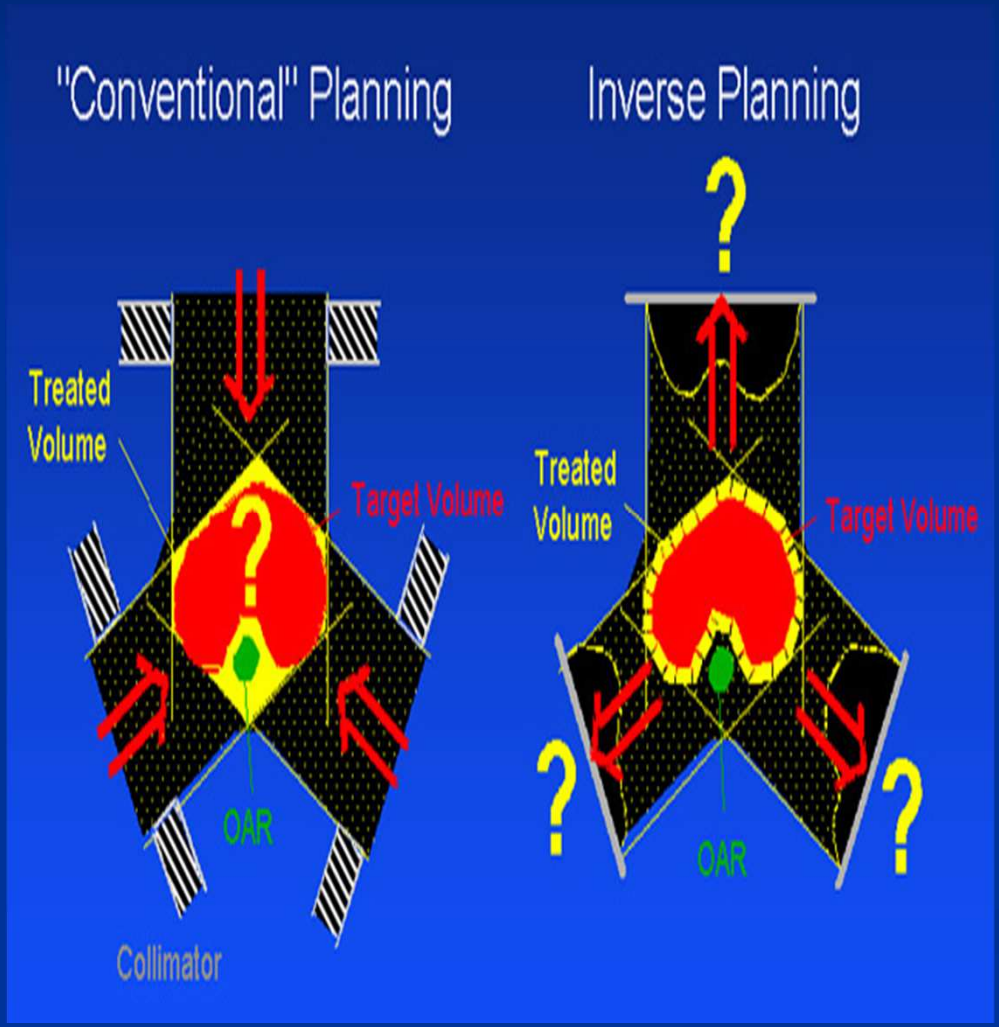


- 10 x 10 cm port is divided into 1cm^2 beamlets
- There are now 10^{+2} beams in the port
- Each can have an intensity weight of 0 – 100%
- Then we have 10^{+200} possibilities
- If we use 5 ports we have 10^{+1000} possibilities

Inverse Planning

- We need to optimize Beam location, energy, modality
- High speed computer tests all the possibilities of a human decision for a best possible solution
- The mathematical process of defining a solution is known as "Inverse planning"

Computer Optimization



- **Forward Planning:**

  The beam geometry i.e beam angle, shape, modifier, weights etc. is first defined, followed by calculation of the 3D dose distribution.

- **Inverse Planning:**

  The user specifies the goals, the computer then adjusts the beam parameters to achieve the desired outcome.

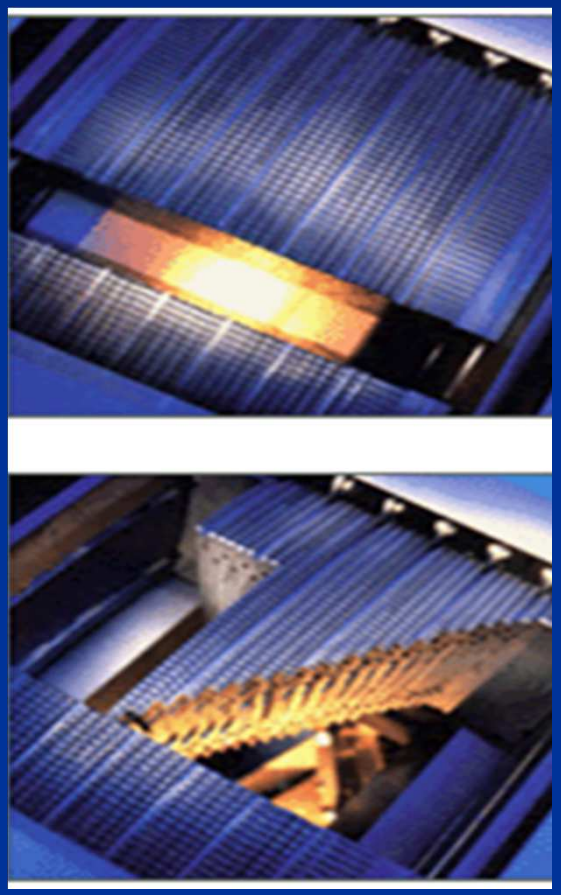
VAR

IMRT

Primary advantage of this technology

- Treating target volumes adjacent to critical or sensitive normal tissues
- Delivery of therapeutic radiation doses to target
- Minimizing normal tissue toxicity.

I M R T delivery techniques



1. Slit MLC:

- Narrow rectangular slit MLC
- Rotates in an arc around the patient
- Treats a target vol with multiple thin slices.

2. Tomotherapy:

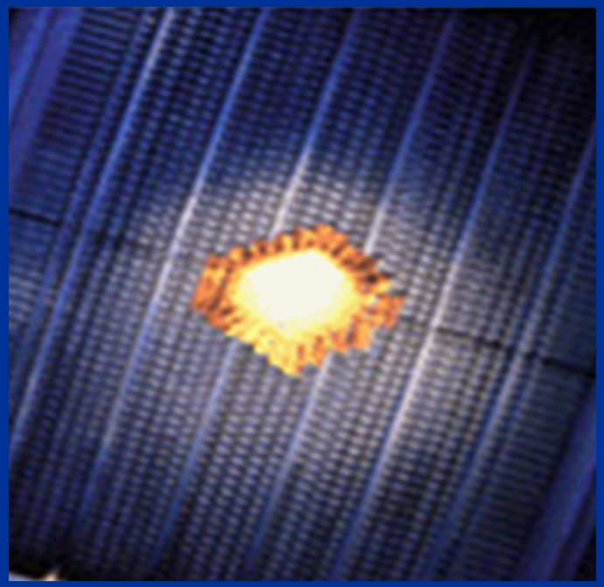
- Actively modulated narrow slit beams
- As the treatment gantry and MLC rotate

  pt moves through gantry ring on a couch.

VAR

I M R T delivery techniques

Standard MLC :



Beams can be delivered via multiple fixed gantry positions with a standard MLC

3. ‘Step and shoot’

- Delivers Sequential subfields with
- Individualized intensity distributions from each gantry position,
- Radiation beam off between subfields.

4. Dynamic mode

- MLCs move while radiation beam is on

VAR

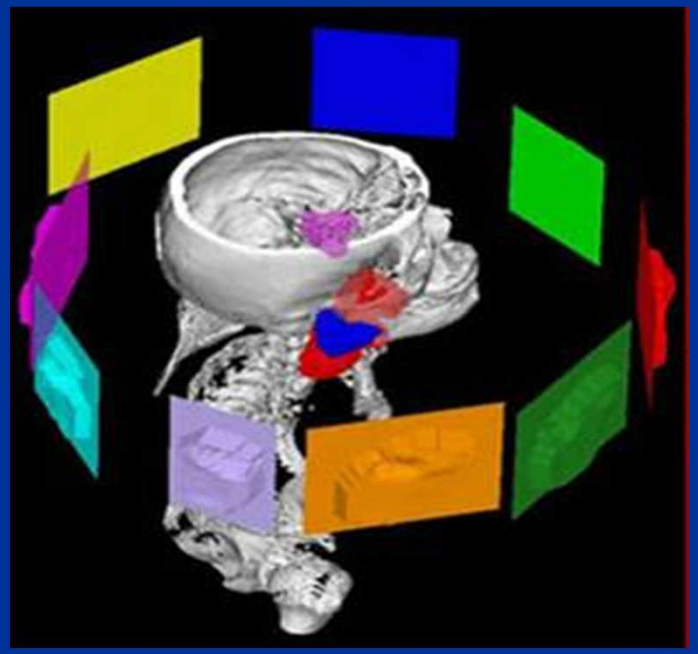
IMRT

Step & shoot or Dynamic

Tomotherapy

Dynamic slit beams,
dynamic gantry & couch

I M R T delivery techniques



5. Intensity modulated Arc therapy (IMAT) combining rotational arcs with dynamic multileaf collimation. (Rapid Arc, VMAT)
6. Fully dynamic systems MLC, gantry, and treatment couch all move independently at some point during beam delivery

Rationale of IMRT in H & N Cancer

1. Anatomically complex H&N region
   - an ideal option - IMRT.
2. Lack of organ motion in the H&N region
   - an ideal region for IMRT.
3. Allows for dose escalation
   - concomitant boost – ideal for H&N

H&N Ca - Radiotherapy Challenges

Tumor

- Very Close proximity of tumor with Critical / normal structures
- Dosimetric Challenges due to
  - Varying Contour
  - Tissue Heterogeneity

Patient

- Poor Nutritional Status and Weight Loss
- Inadequate oral Intake
- Treatment Induced Mucositis

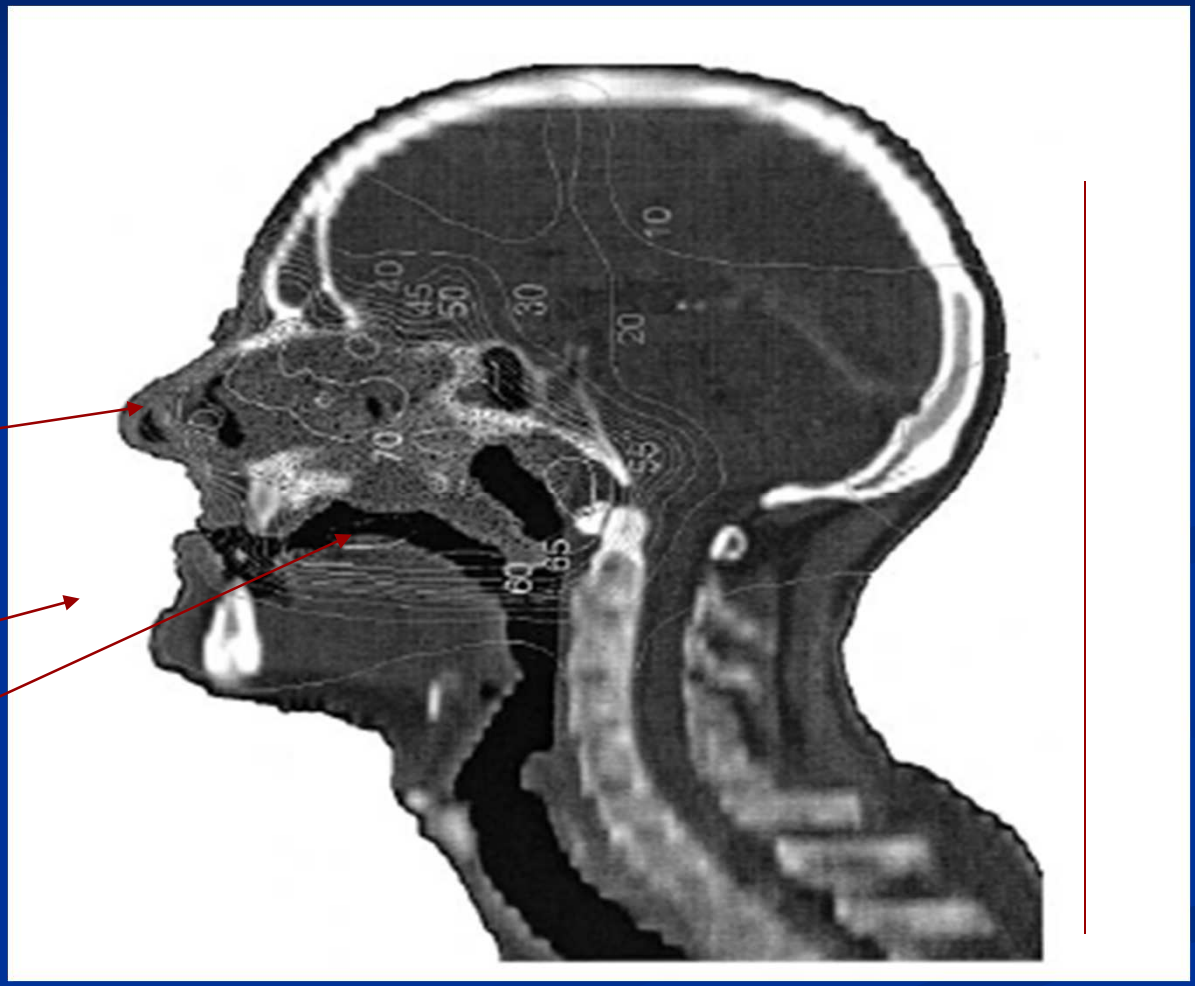
Heterogeneities in H & N areas

Tissue Heterogeneities

Soft Tissue

Bone

Air Sinuses



Varying Contour

Heterogeneities pose difficulty in treatment planning and dose delivery

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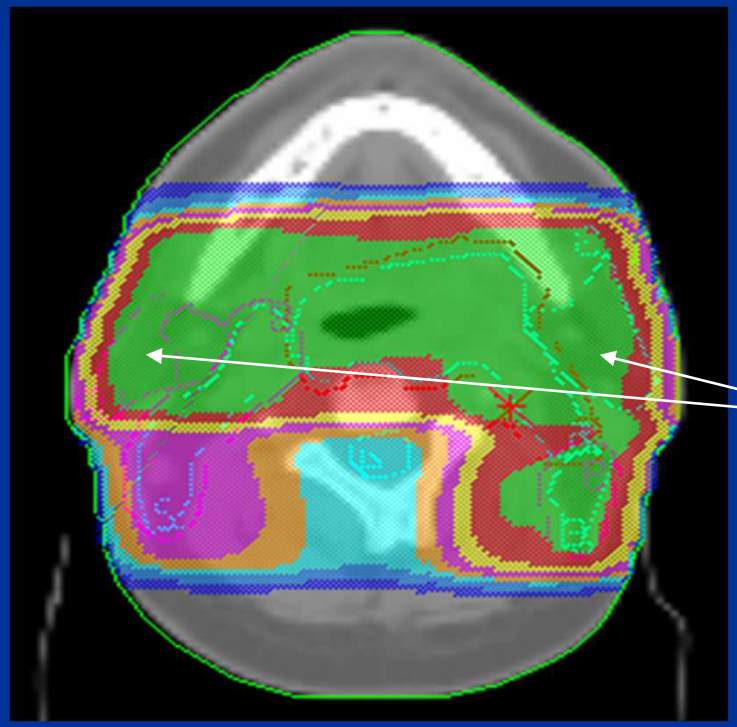
Rationale for parotid sparing IMRT

- Parotid glands produce 80% of saliva
- Innocent bystander in lateralized tumors!
- Opposed lateral fields causes severe xerostomia in 90% of treated patients
- Reduces QoL and causes complications
- IMRT can reduce the dose to contra-lateral parotid glands in lateralized cancer

Conventional dose distribution



IMRT **Sites in H&N**

- Nasopharynx
- Sinonasal region
- Parotid gland
- Tonsil
- Buccal mucosa, Gingiva
- Thyroid
- Tumor tracking along the cranial nerves.

- Based on the studies comparing IMRT and other treatment approaches

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Steps of IMRT

- Clinical evaluation & assessment
- Simulation
- Planning CT/MRI/PET-CT scan
- Target vol Delineation GTV, CTV, PTV
- IMRT Planning, Dose Vol Histogram
- QA
- Execution of IMRT

Steps of IMRT in H&N Cancer

Clinical Assessment

- Pt is seen by Surgeon, RO, MO
- Examination of the H&N region
  - Indirect laryngoscopy
  - Fiberoptic nasopharyngolaryngoscopy
- An illustration of the physical findings
  - Demonstrating the primary tumor extent
  - Lymph-adenopathy

Steps of IMRT in H&N Ca …

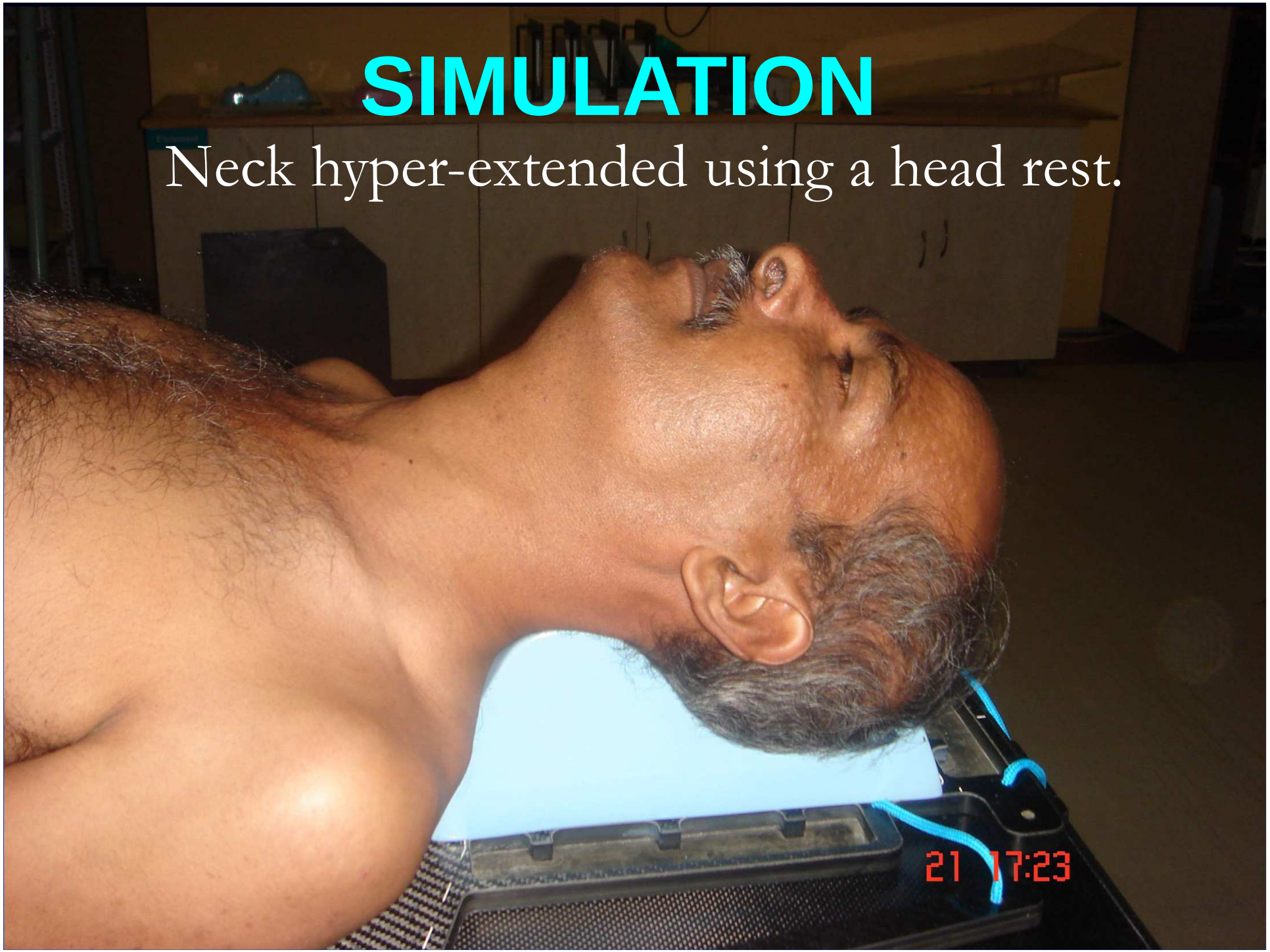
Clinical Assessment…

- Pretreatment dental consultation
  - Extraction of bad teeth
  - Initiation of prophylactic fluoride therapy.
- Pretreatment ophthalmology and audiology consults
- Thyroid function tests baseline.
- Review of imaging studies and further workup


