



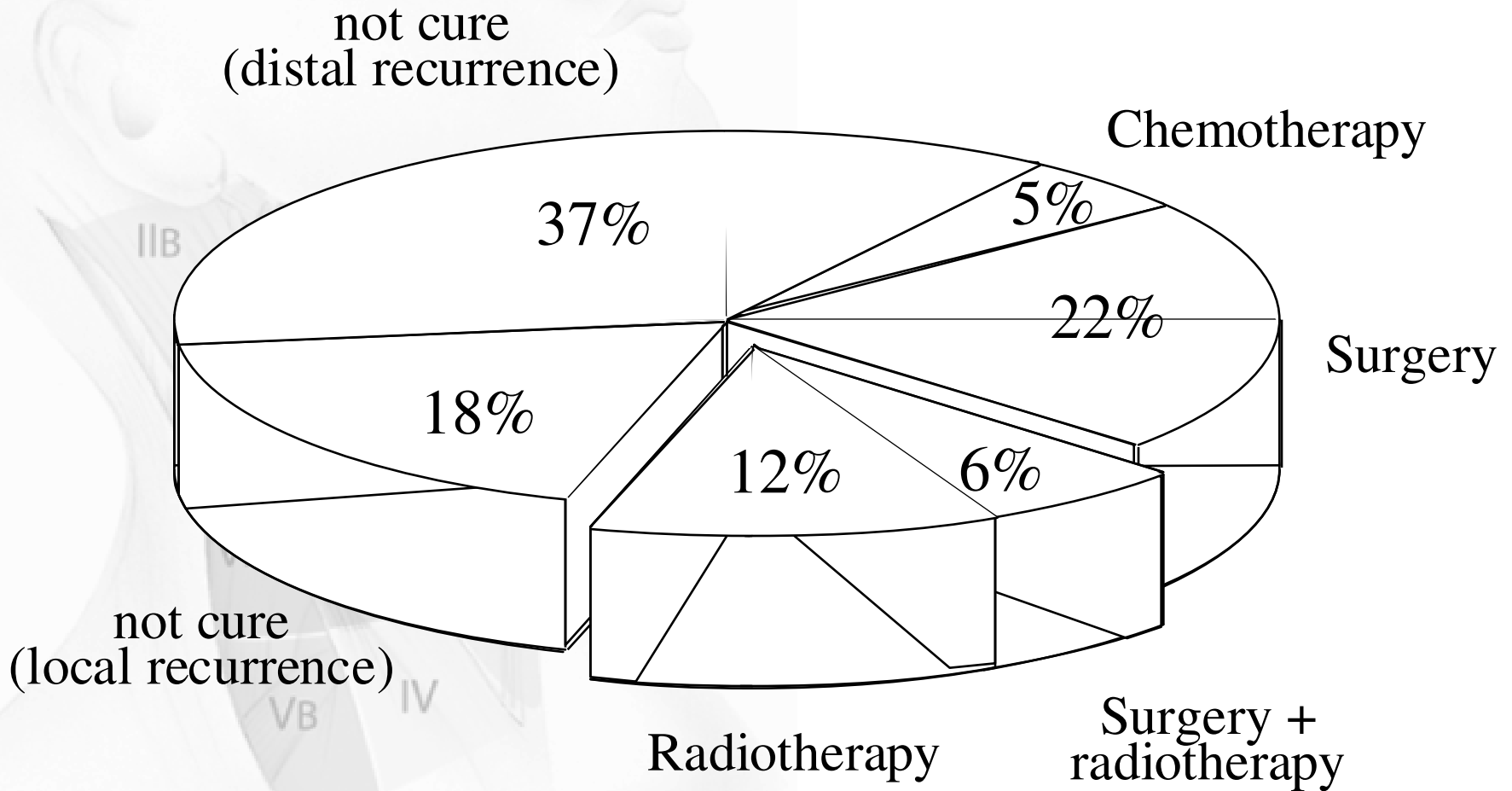
Adaptive radiotherapy of HNSCC: advantages, limits and clinical applications in the treatment of oropharyngeal carcinoma.