Simulation/CT simulation in the treatment position
• Conventional simulation followed by a CT or
• CT Simulation.
21 16:26

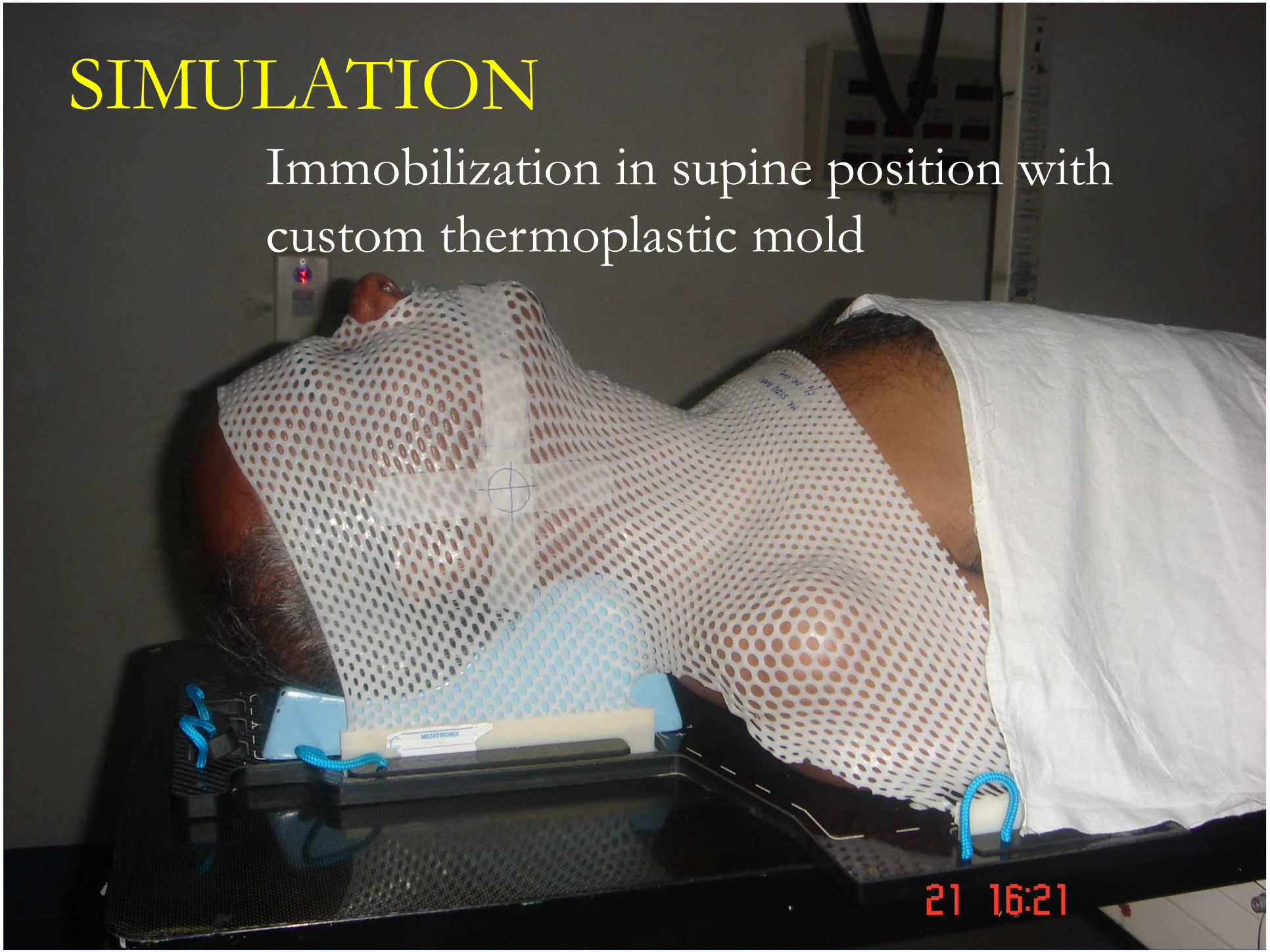
SIMULATION

Neck hyper-extended using a head rest.



SIMULATION

Immobilization in supine position with custom thermoplastic mold



SIMULATION

- Shoulder traction to minimize shoulder in RT fields
- Palpable masses & incisional scars are outlined by ….
- For CT, use iv contrast to diff vessels from masses or LN

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Image registration & Tumor volume delineation

- Planning CT scan
  - with i.v contrast in the treatment position
- MRI
  - better delineation of normal tissue & tumor
- FDG-PET-CT
  - Improve tumor delineation better than CT alone

It is imperative that the radiation oncologist be trained in the interpretation of all images used for structure localization

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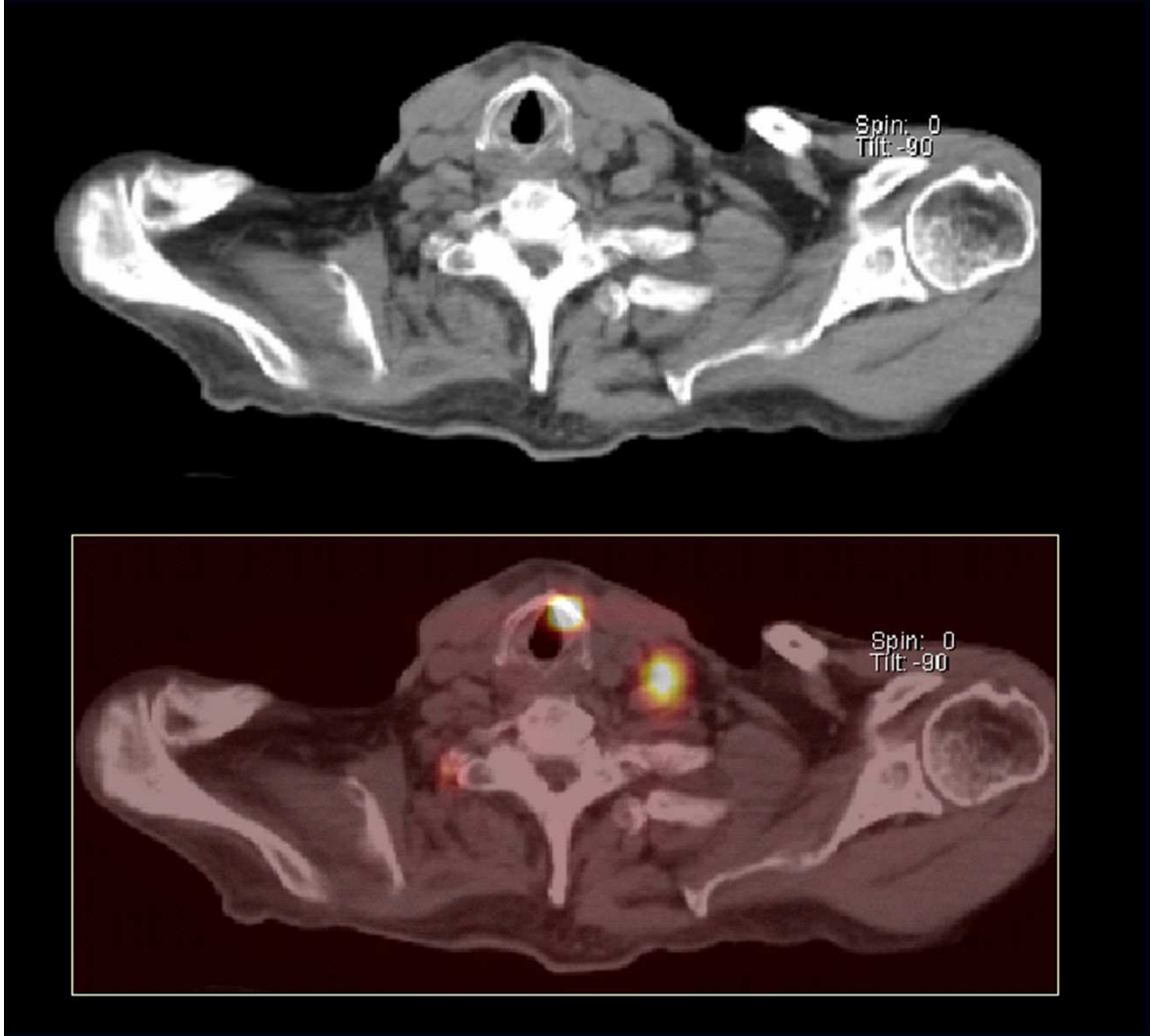
PET Scores over others!



CT, MRI

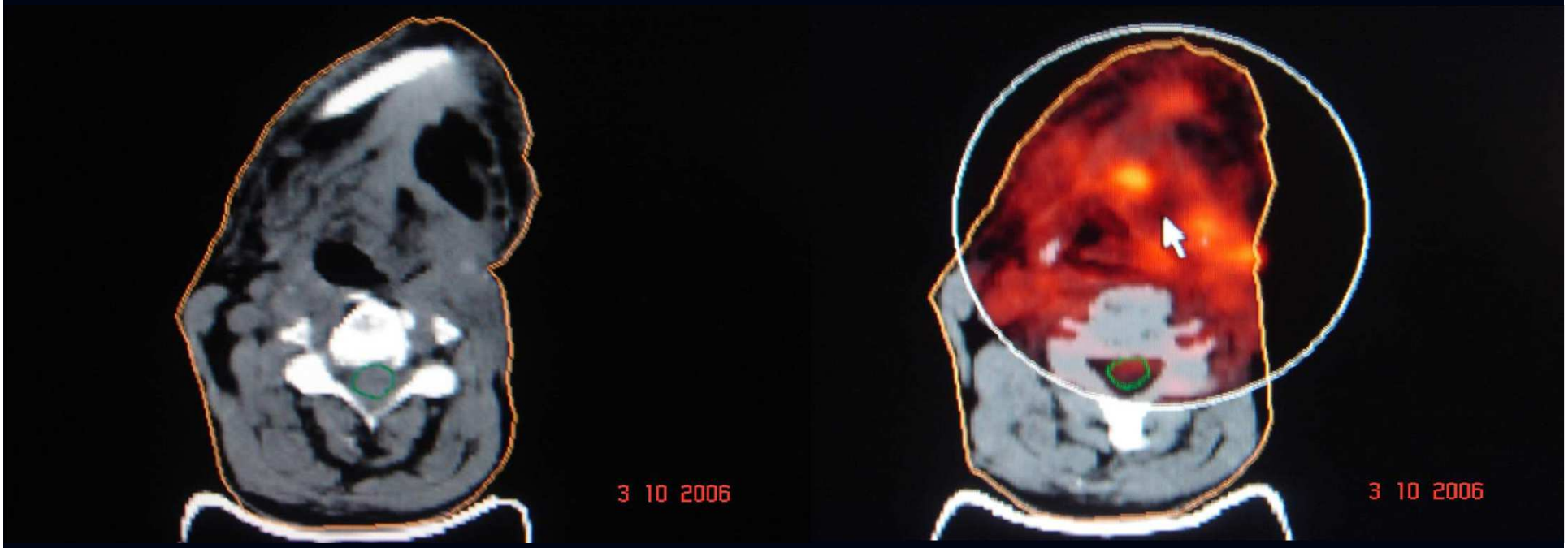
Anatomical imaging

PET

is functional imaging

Active viable tumor

Advantages of Biological Imaging..



Will not be affected with post op anatomical disturbances!

Clinical applications of FDG-PET in Target volume delineation…

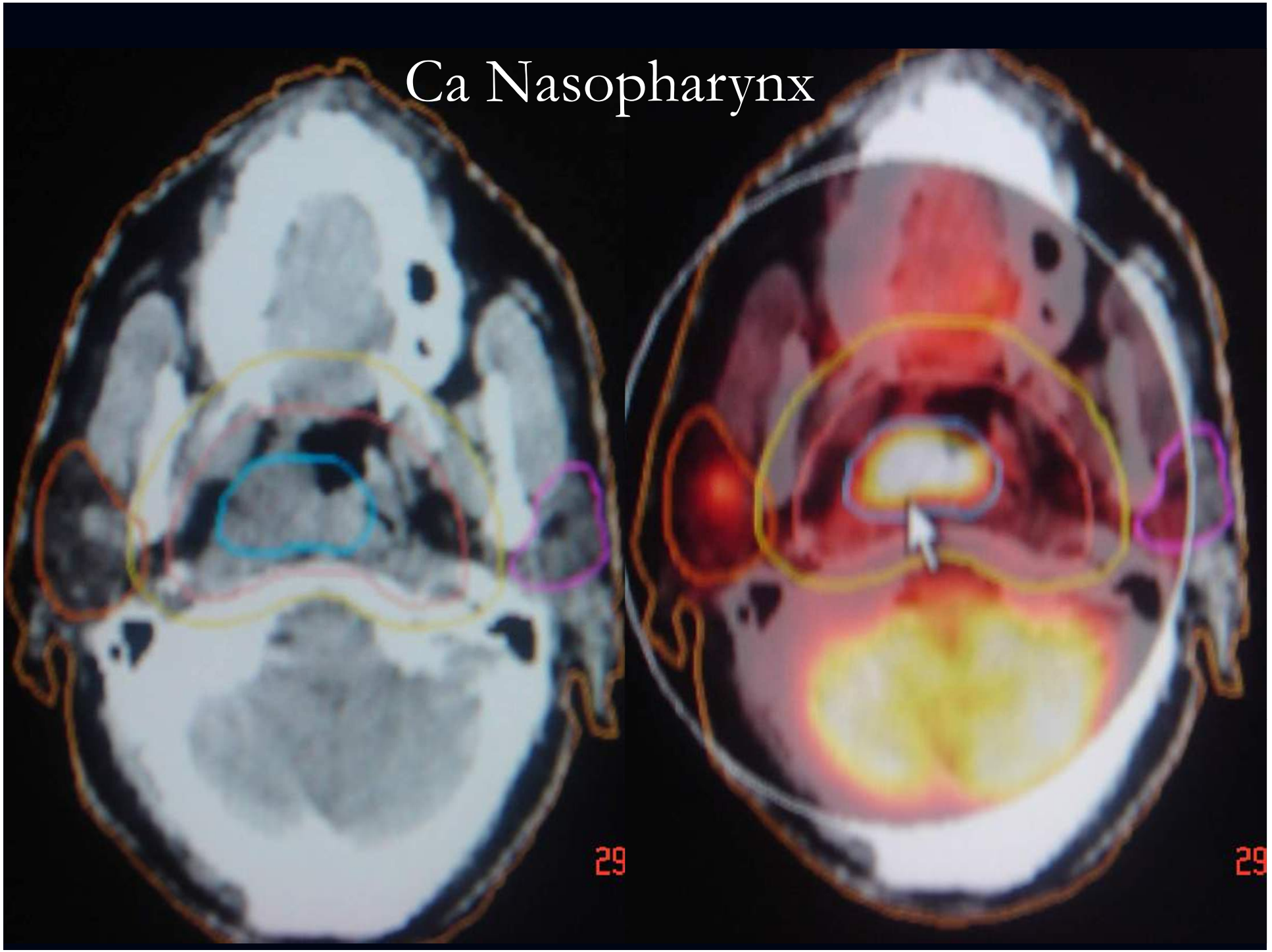
- Lung Cancer
- Head and Neck Cancer
- Gynecological Cancers
- GI tract Cancers
- Brain tumors
- Lymphomas

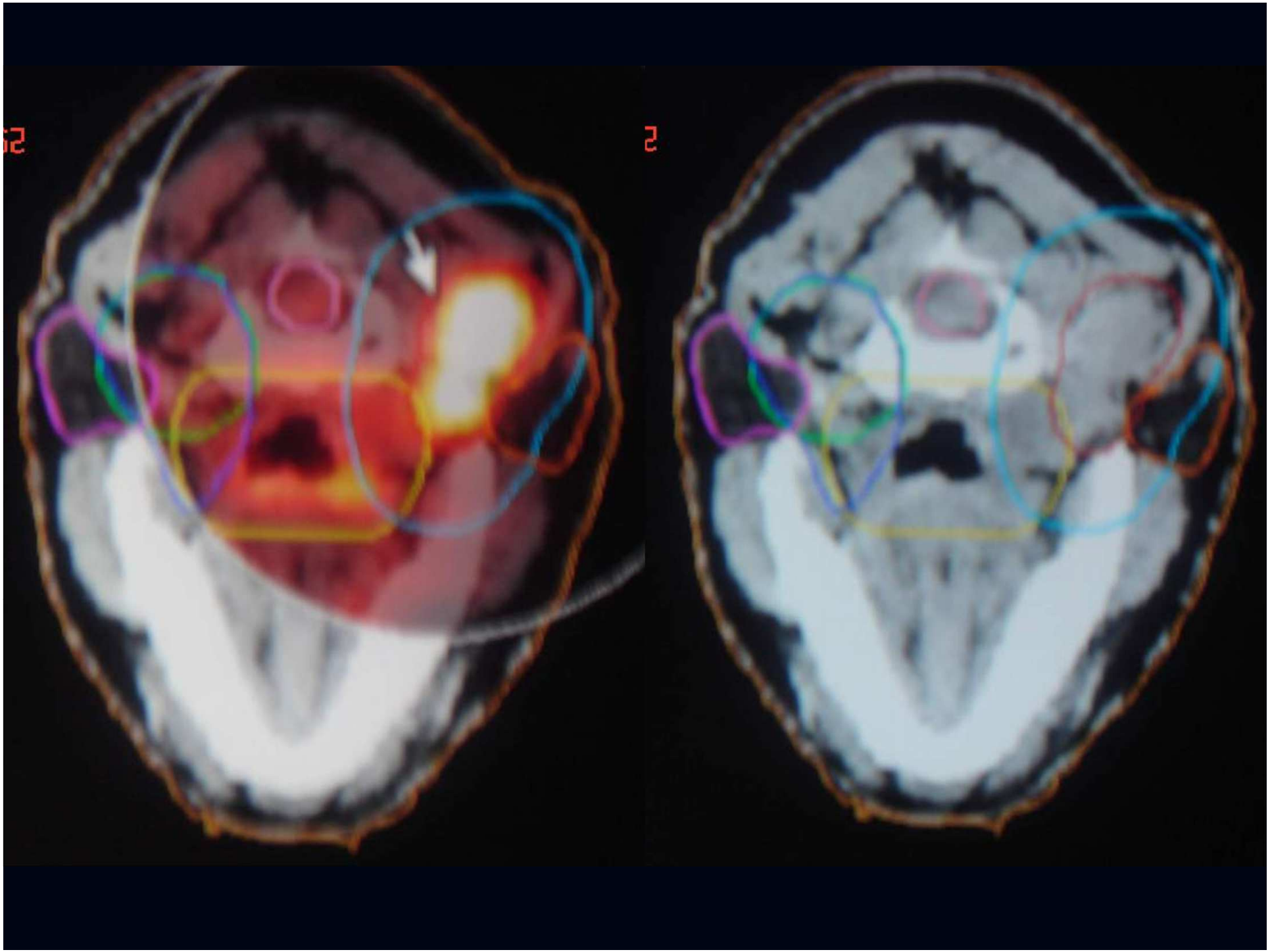
Impact of PET-CT in H & N Ca

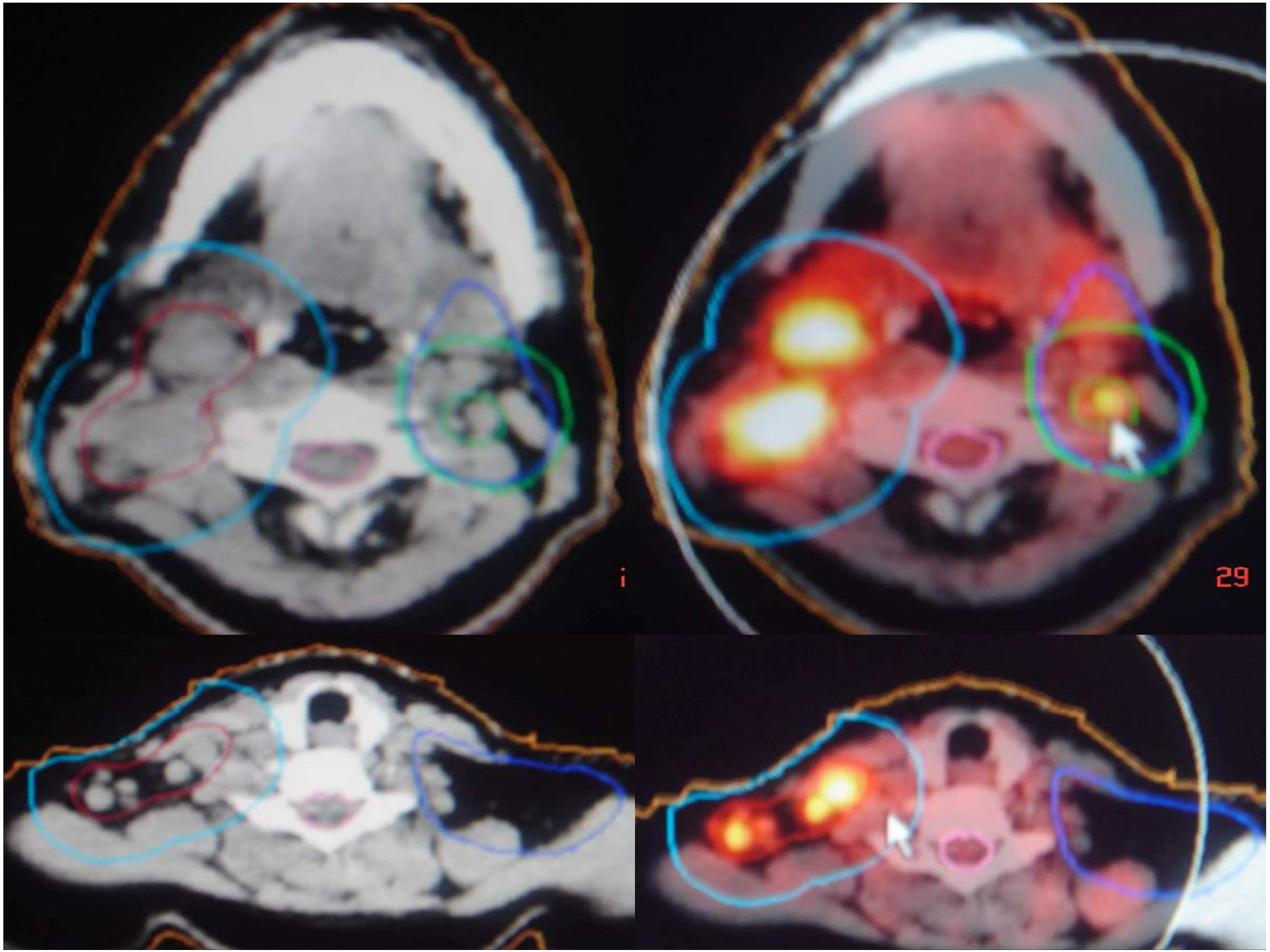
Author	Patients	Change of GTV using PET	Increase in GTV	Decrease in GTV	Remarks
Rahn, 1998	22(prim)	41%	41%	0%	No image fusion
	12(recur)	58%	58%	0%	
Nishioka, 2002	21	71%	0%	71%	PET/CT/MRI fusion
Ciernik, 2003	12	50%	17%	33%	Integrated PET-CT
Daisne, 2004	29	93%	18%	75%	CT-PET image fusion
Paulino, 2005	40	100%	-	-	PET/CT/MRI and surgical specimen image fusion

VAR

Ca Nasopharynx



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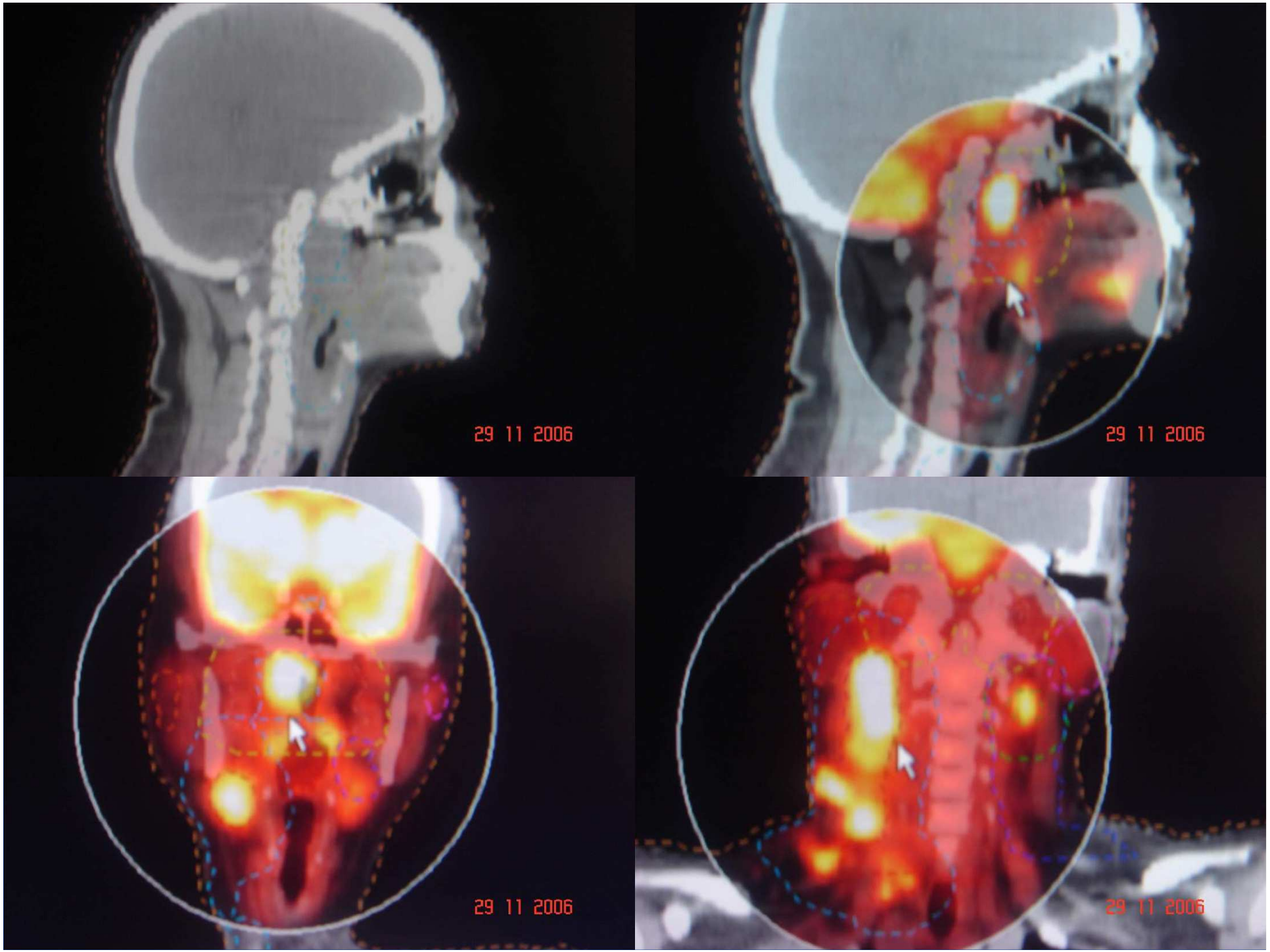
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I M R T - Target volume

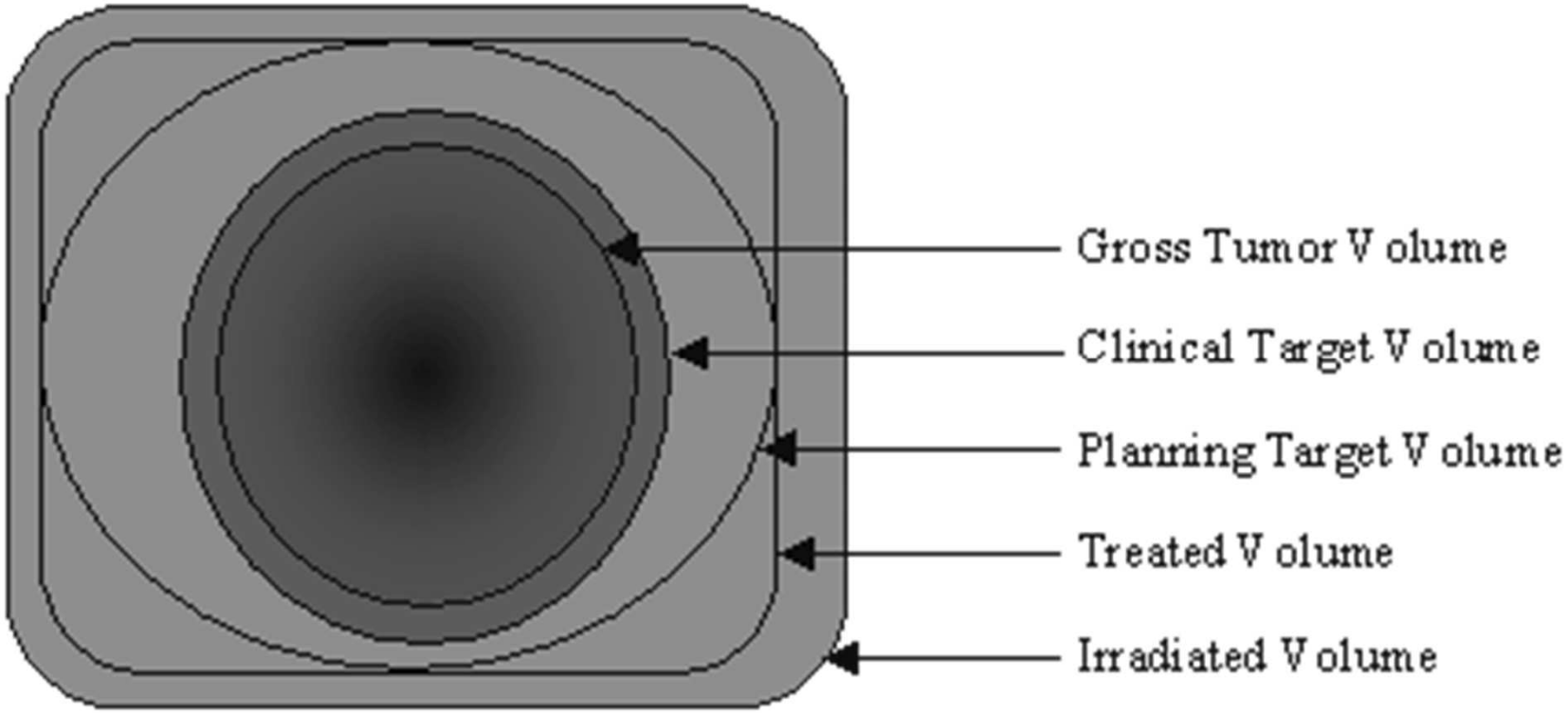
- IMRT requires a thorough understanding of target delineation in the complex H&N
- Areas to be delineated on the planning CT
  - Gross tumor volume (GTV)
  - Subclinical disease (CTV)

Target volumes

- Gross tumor volume GTV (Primary & LN)
- Clinical Target volume CTV
  - Primary incl subclinical + elective nodal regions
- Planning Target volume (gross)
  - 1 cm margin everywhere
  - except post along the skull (0.5 cm margin)
- Planning Target volume PTV (elective)
  - Uniform .5 cm margin all round

IMRT Target Volume Specification (CWG recommendation)

Target volume(s) should follow the recommendations of ICRU Reports 50 and 62.



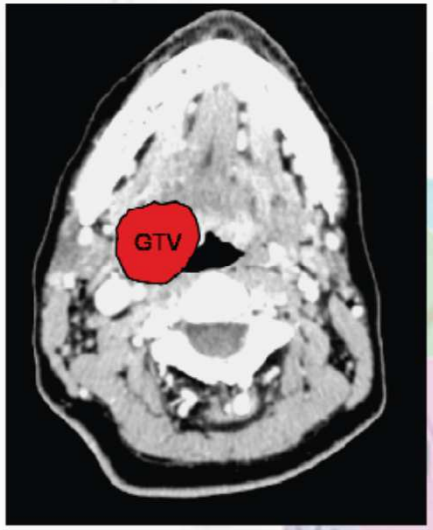
Clinical Target Volume (CTV)

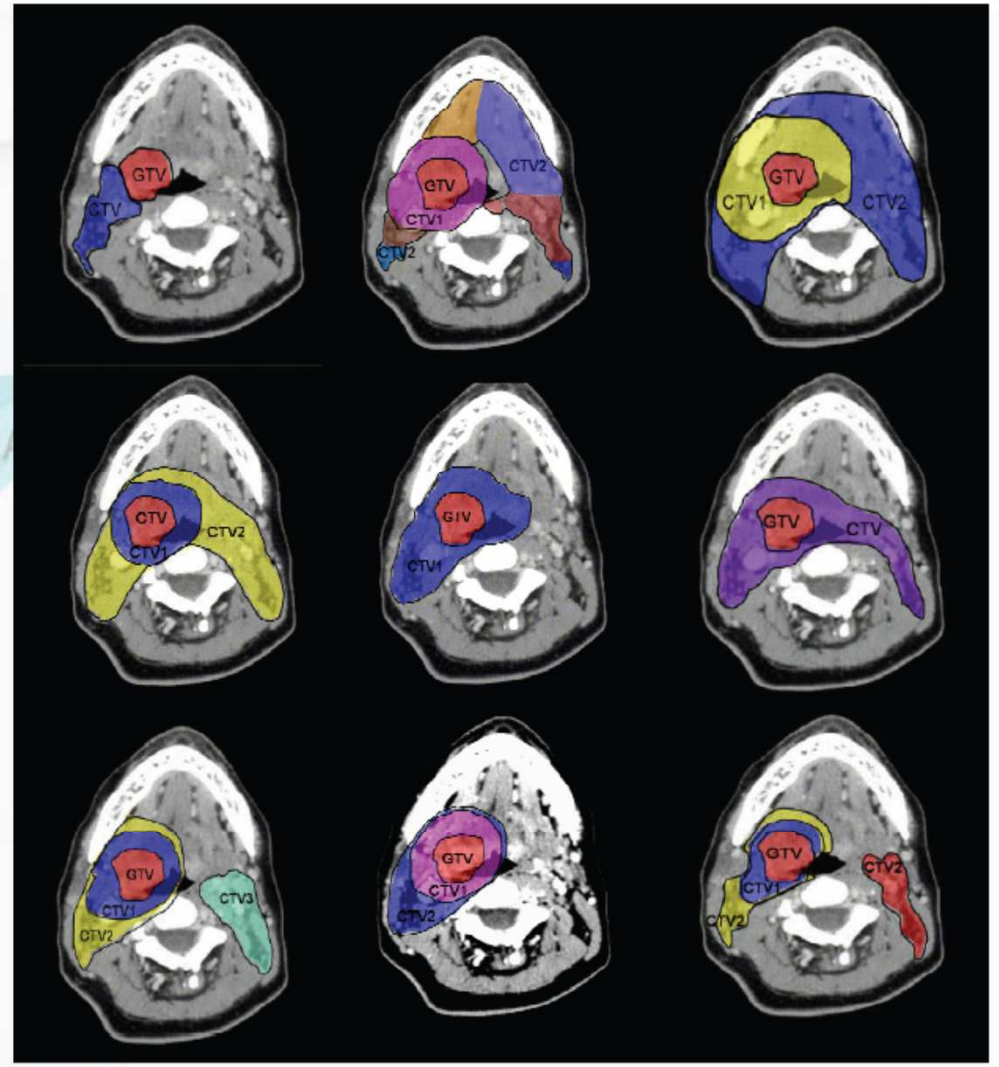
- *targeting the sub-clinical disease*

- Every primary in H&N region there are associated LN regions or levels, that are at risk
- Knowledge of these levels and their anatomic boundaries is essential.
- RTOG, EORTC & DAHANCA imaging based nodal atlases

CTV guidelines for the clinically & radiographically negative, surgically nonviolated neck

H&N IMRT practice heterogeneity



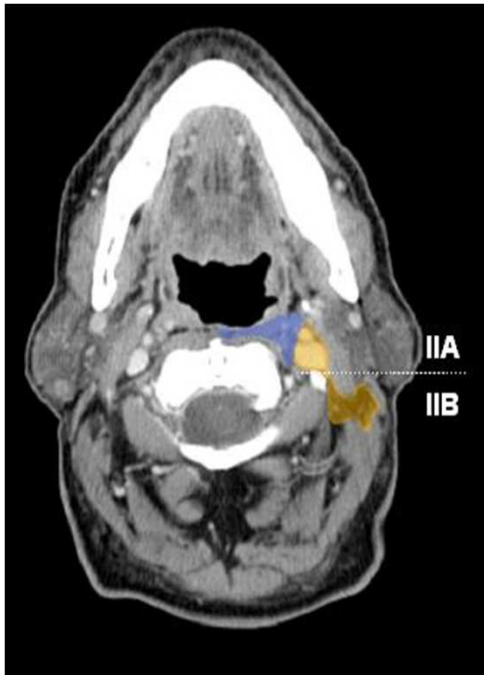


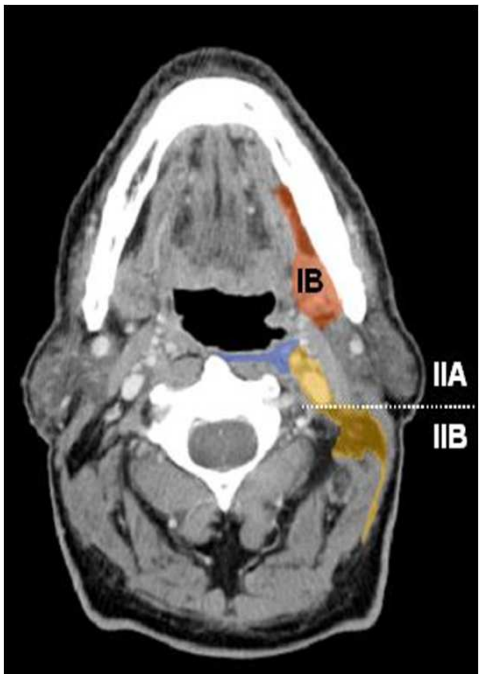
Atlases?