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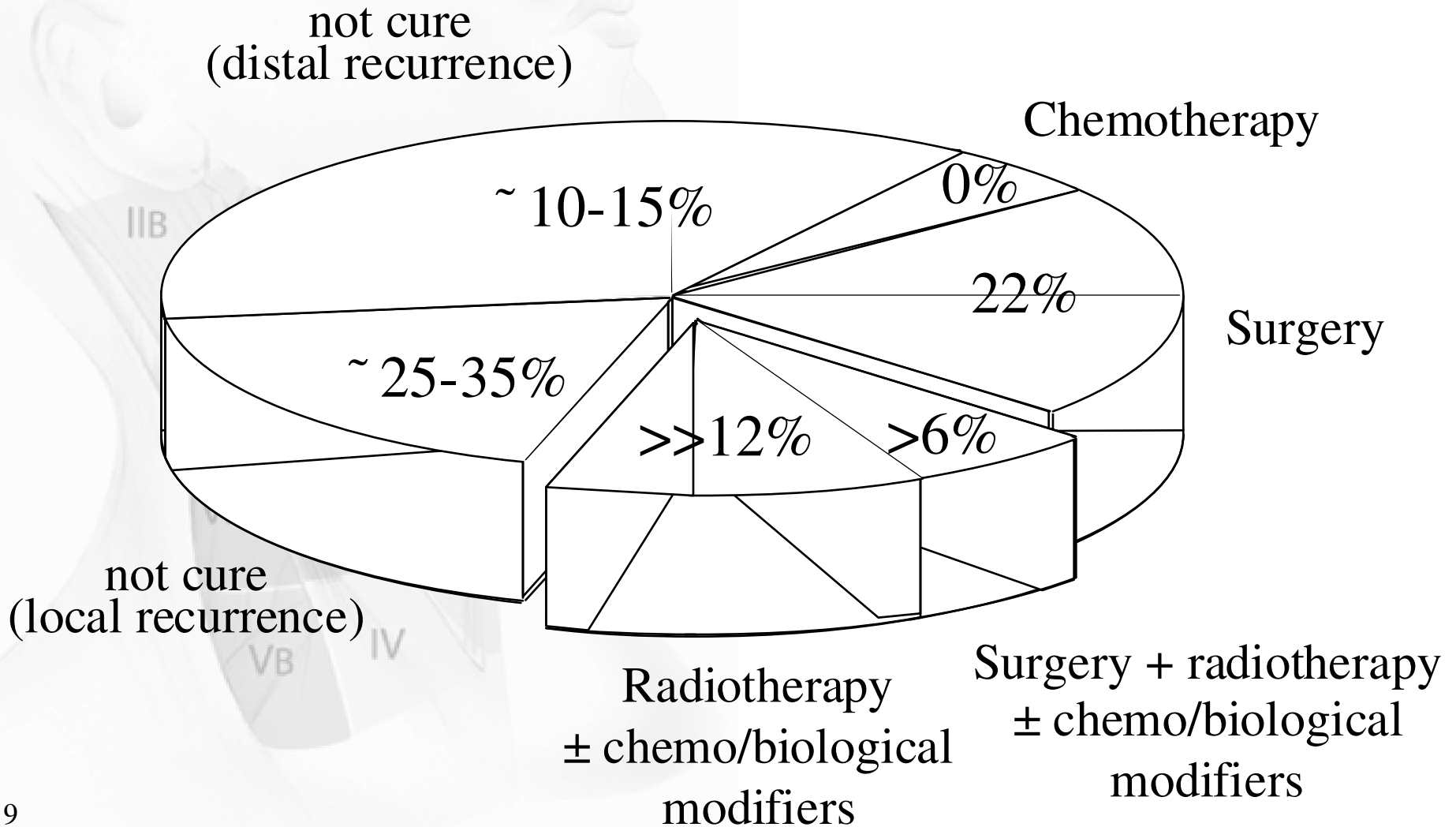


Myths and facts in Oncology: the challenge of local therapies





Myths and facts in Oncology: the challenge of local therapies in ...HNSCC...