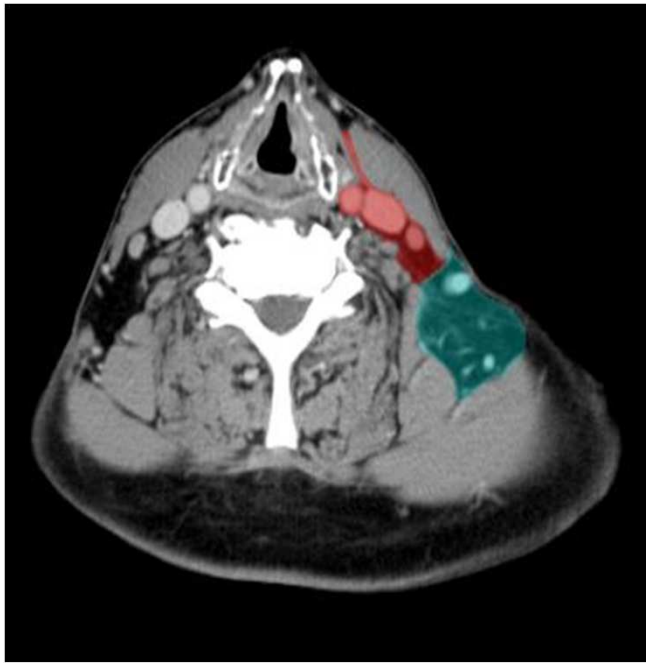
MAESTRO
Jan. 2007

Harari et al., 2005

Radiotherapy & Oncology 69: 227, 2003
http://www.rtog.org/hnatlas/main.html





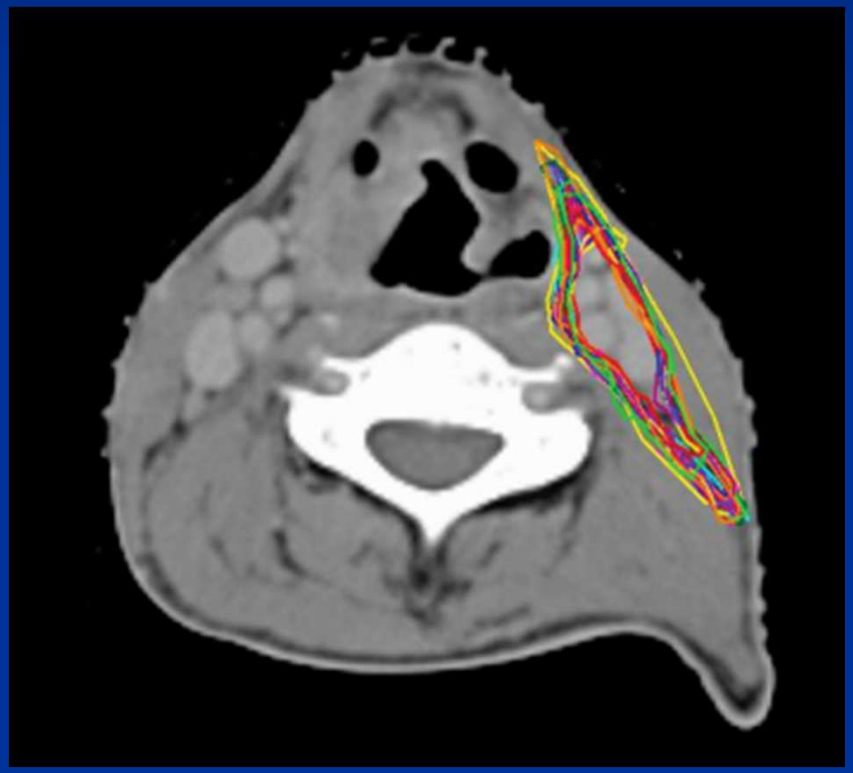


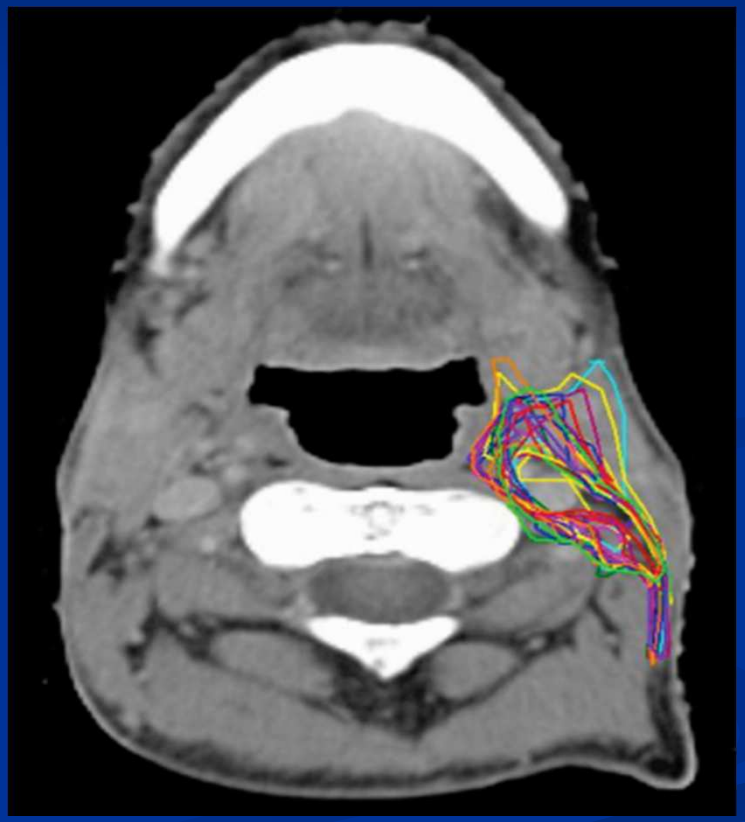
Level I | Level II | Level III | Level IV | Level V | Level VI | RP

CT-based delineation of lymph node levels and related CTVs in the node-negative neck: DAHANCA, EORTC, GORTEC, NCIC, RTOG consensus guidelines

Vincent Grégoire[a,*,1], Peter Levendag[b,1], Kian K. Ang[c], Jacques Bernier[d], Marijel Braaksma[b], Volker Budach[e], Cliff Chao[c], Emmanuel Coche[f], Jay S. Cooper[c], Guy Cosnard[f], Avraham Eisbruch[c], Samy El-Sayed[g], Bahman Emami[c], Cai Grau[h], Marc Hamoir[i], Nancy Lee[c], Philippe Maingon[j], Karin Muller[b], Hervé Reychler[k]

H&N IMRT practice heterogeneity among Dutch Radiation Oncologists





Rasch et al., 2007

VAR

Steps…

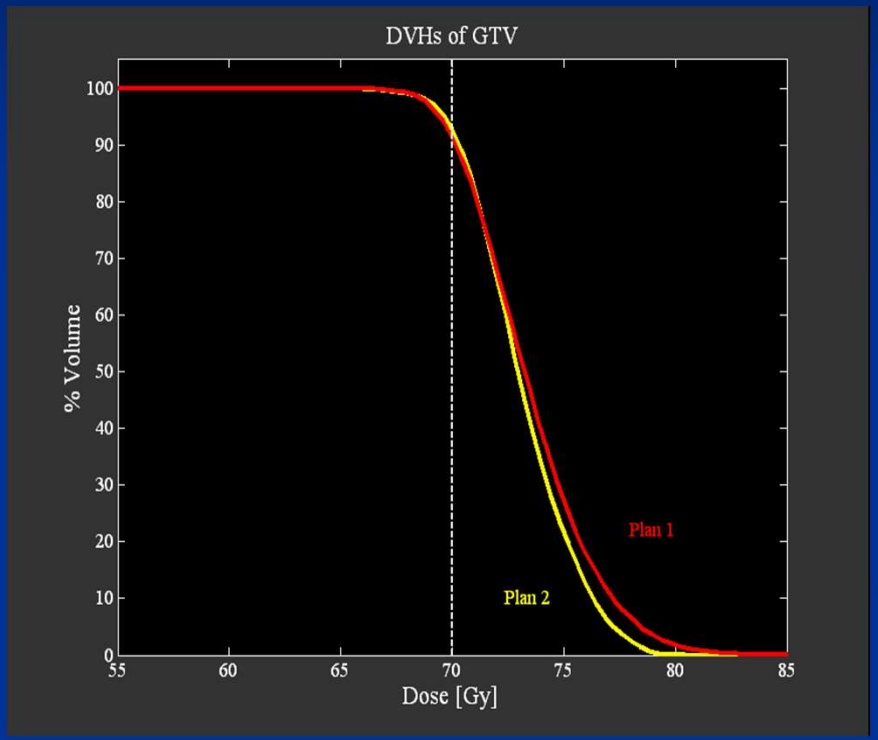
Dose volume histograms (DVHs)

Accurate calculation of DVHs

Biological indices (e.g., normal tissue complication probability)

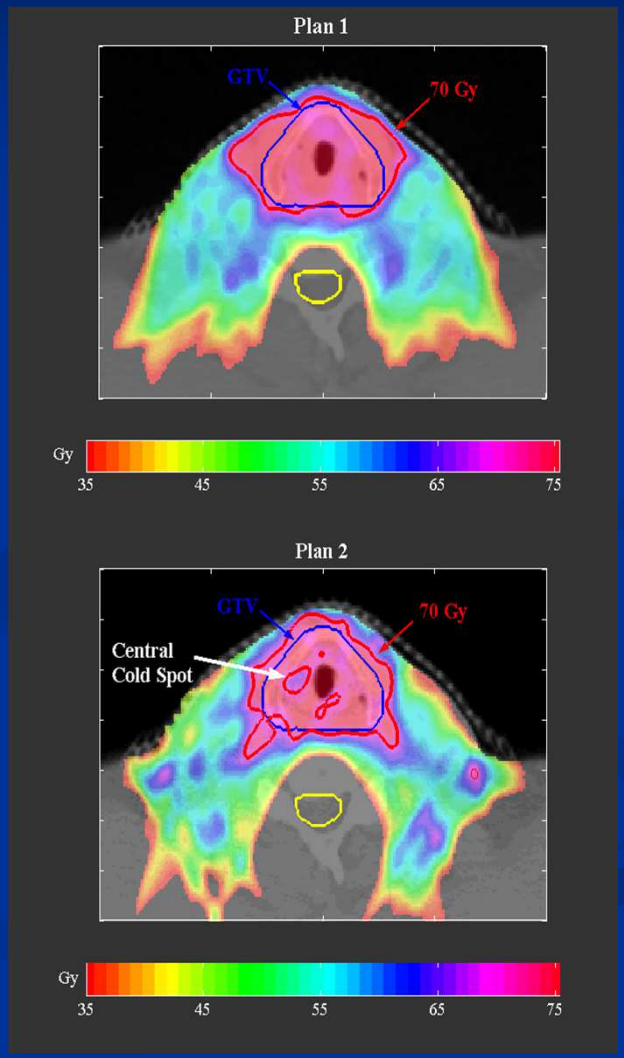
Mandate the inclusion of the entire extent of the relevant structures

What does an IMRT DVH tell us?



Plan1 has peripheral cold spots
Plan2 has central cold spots

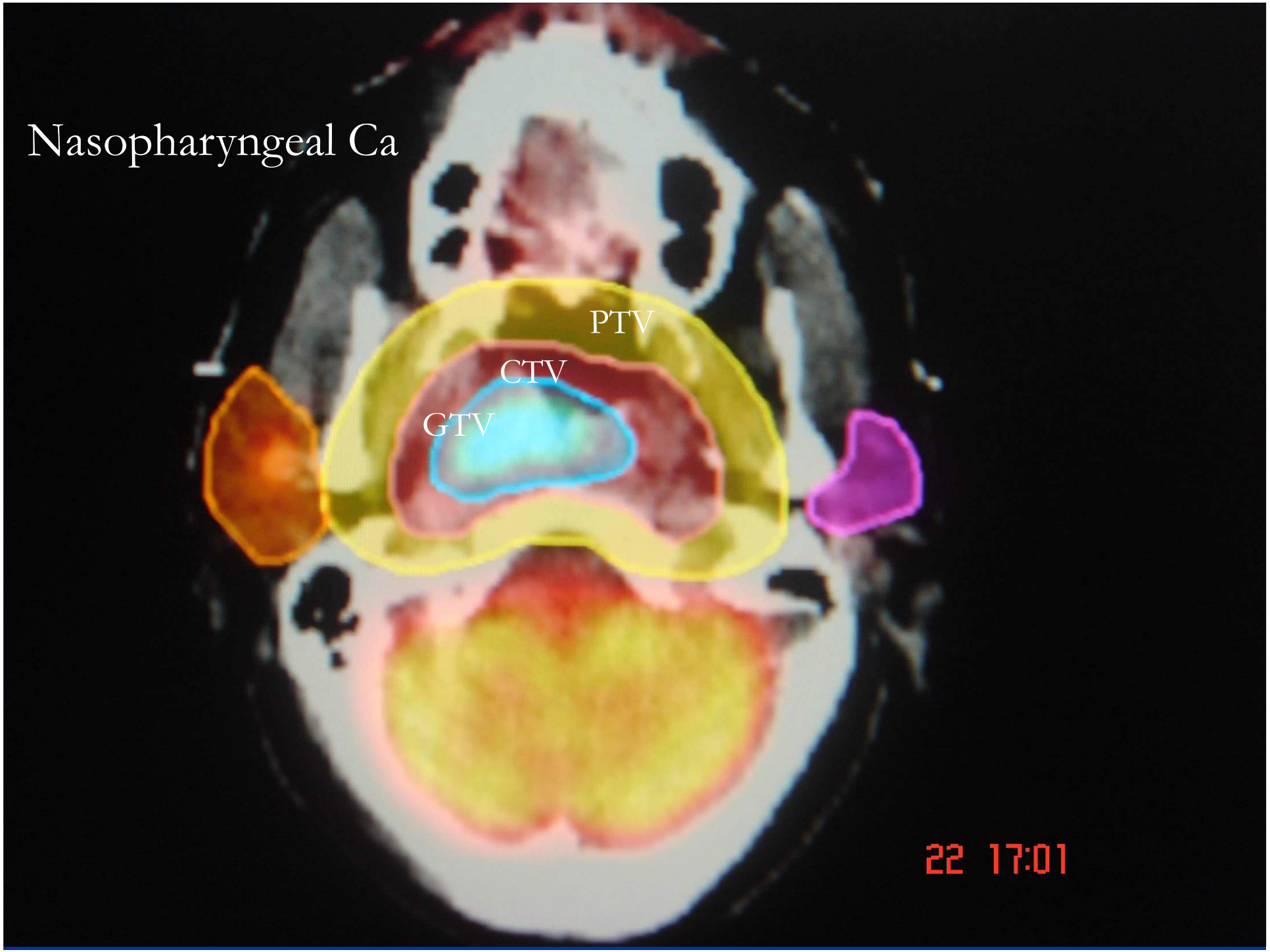
It is all the same to a DVH : Therefore, it is imperative that the dose distribution is reviewed on trans-axial CT slices

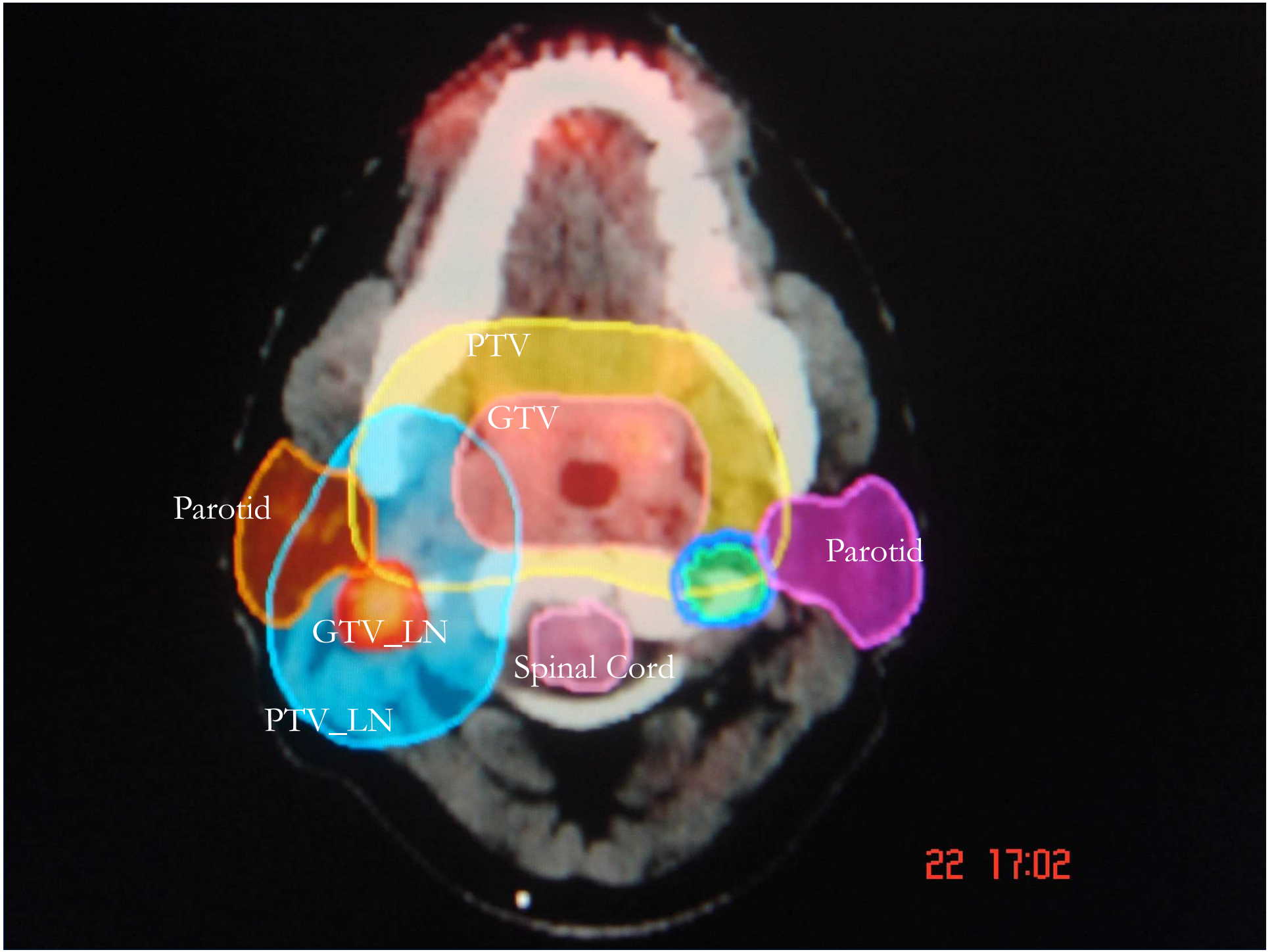


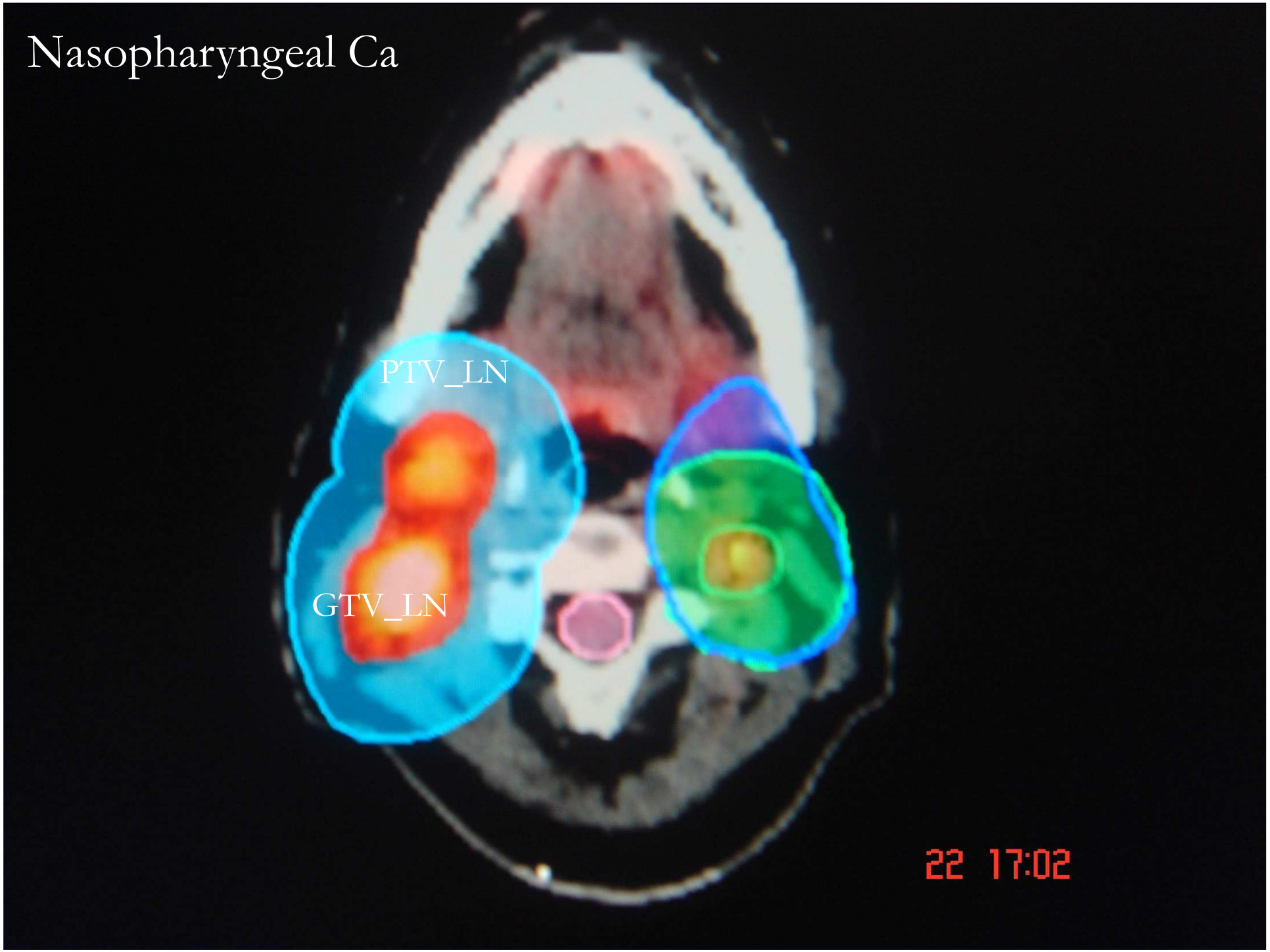
VAR

Normal tissues Contouring…

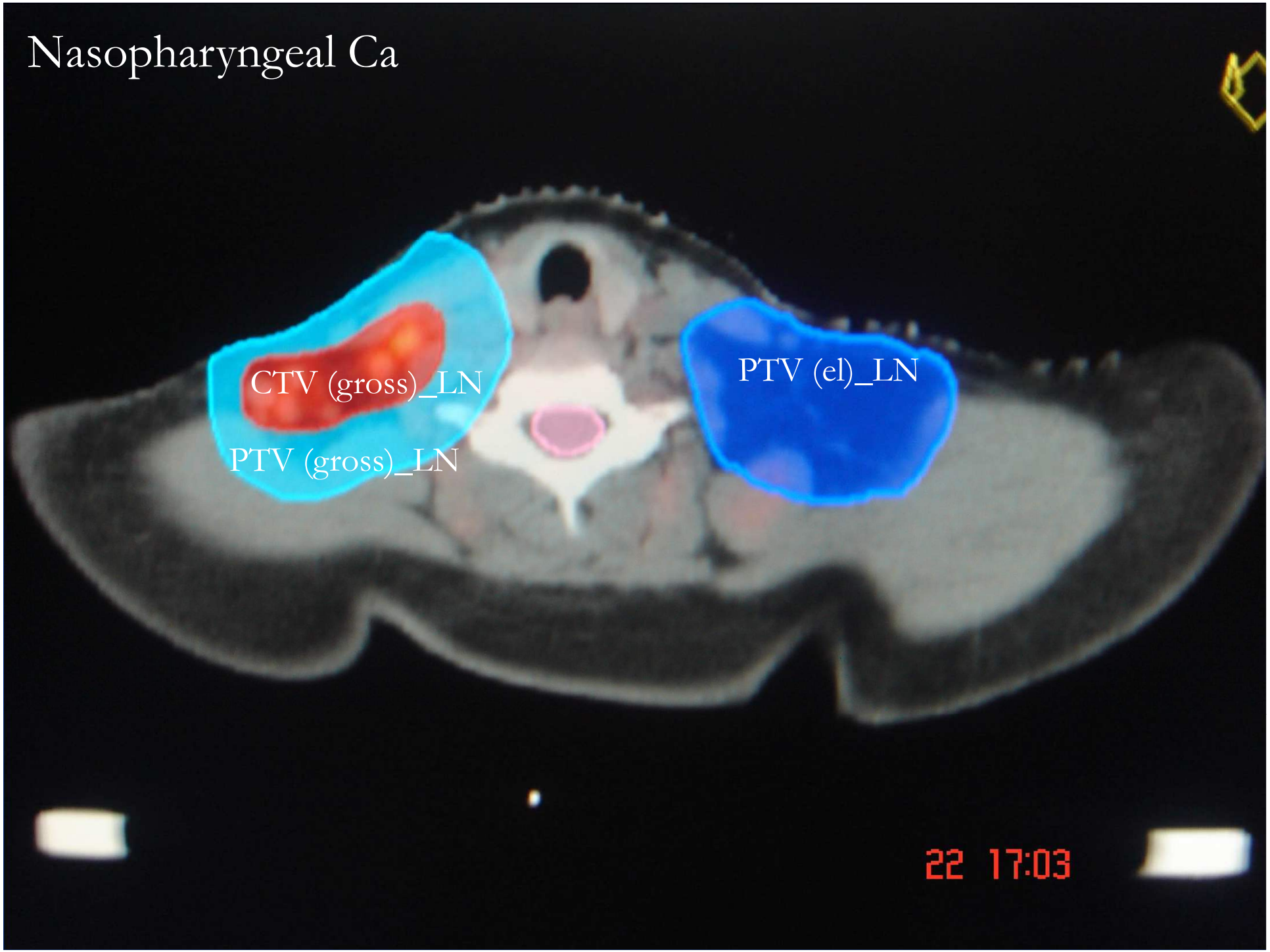
- Parotid glands
- Spinal cord
- Brainstem
- Cochlea
- Optical structures
- Pituitary gland

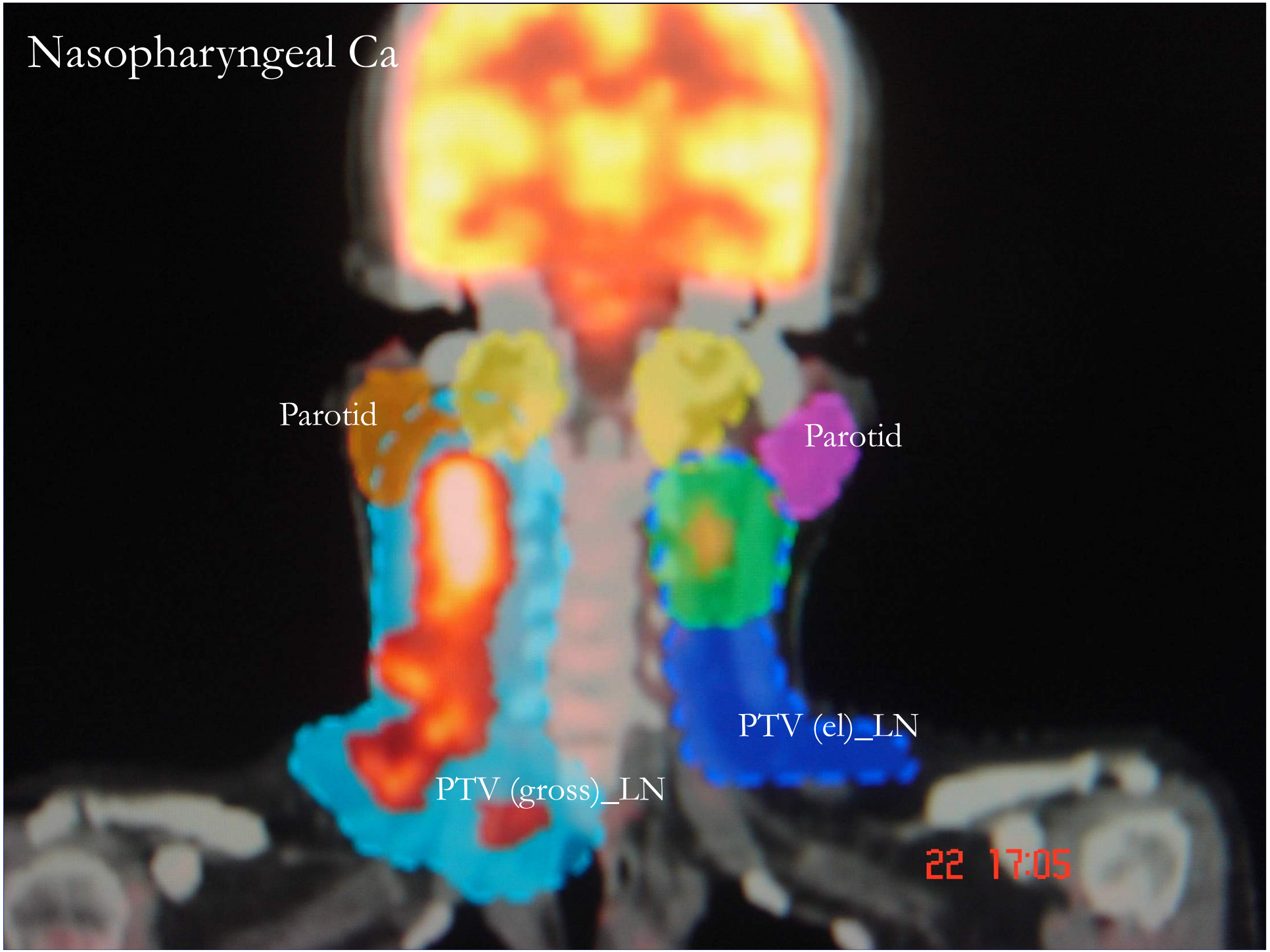

Nasopharyngeal Ca
PTV
CTV
GTV
22 17:01

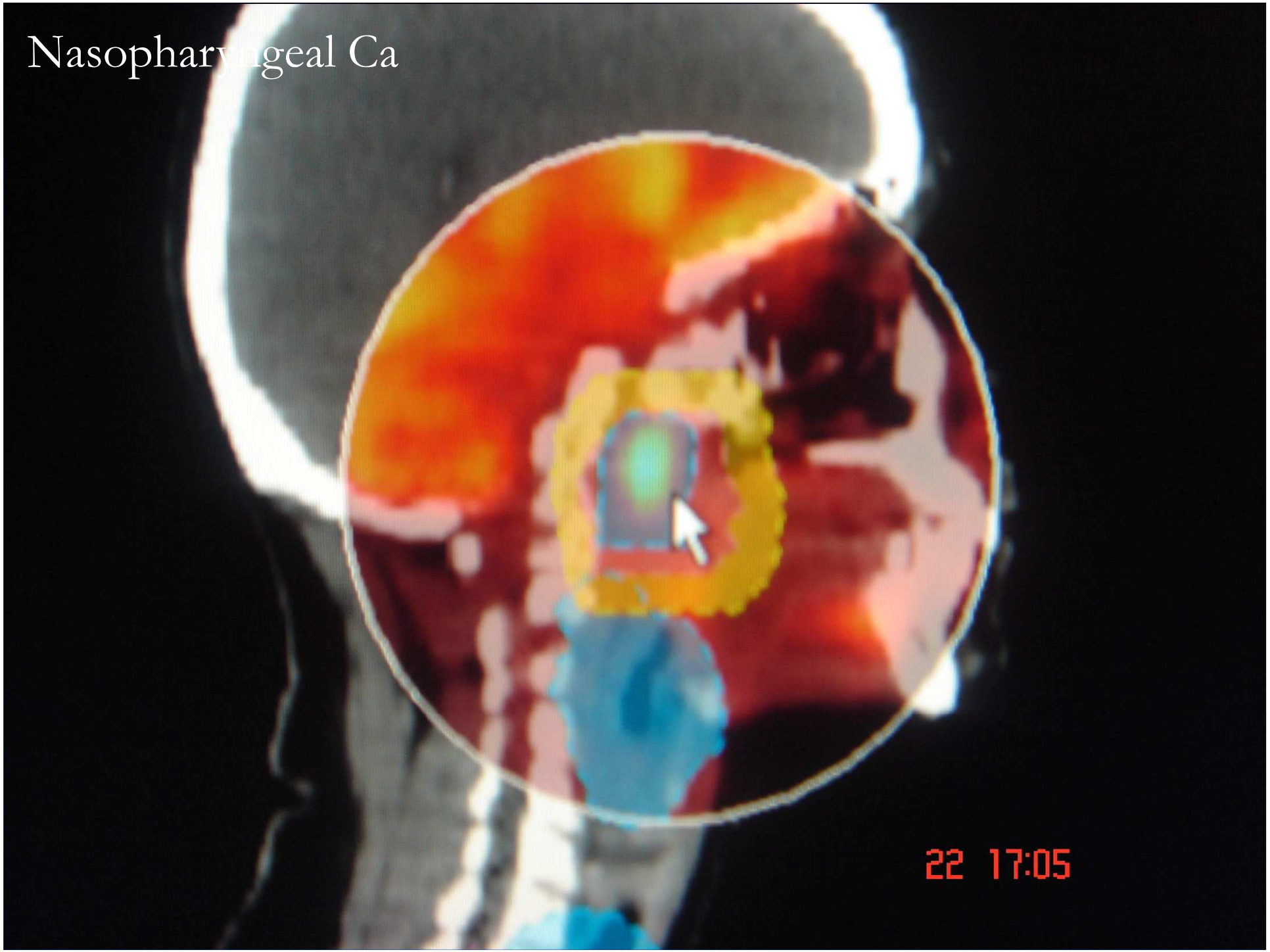

PTV
GTV
Parotid
Parotid
GTV_LN
Spinal Cord
PTV_LN
22 17:02

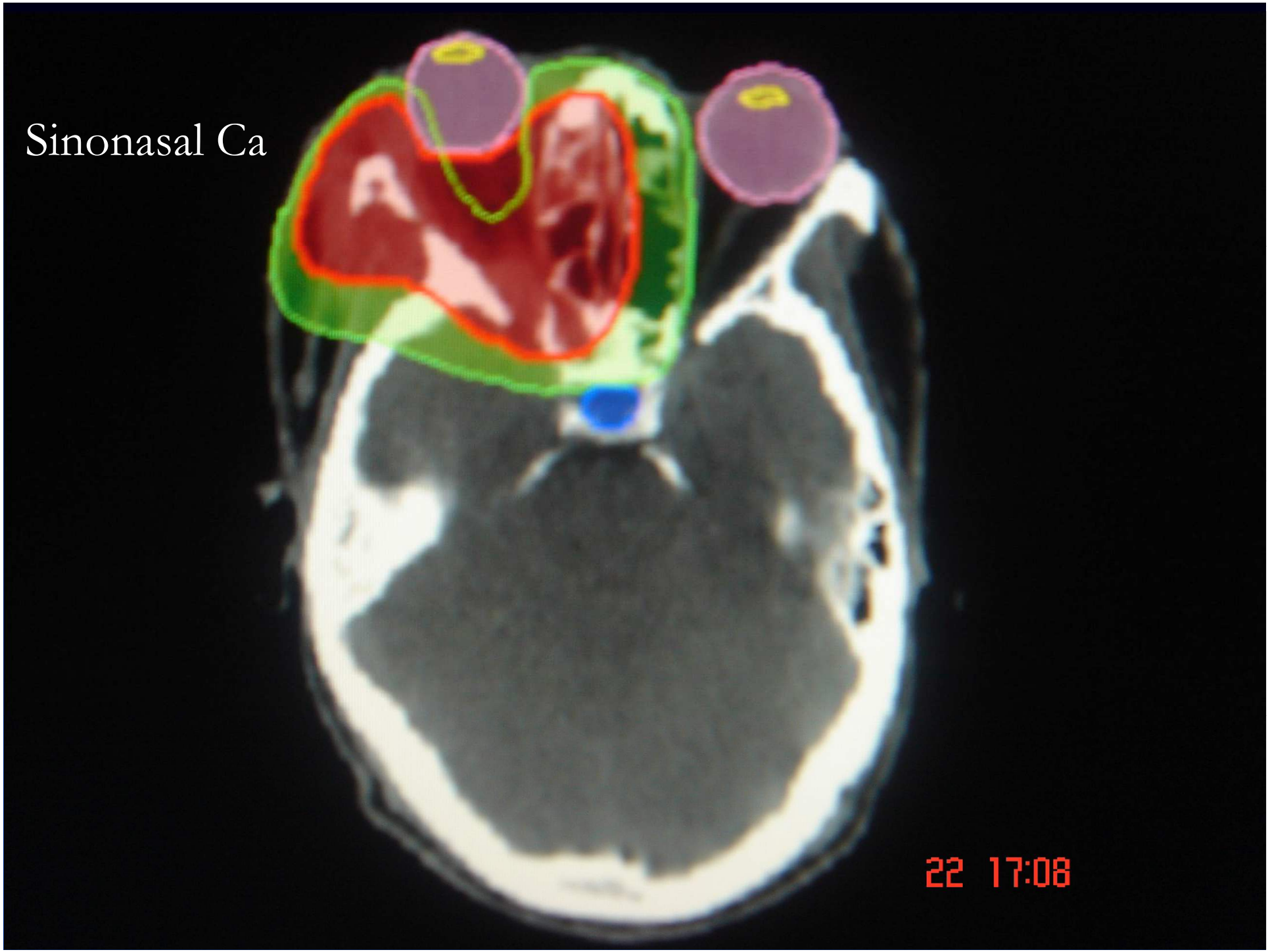

Nasopharyngeal Ca
PTV_LN
GTV_LN
22 17:02

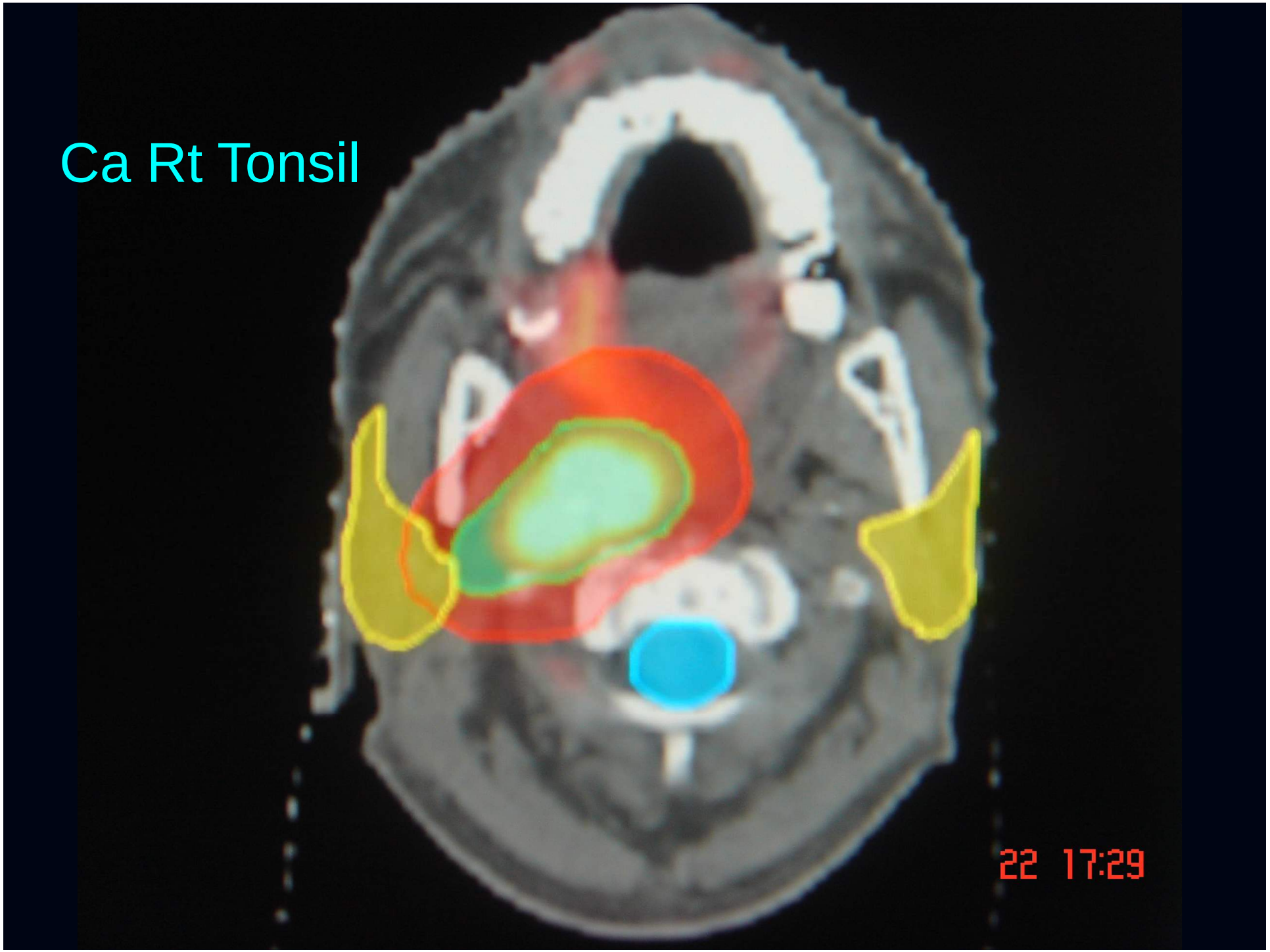
Nasopharyngeal Ca




Nasopharyngeal Ca
Parotid
Parotid
PTV (el)_LN
PTV (gross)_LN
22 17:05


Nasopharyngeal Ca
22 17:05


Sinonasal Ca
22 17:08


Ca Rt Tonsil
22 17:29

Discussion with Physicist..

Communicating pertinent information

- Brief clinical findings
- Location of the primary
- Adenopathy
- High risk regions
- Adjacent critical structures

IMRT
Head & Neck studies

LANDMARK PUBLICATIONS ON IMRT IN H&N CANCERS

CLINICAL INVESTIGATION — **Head and Neck**

XEROSTOMIA AND ITS PREDICTORS FOLLOWING PAROTID-SPARING IRRADIATION OF HEAD-AND-NECK CANCER

AVRAHAM EISBRUCH, M.D.,* HYUNGJIN M. KIM, SC.D.,† JEFFREY E. TERRELL, M.D.,‡

CLINICAL INVESTIGATION — **Head and Neck**

INTENSITY-MODULATED RADIATION THERAPY FOR HEAD-AND-NECK CANCER: THE UCSF EXPERIENCE FOCUSING ON TARGET VOLUME DELINEATION

NANCY LEE, M.D.,* PING XIA, PH.D.,* NANCY J. FISCHBEIN, M.D.,† PAM AKAZAWA, C.M.D.,*

CLINICAL INVESTIGATION — **Head and Neck**

DYSPHAGIA AND ASPIRATION AFTER CHEMORADIOTHERAPY FOR HEAD-AND-NECK CANCER: WHICH ANATOMIC STRUCTURES ARE AFFECTED AND CAN THEY BE SPARED BY IMRT?