“My” vision of Radiation Oncology in 2009 and beyond ...

- RO will be (even more) multidisciplinary...
- RO will be conformal (e.g. IMRT, proton, hadrons)...
- RO will be tailored (based on imaging and molecular profiling) and adaptive ...
- RO will be associated with targeted agents ...



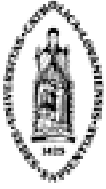
“My” vision of Radiation Oncology in 2009 and beyond ...

- RO will be conformal (e.g. IMRT, proton, hadrons) ...
- RO will be tailored (based on imaging and molecular profiling) and adaptive ...



Challenges in Head & Neck loco-regional treatment

- Target selection and delineation
- **Adaptive IMRT: geometrical, biological & dosimetric**
 - **which imaging modalities?**
 - **which biological pathways?**
 - **which volume/dose registration algorithms?**
 - **how frequently?**
- Concomitant association with drugs and/or "small molecules"



“2D” Radiotherapy in oropharyngeal cancers



Table 2. Tonsillar Squamous Cell Carcinoma: Local Control

Institution (ref)	Treatment	Patients		Local Control Rate (%)				Overall
		No.	% With T4 Disease	T1	T2	T3	T4	
Washington University Medical Center, St Louis, MO ¹⁶	Surgery + RT	230	14	80*	71*	65*	58*	68*
Mayo Clinic, Rochester, MN ¹⁷	Surgery ± RT	72	3	78*	76*	44*	0/2	71*
Roswell Park Cancer Institute, Buffalo, NY ¹	Surgery	56	ND	ND	ND	ND	ND	75*
Memorial Medical Center, Long Beach, CA ¹⁸	RT — ¹⁹² Ir	80	24	ND	ND	ND	ND	84*
Center Alexis Vautrin, Vandoeuvre-les-Nancy, France ¹⁹	RT — ¹⁹² Ir	361	1	89†	85†	67	ND	80†
Institut Curie, Paris, France ²⁰	RT	465	35	90†	84†	64†	47†	64†
M.D. Anderson Cancer Center, Houston, TX ²¹	RT	150	5	94*	81*	67*	63*	75*
Washington University Medical Center, St Louis, MO ¹⁶	RT	154	23	76*	63*	59*	33*	56*
University of Maryland Hospital, Baltimore, MD ²²	RT	185	14	94‡	80‡	51‡	19‡	58‡
University of Florida, Gainesville, FL (present series)	RT	400	17	83†	81†	74†	60†	76†

Abbreviations: RT, radiation therapy; ND, no data; ¹⁹²Ir, iridium-192 boost.

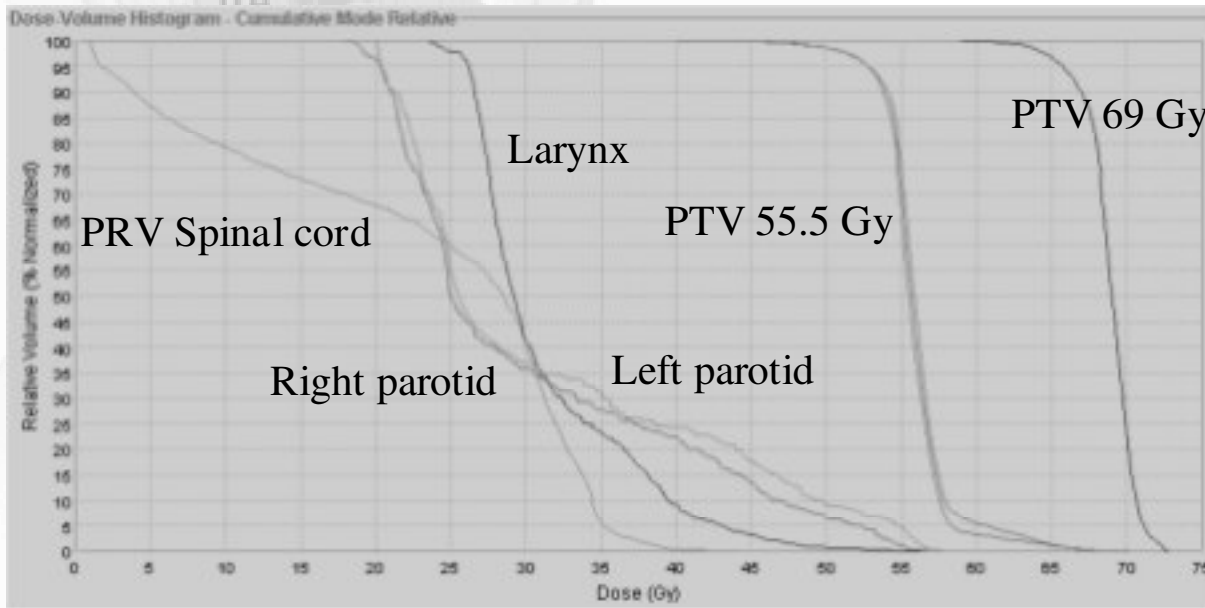
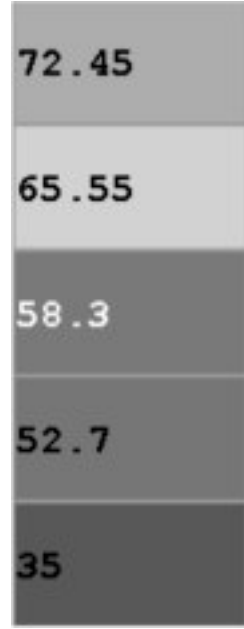
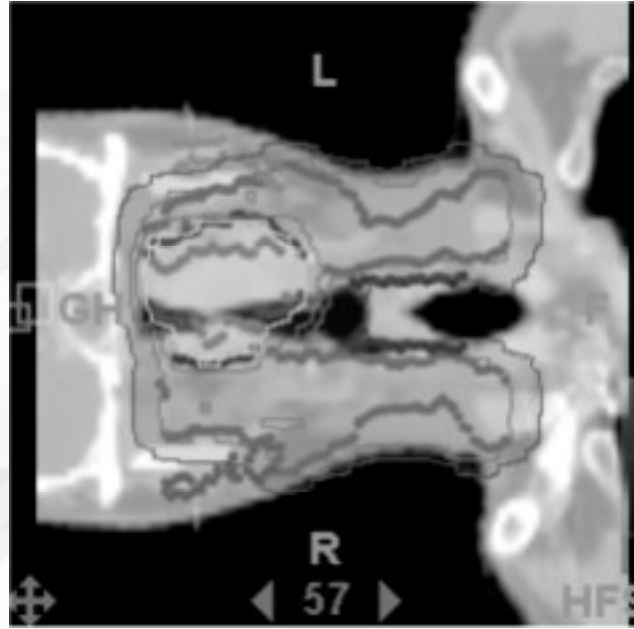
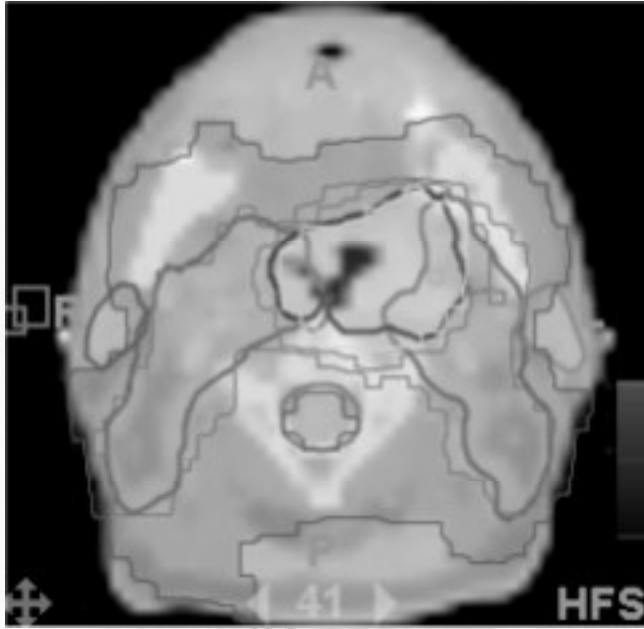
*Crude local control rates.