AVRAHAM EISBRUCH, M.D.,* MARCO SCHWARTZ, M.SC.,† COEN RASCH, M.D.,†

CLINICAL INVESTIGATION — **Head and Neck**

DETERMINATION AND DELINEATION OF NODAL TARGET VOLUMES FOR HEAD-AND-NECK CANCER BASED ON PATTERNS OF FAILURE IN PATIENTS RECEIVING DEFINITIVE AND POSTOPERATIVE IMRT

K. S. CLIFFORD CHAO, M.D.,* FRANZ J. WIPPOLD, II, M.D.,† GOKHAN OZYIGIT, M.D.,*

CLINICAL INVESTIGATION — **Head and Neck**

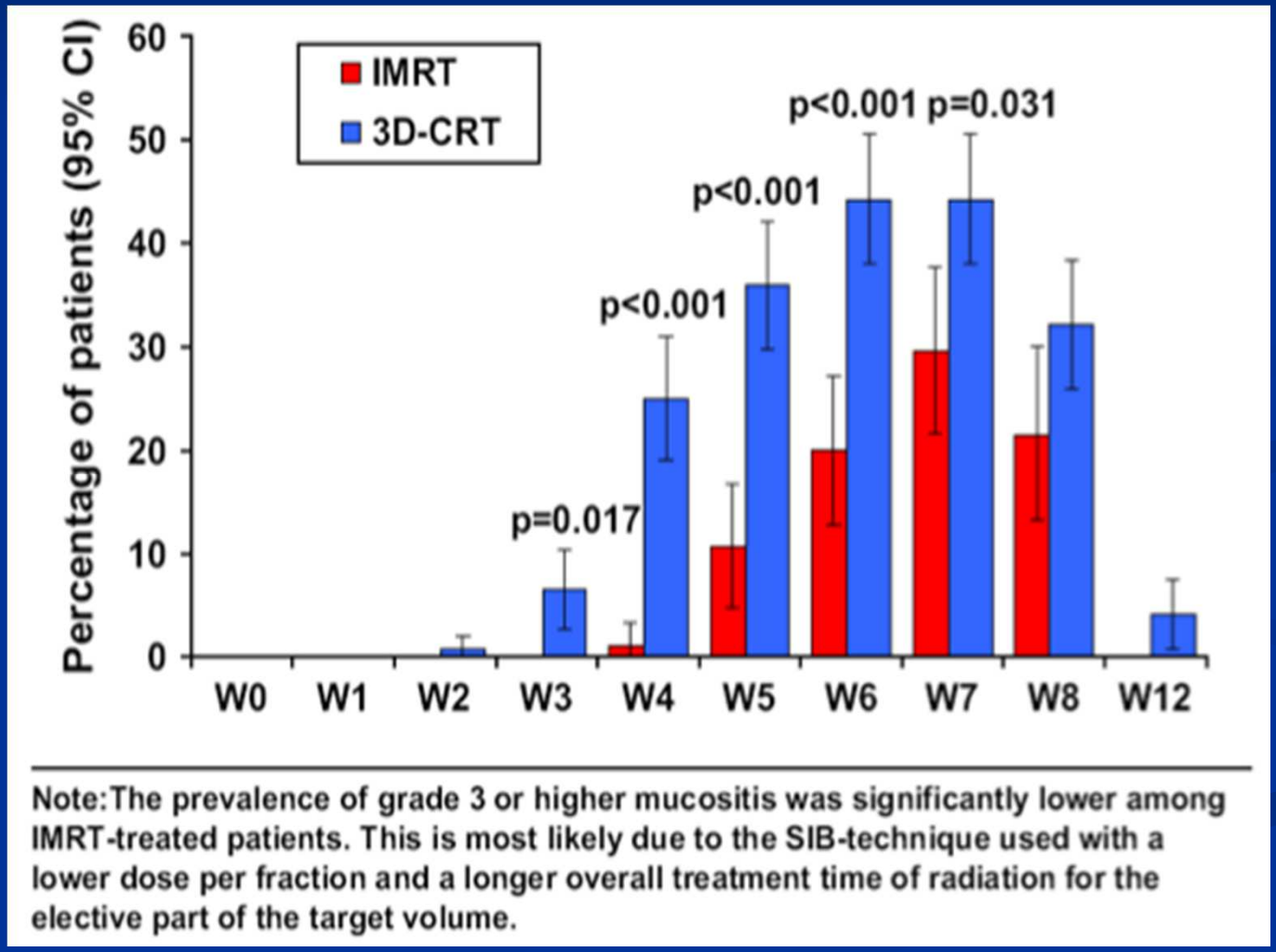
RECURRENCES NEAR BASE OF SKULL AFTER IMRT FOR HEAD-AND-NECK CANCER: IMPLICATIONS FOR TARGET DELINEATION IN HIGH NECK AND FOR PAROTID GLAND SPARING

AVRAHAM EISBRUCH, M.D.,* LON H. MARSH, C.M.D.,* LAURA A. DAWSON, M.D.,*

VAR

Acute toxicity with IMRT

≥ grade 3 mucositis: IMRT vs 3D-CRT

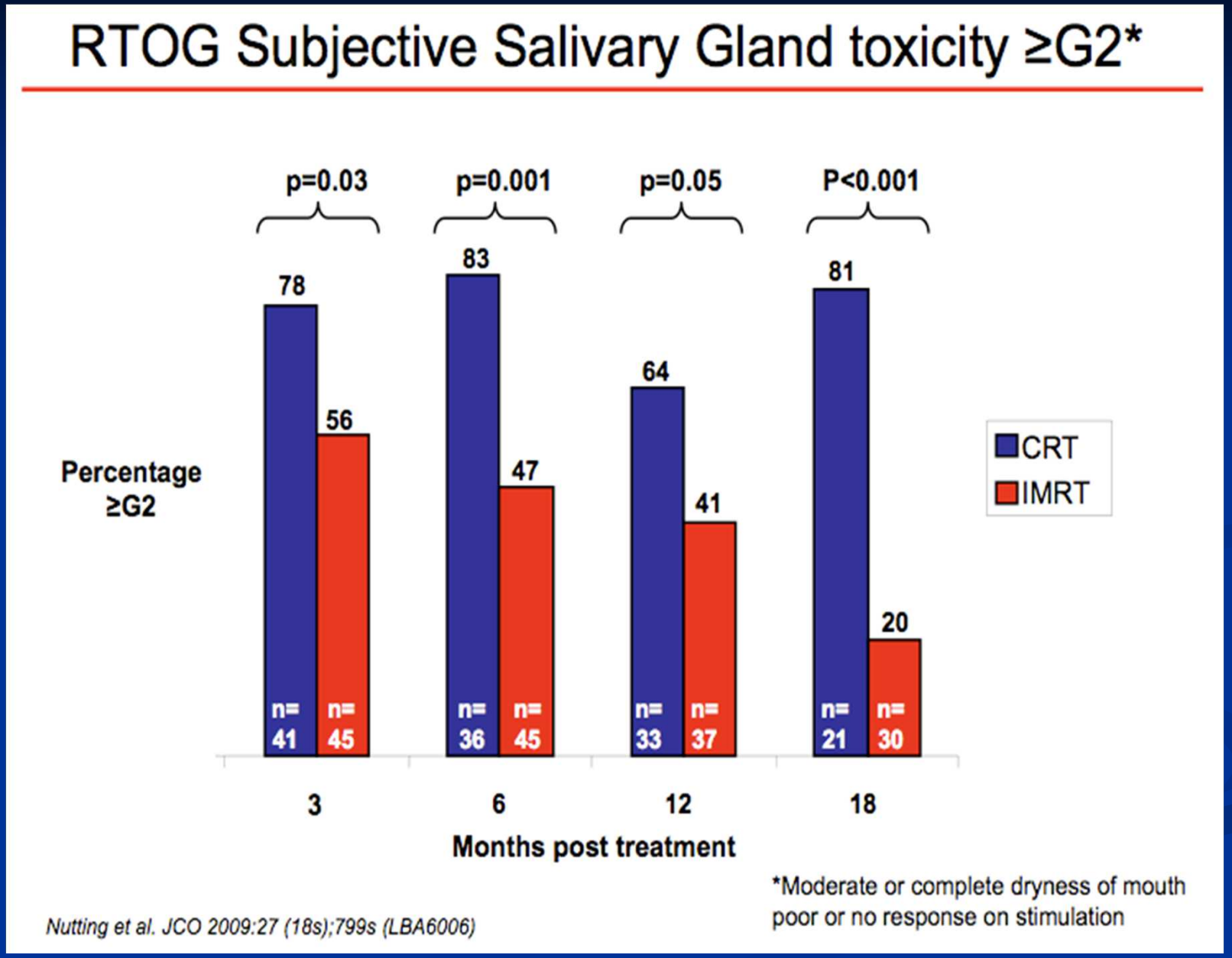


Note:The prevalence of grade 3 or higher mucositis was significantly lower among IMRT-treated patients. This is most likely due to the SIB-technique used with a lower dose per fraction and a longer overall treatment time of radiation for the elective part of the target volume.

VAR

Vergeer, 2009

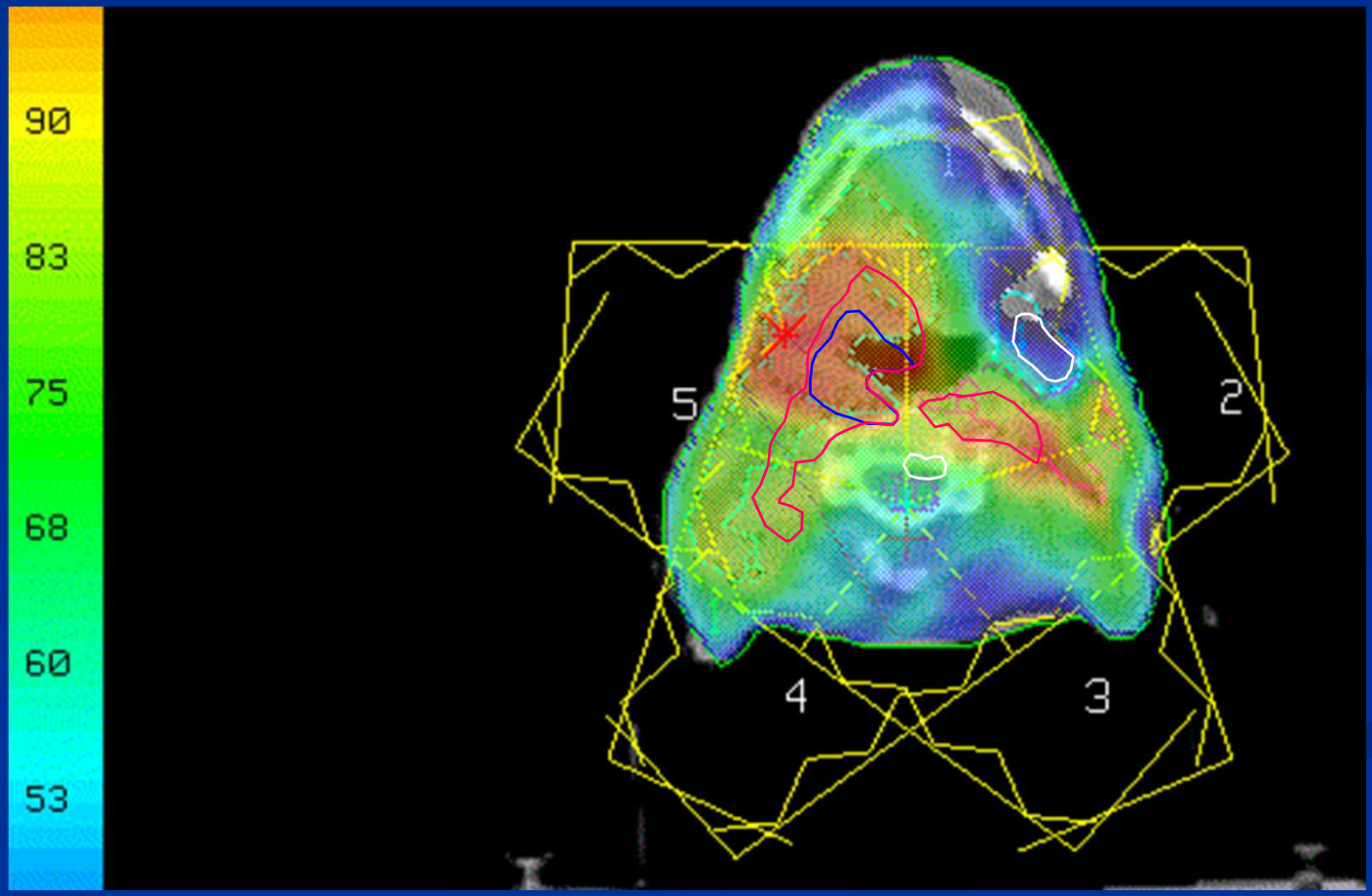
Parotid gland sparing in IMRT for HNSCC



VAR

Nutting, 2009

IMRT - Reduction of Xerostomia in Oropharyngeal Tumors



VAR

Parotid-sparing intensity modulated versus conventional radiotherapy in head and neck cancer (PARSPORT): a phase 3 multicentre randomised controlled trial

*Christopher M Nutting, James P Morden, Kevin J Harrington, Teresa Guerrero Urbano, Shreerang A Bhide, Catharine Clark, Elizabeth A Miles, Aisha B Miah, Kate Newbold, MaryAnne Tanay, Fawzi Adab, Sarah J Jefferies, Christopher Scrase, Beng K Yap, Roger P A'Hern, Mark A Sydenham, Marie Emson, Emma Hall, on behalf of the PARSPORT trial management group**

Summary

Background Xerostomia is the most common late side-effect of radiotherapy to the head and neck. Compared with conventional radiotherapy, intensity-modulated radiotherapy (IMRT) can reduce irradiation of the parotid glands. We assessed the hypothesis that parotid-sparing IMRT reduces the incidence of severe xerostomia.

Methods We undertook a randomised controlled trial between Jan 21, 2003, and Dec 7, 2007, that compared conventional radiotherapy (control) with parotid-sparing IMRT. We randomly assigned patients with histologically confirmed pharyngeal squamous-cell carcinoma (T1–4, N0–3, M0) at six UK radiotherapy centres between the two radiotherapy techniques (1:1 ratio). A dose of 60 or 65 Gy was prescribed in 30 daily fractions given Monday to Friday. Treatment was not masked. Randomisation was by computer-generated permuted blocks and was stratified by centre and tumour site. Our primary endpoint was the proportion of patients with grade 2 or worse xerostomia at 12 months, as assessed by the Late Effects of Normal Tissue (LENT SOMA) scale. Analyses were done on an intention-to-treat basis, with all patients who had assessments included. Long-term follow-up of patients is ongoing. This study is registered with the International Standard Randomised Controlled Trial register, number ISRCTN48243537.

Findings 47 patients were assigned to each treatment arm. Median follow-up was 44·0 months (IQR 30·0–59·7). Six patients from each group died before 12 months and seven patients from the conventional radiotherapy and two from the IMRT group were not assessed at 12 months. At 12 months xerostomia side-effects were reported in 73 of 82 alive patients; grade 2 or worse xerostomia at 12 months was significantly lower in the IMRT group than in the conventional radiotherapy group (25 [74%; 95% CI 56–87] of 34 patients given conventional radiotherapy *vs* 15 [38%; 23–55] of 39 given IMRT, p=0·0027). The only recorded acute adverse event of grade 2 or worse that differed significantly between the treatment groups was fatigue, which was more prevalent in the IMRT group (18 [41%; 99% CI 23–61] of 44 patients given conventional radiotherapy *vs* 35 [74%; 55–89] of 47 given IMRT, p=0·0015). At 24 months, grade 2 or worse xerostomia was significantly less common with IMRT than with conventional radiotherapy (20 [83%; 95% CI 63–95] of 24 patients given conventional radiotherapy *vs* nine [29%; 14–48] of 31 given IMRT; p<0·0001). At 12 and 24 months, significant benefits were seen in recovery of saliva secretion with IMRT compared with conventional radiotherapy, as were clinically significant improvements in dry-mouth-specific and global quality of life scores. At 24 months, no significant differences were seen between randomised groups in non-xerostomia late toxicities, locoregional control, or overall survival.

Interpretation Sparing the parotid glands with IMRT significantly reduces the incidence of xerostomia and leads to recovery of saliva secretion and improvements in associated quality of life, and thus strongly supports a role for IMRT in squamous-cell carcinoma of the head and neck.

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See Comment page 110

*Details given in the webappendix (p 2)

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Table 1. Locoregional Control After IMRT for Head and Neck Cancer

Study	No. of Patients	Primary Site	RT		Follow-Up (months)		Control		
			Definitive	Postoperative	Median	Range	Local (%)	Regional (%)	Interval (years)
Chao et al[19]	126	Various	52	74	26	12-55		85	2
Lee et al[5]	67	NPX	67	0	31	7-72		98	4
Chao et al[20]	74	OPX	31	43	33	9-60		87	4
Eisbruch et al*[21]	133	Various, non-NPX	60	73	32	6-107		82	3
Kam et al[33]	63	NPX	63	0	29	8-45	92	98	3
Kwong et al[34]	33	NPX	33	0	29	11-42	100	92	3

Abbreviations: IMRT, intensity-modulated radiotherapy; RT, radiotherapy; NPX, nasopharynx; OPX, oropharynx.

*Patients treated from 1994 to 2002; three-dimensional conformal radiotherapy was used before 1996, and IMRT thereafter.

JCO, 2006

IMRT ± Chemo for NPC
(Single Institutions)

Center	N	Stage	FU (mo)	LC	DM-Free
Bucci IJROBP, 2004(abs)	118	50% T3-4	30	96% (4-year data)	72%
Kam IJROBP, 2004	63	51% T3-4	29	92% (3-year data)	79%
Wolden IJROBP, 2006	74	51% T3-4	35	91% (3-year data)	78%

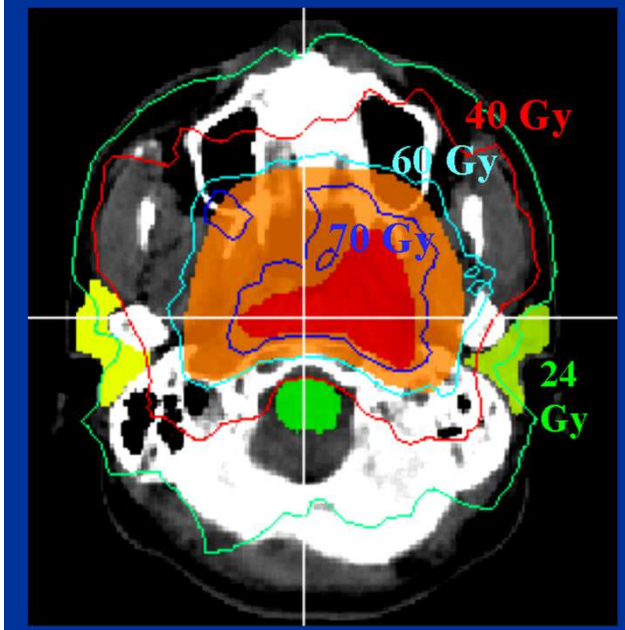
VAR

IMRT for NPC
RTOG Protocol H-0225 (Lee & Garden)

Stage: I-IVb

Histology:

WHO I-III



R E G I S T E R

IMRT:

2.12 Gy/F/d X 33 F
to ≥ 95% of GTV

1.8 Gy/F/d X 33 F
to ≥ 95% of CTV

Chemotherapy (≥T2b or N+)

Concurrent: Cisplatin x 3

Adjuvant: Cisplatin + 5-FU

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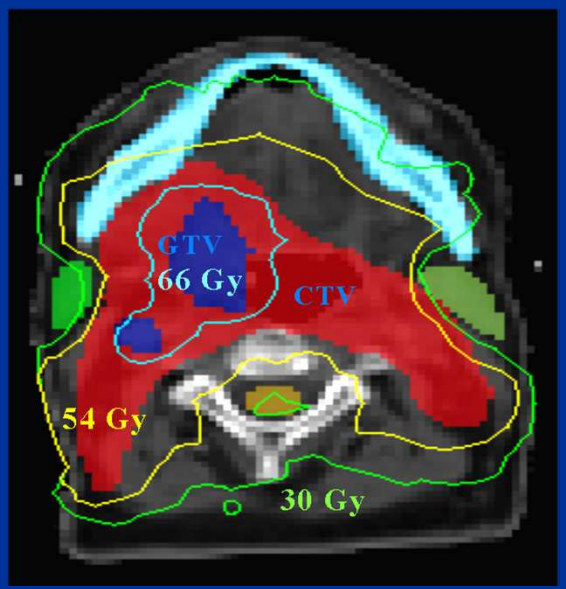
IMRT for Oropharyngeal SCC

RTOG Protocol H-0022 (Eisbruch & Chao)

Stage: T1-2 N-1

Site:
Tonsil, BOT, Soft Palate



R E G I S T E R

Gross disease PTV:

66 Gy/30 FX

Subclinical disease PTV:

54-60 Gy/30 FX

Boost of 4-6 Gy/2-3 FX to the tumor PTV allowed

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RTOG 0022 – ASTRO 2006

- Study population: 67 patients (14 centers)
- Tumor: tongue base-20 (39%),
  tonsil-33 (49%), soft palate 8 (12%)
- Stage: T1-25%, T2-75%; N0-57%, N1-43%
- Median follow-up: 1.6 (0.2-3.8) years
- LR progression: 3 patients (4.9%)
- No metastatic disease observed

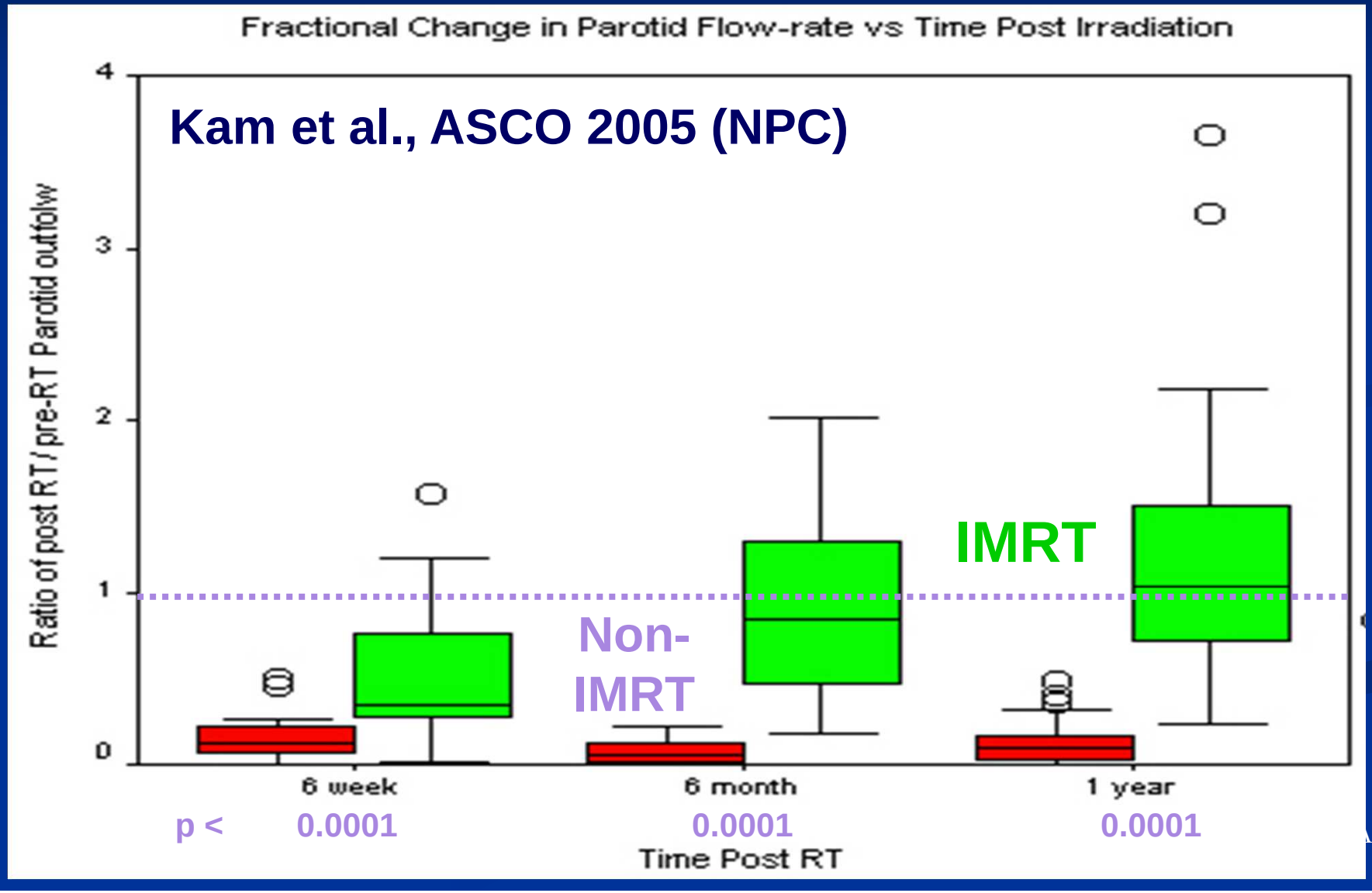
A Eisbruch, J Harris, A Garden, C Chao, W Straube, C Schultz, G Sanguineti, C Jones, W Bosch, K Ang

IMRT for Oropharynx Cancer

- 2000-June 2003: 133 patients
- Age: 30-75 (53) years; 85% male
- Site: tonsil-52%; tongue base-40%
- T1-2(x): 114; T3-4: 19
- Chemotherapy: 28 (T3-4 or N2-3)
- 3-Y local control: 95%
- 3-Y overall survival: 93%

Garden et al., 2005

Recovery of Saliva Flow (A vs C)



Advantages – Variable doses

- Boosting doses within targets

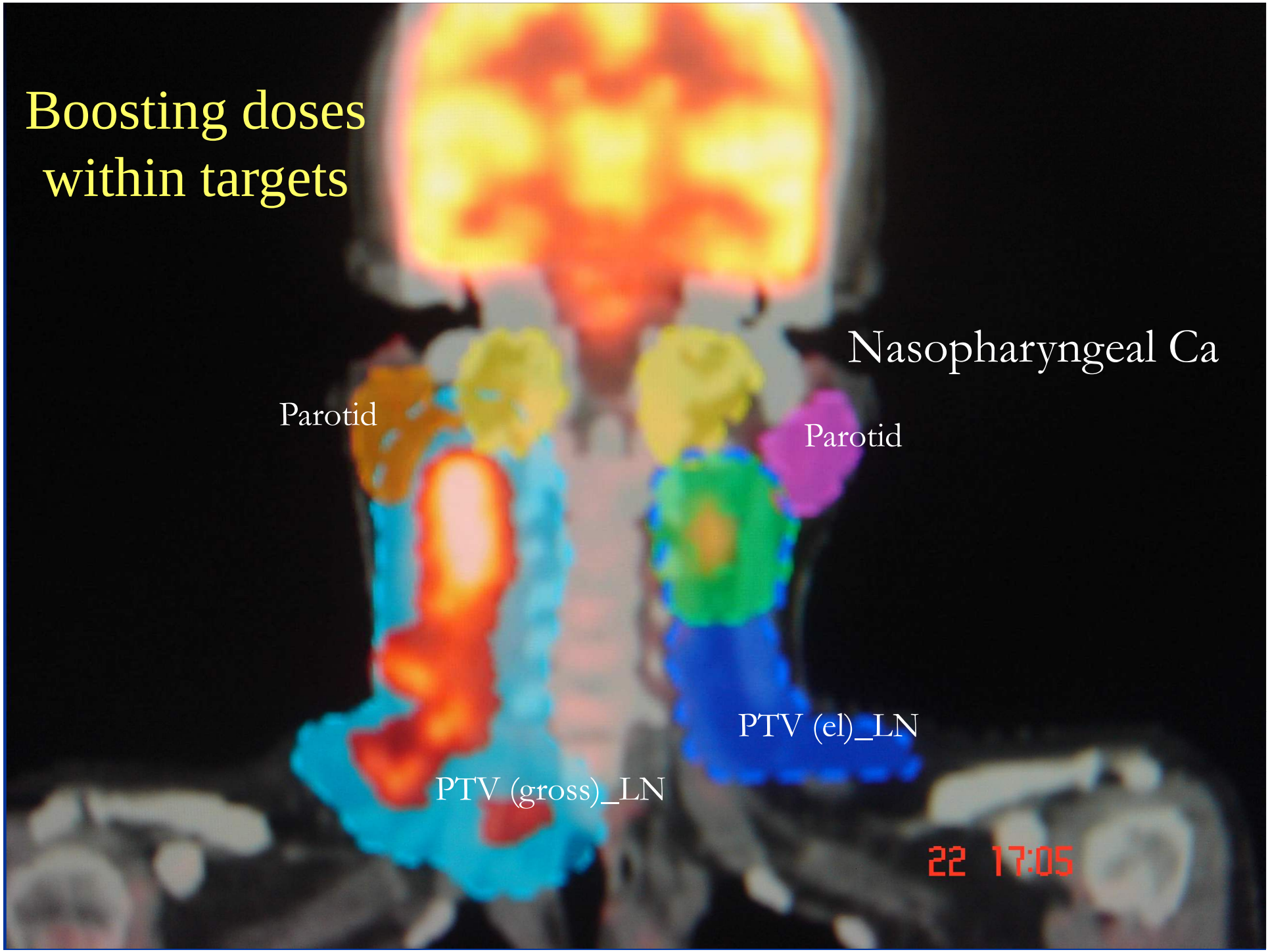
  Diff doses per fraction to multiple target vol within a treatment field.

- Simultaneous Integrated Boost

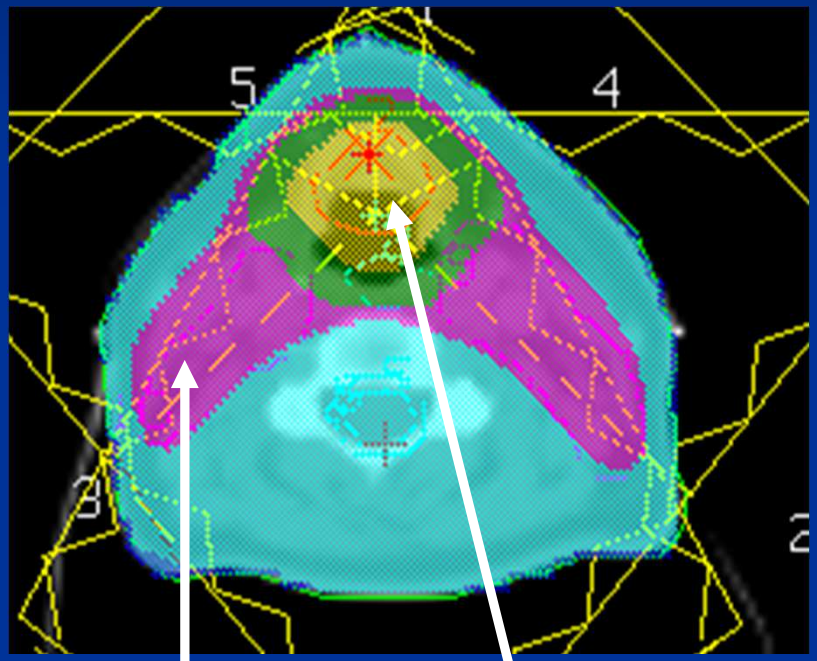
  Concomitantly with standard doses to the remainder of targets

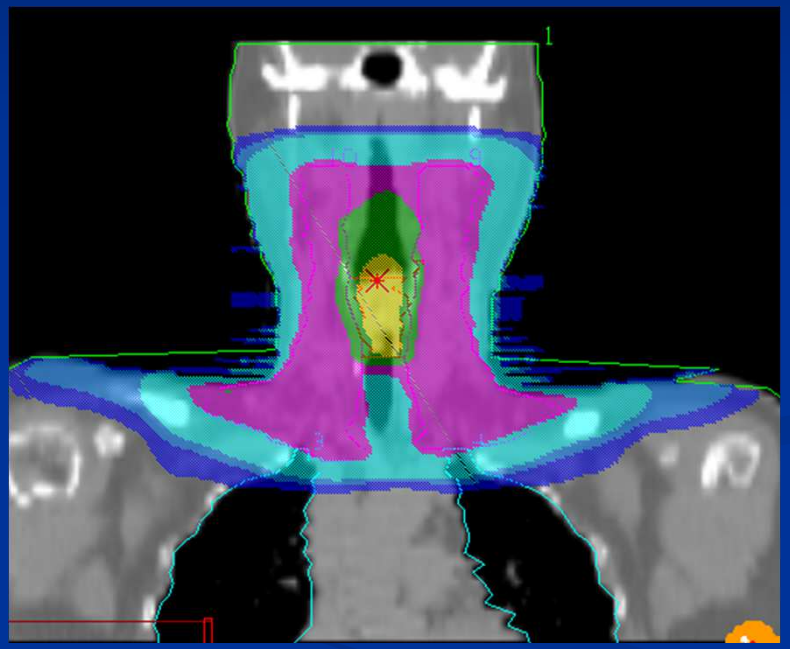
- 70Gy vs 45-55Gy within the target vol

VAR


Boosting doses within targets
Nasopharyngeal Ca
Parotid
Parotid
PTV (el)_LN
PTV (gross)_LN
22 17:05

IMRT dose distribution - SIB





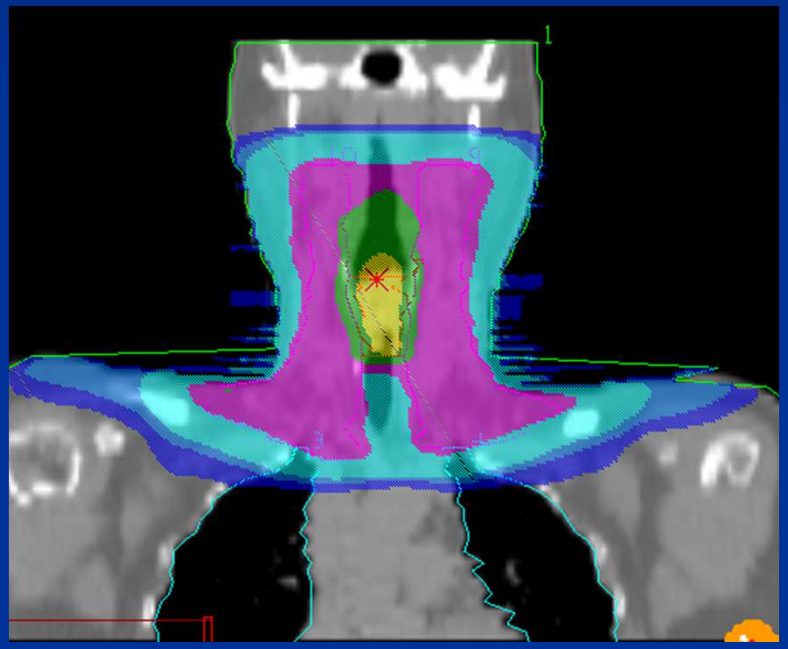
1.8Gy/# 2.25Gy/# X 28#

Dose 50.4 and 63 Gy

- Single-phase plan
- 10-15 minutes to deliver

VAR

Advantages of I M R T…



•Single-phase plan

•No electrons

Eliminate the need for standard fields

- Low anterior neck field
- Electron boost

Advantages of I M R T…

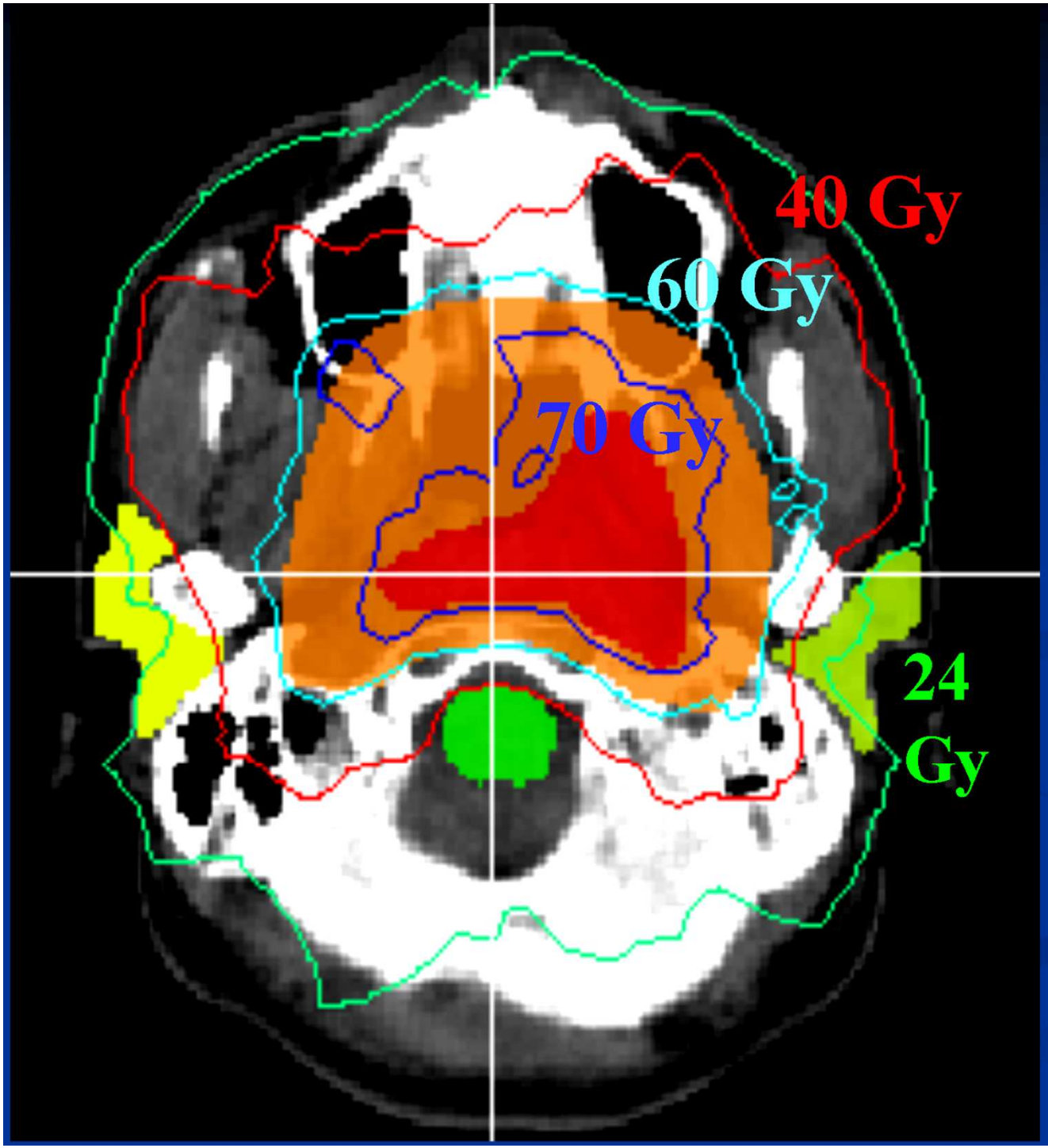
Re-treatment

Re-treatment of radiated H&N ca Possible due to its ability to spare adjacent normal tissues with acceptable target dose uniformity.

Sparing of normal tissues

Uninvolved tissue sparing of multiple sites to reduce short and long term side effects

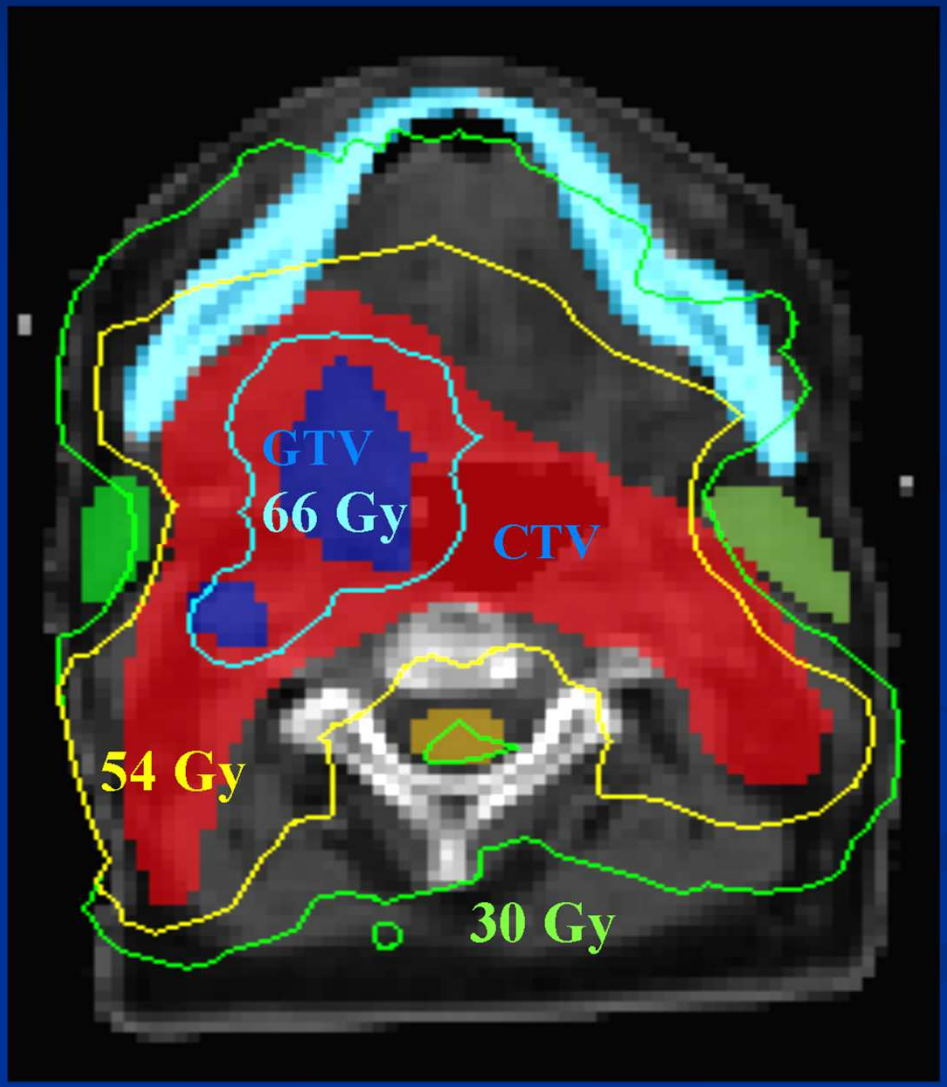
- Major and minor salivary glands, most notably parotids, mandible, oral cavity, larynx and pharynx.
- Critical structures - Cochlea, temporal lobes, optic pathways, spinal cord, brainstem & brain



IMRT Ca NP

VAR

IMRT - Ca Oropharynx



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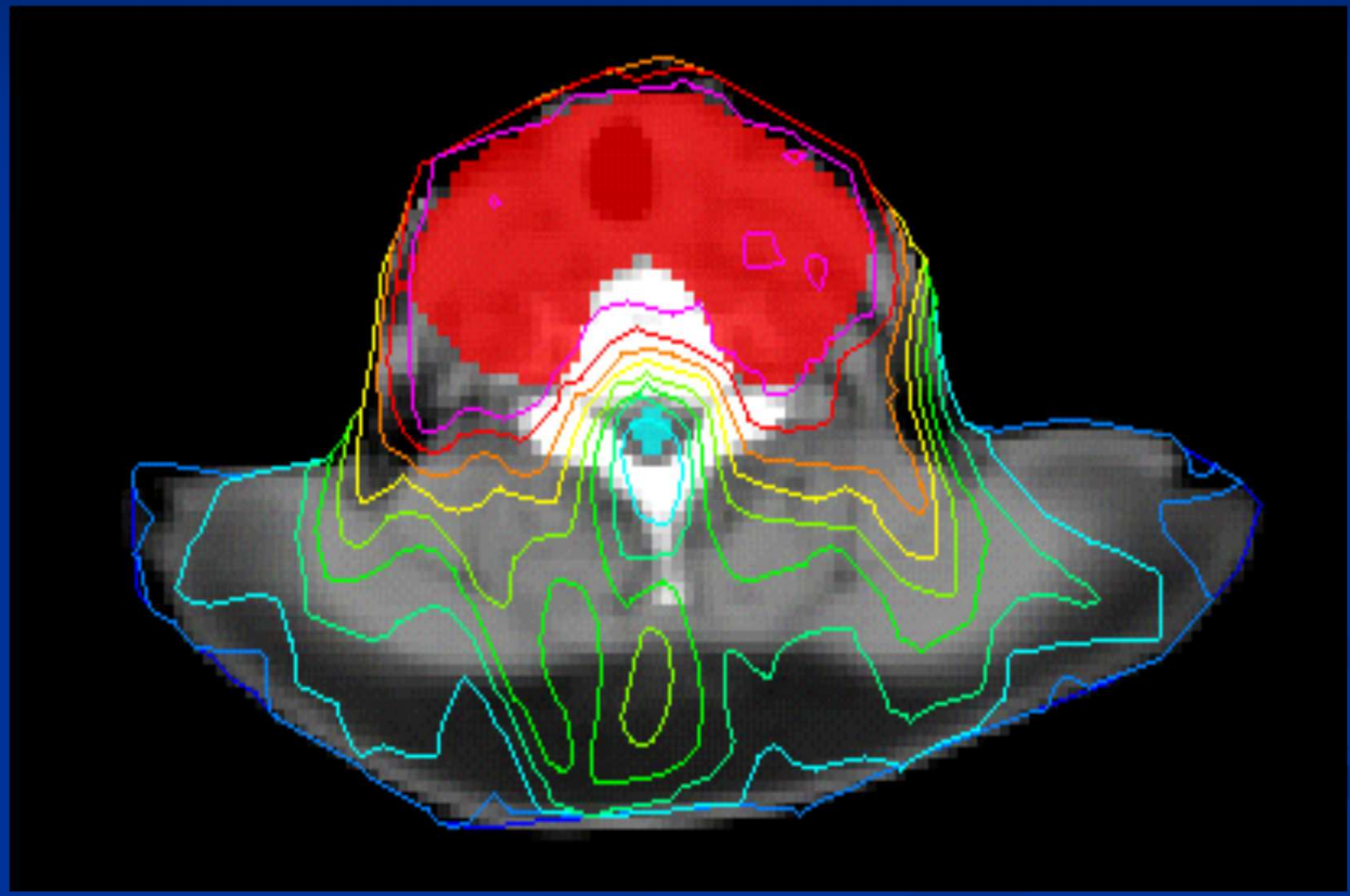
IMRT - Thyroid



VAR

Maxillary Antrum

Comparison of treatments

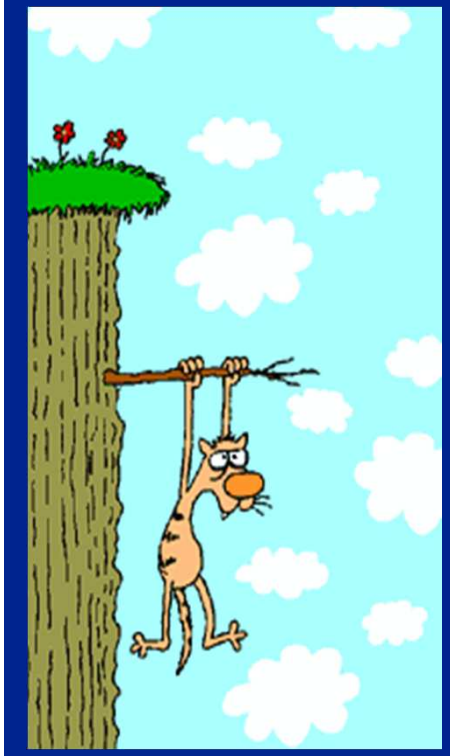
		conv RT	3DCRT	IMRT
PTV	Min (Gy)	56.4	56.3	55.8
	Max (Gy)	69.9	69.9	69.7
	%V<95%	14.7	15.1	8.5
	%V>105%	15.4	15.8	9.1
c/l Opt Nerve	Max (Gy)	65.7	64.2	56.4
i/l Opt Nerve	Max (Gy)	65.7	65.7	58.7
i/l parotid	Mean (Gy)	42.4	27.7	22.8

VAR

Maxillary Antrum : IMRT

- PTV
  - IMRT improved dose homogeneity and target coverage
- OAR
  - IMRT reduced OAR doses
    - I/L Optic nerve by 10% c.f. 3DCRT
    - c/L Optic nerve by 12% c.f. 3DCRT
    - parotid gland to within tolerance

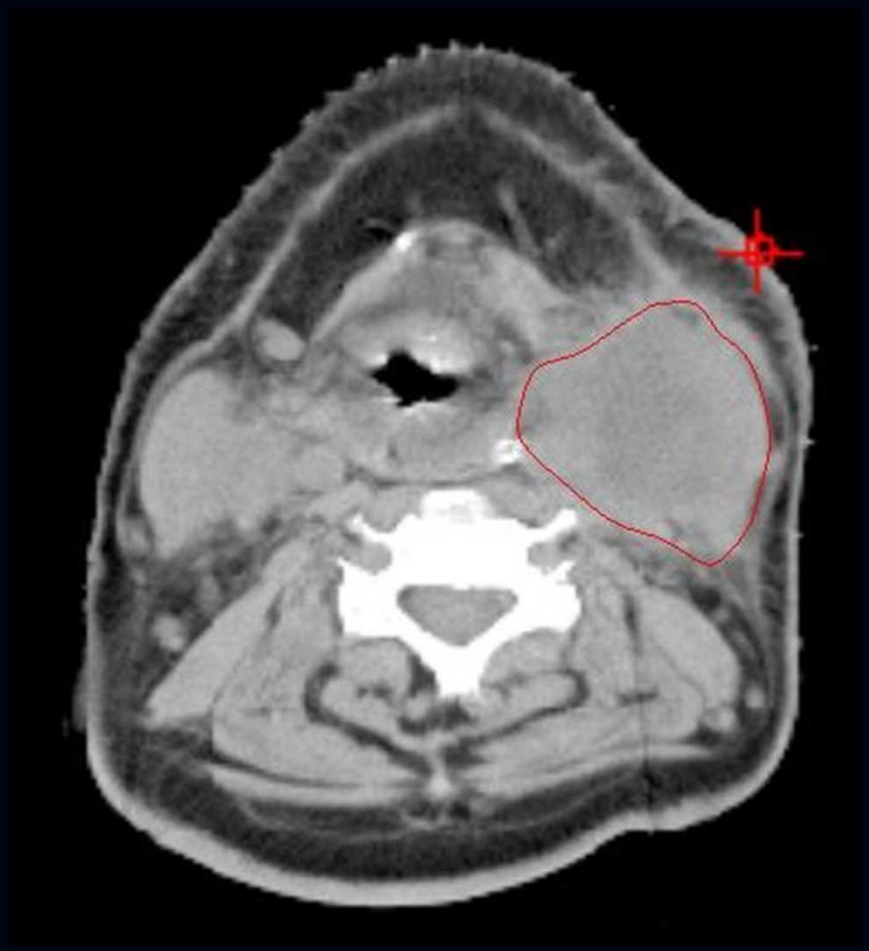
Pit falls ….



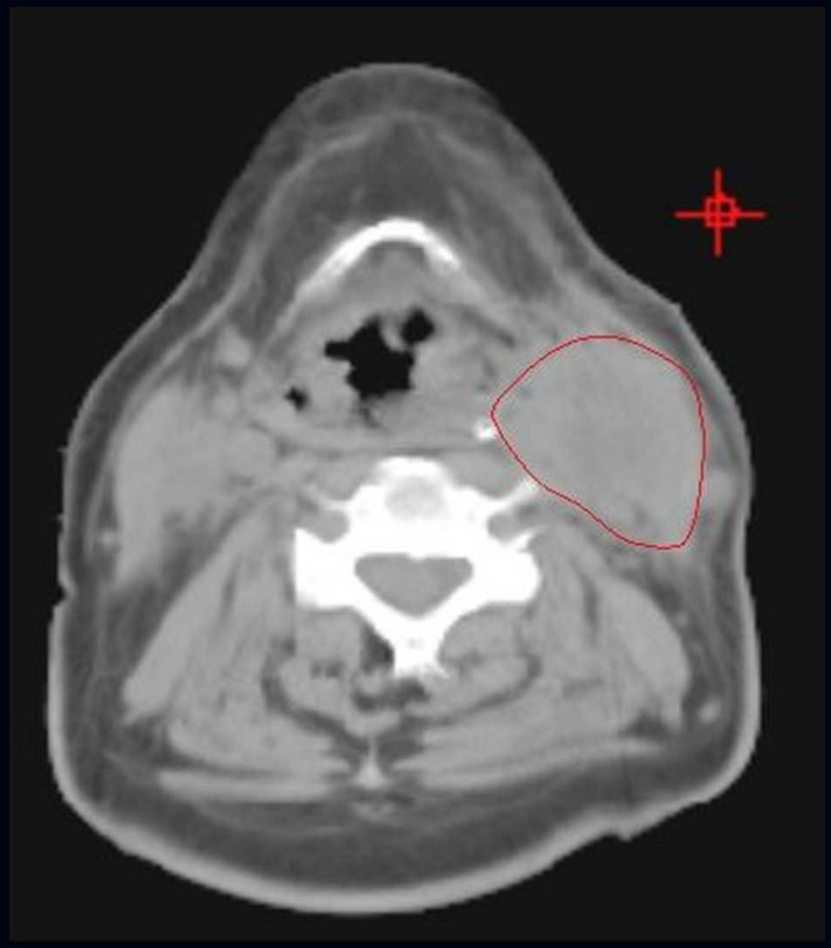
- Smaller PTV margins, Sharper dose fall-off can allow for geographic misses if target localization and immobilization are not accurate
- Change of anatomy with treatment – reducing tumor size, loss of wt etc
- Lack of uniformity – no IMRT planning standards for every anatomical site.
- Diff to compare data between institutions

Changes in Anatomy during course of Rx

Planning CT

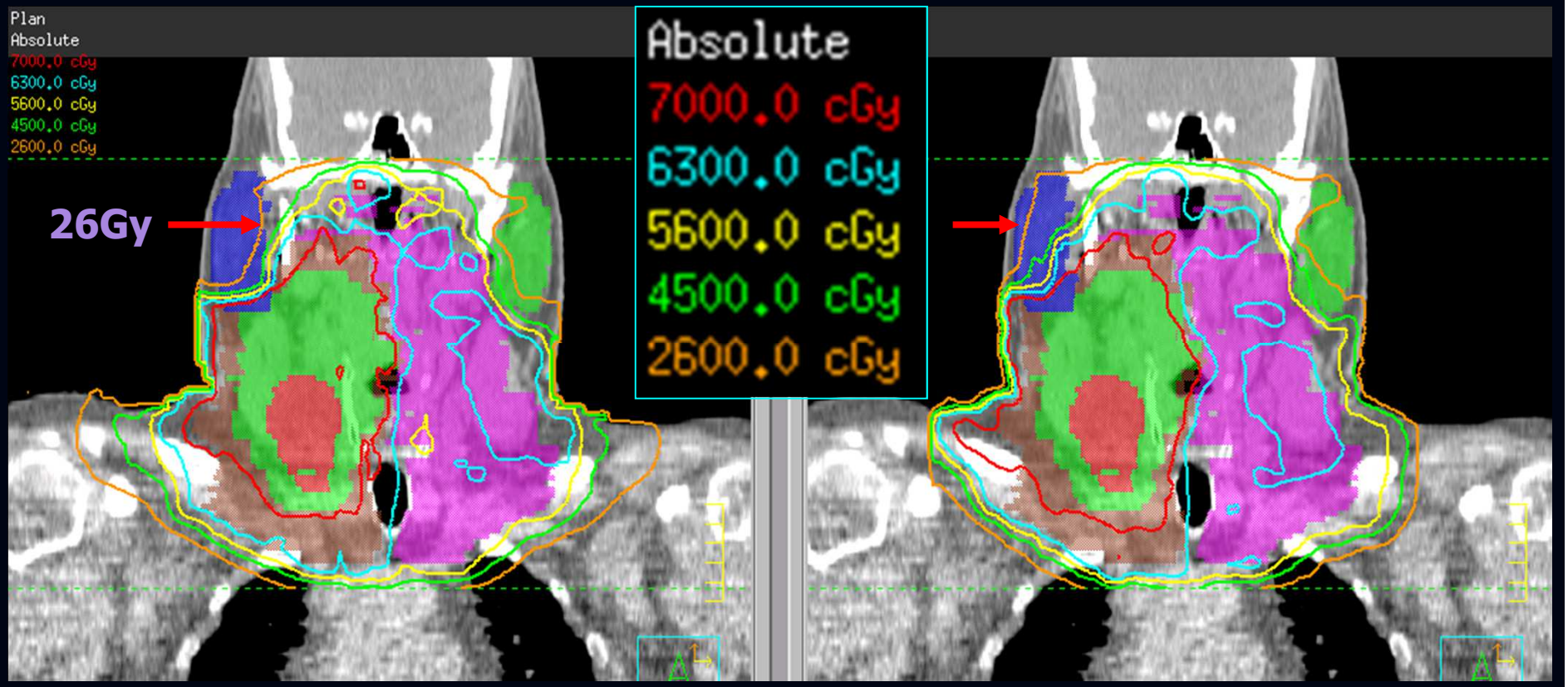


Three Weeks into RT



Barker et al. *IJROBP* 59:960, 2004 & Lei Dong et al. (MDACC)

Dosimetric Impact of Anatomic Changes



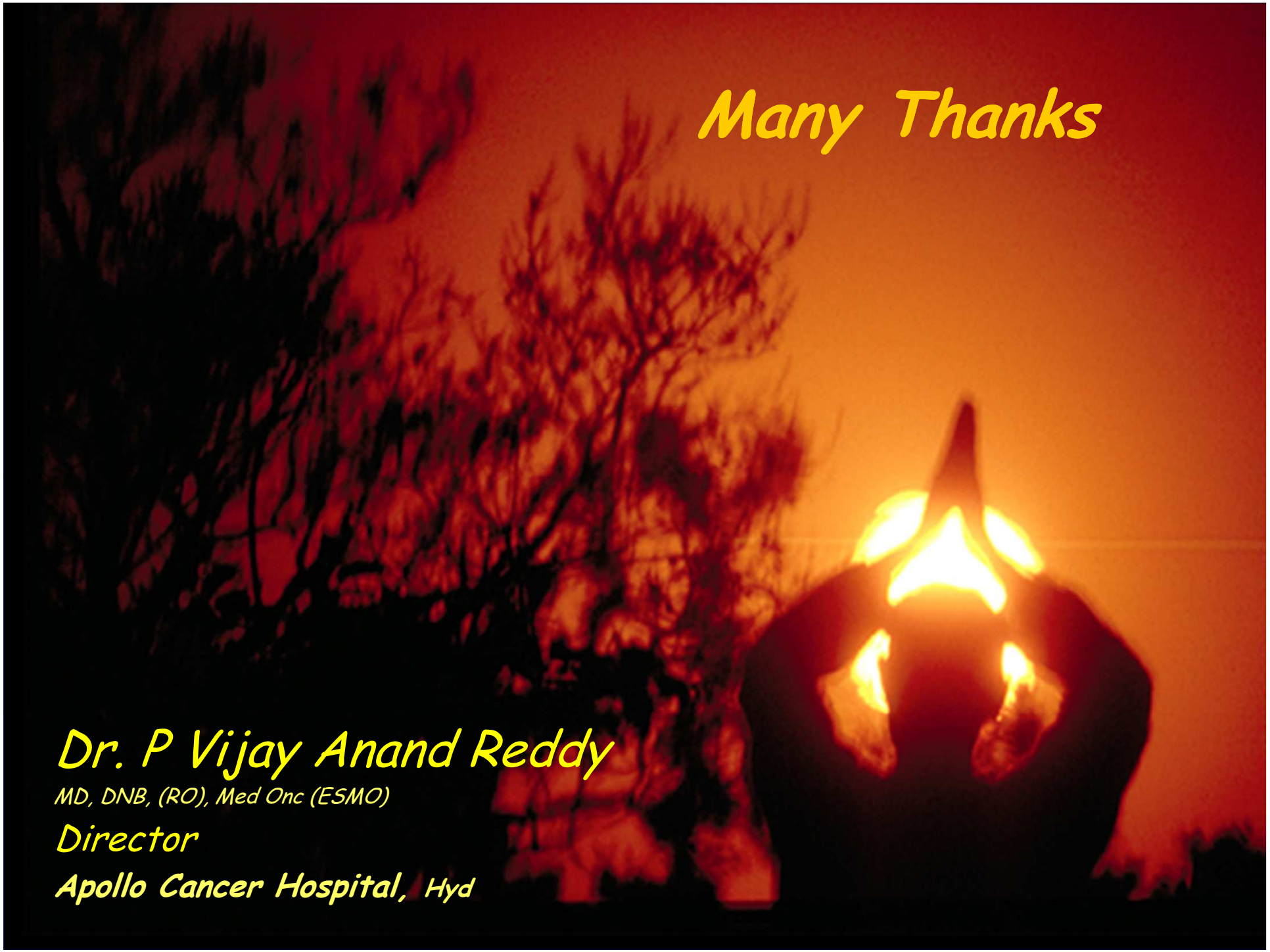
Original Plan

Four Weeks Later (Mapped back to the original planning CT using deformable registration)

Barker et al. IJROBP 59:960, 2004 & Lei Dong et al. (MDACC)

Conclusions

- IMRT is an obvious choice for H&N Ca
  - NP,OP,PNS etc
- Longer follow up to testify its advantage
- Obtains tight dose gradients around gross & sub-clinical disease when desirable
- Tumor in close vicinity of the cord, parotids & brain stem
- Re-irradiation possible
- ***Requires expertise***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