†Actuarial local control rates.

‡Patients who died with intercurrent disease less than 2 years after treatment were excluded.



IMRT for Head and Neck Tumors



Oropharyngeal SCC
 T2-N0-M0
 SIB-IMRT: 30x2.3 Gy
 30x1.85 Gy



IMRT for Head and Neck Tumors



Oropharyngeal carcinomas

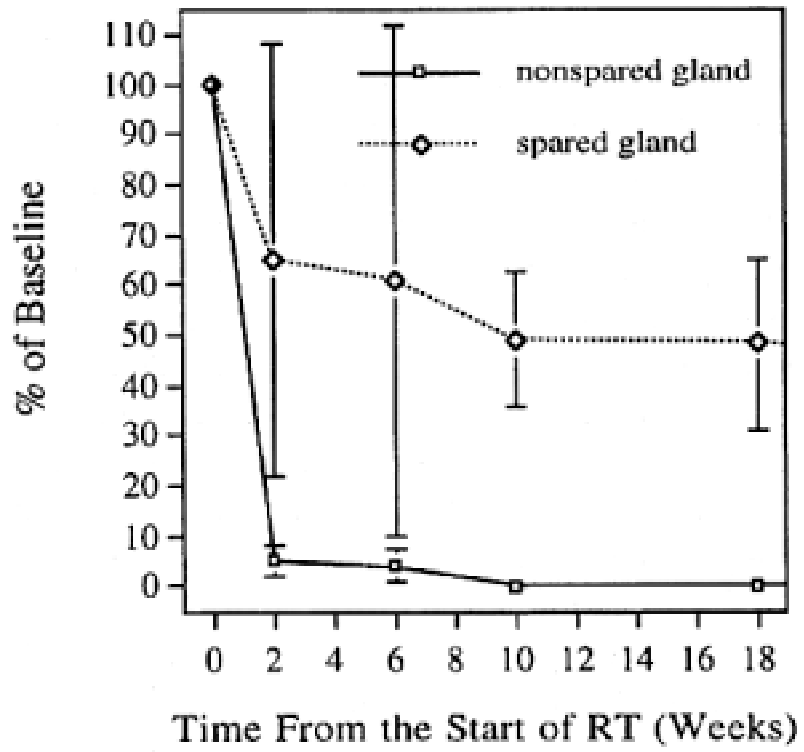
Study	N	Characteristics	Median follow-up (mo)	Time point (y)	Local control	Locoregional control	Disease-free survival	Distant metastasis-free survival	Overall survival
Chao et al ³⁸ (Mallinckrodt)	74	93% stage III or IV	33	4	NR	87%	81%	90%	87%
Garden et al ⁴⁰ (MDACC)	80	T1-2, Tx N+	17	2	NR	94%	NR	NR	NR
Huang et al ⁴¹ (UCSF)	41	T1-4 N0-3	14	2	94%	89%	91%	NR	89%
De Arruda et al ⁴² (MSKCC)	43	Stage III and IV	18	2	97%	85%	NR	72%	100%



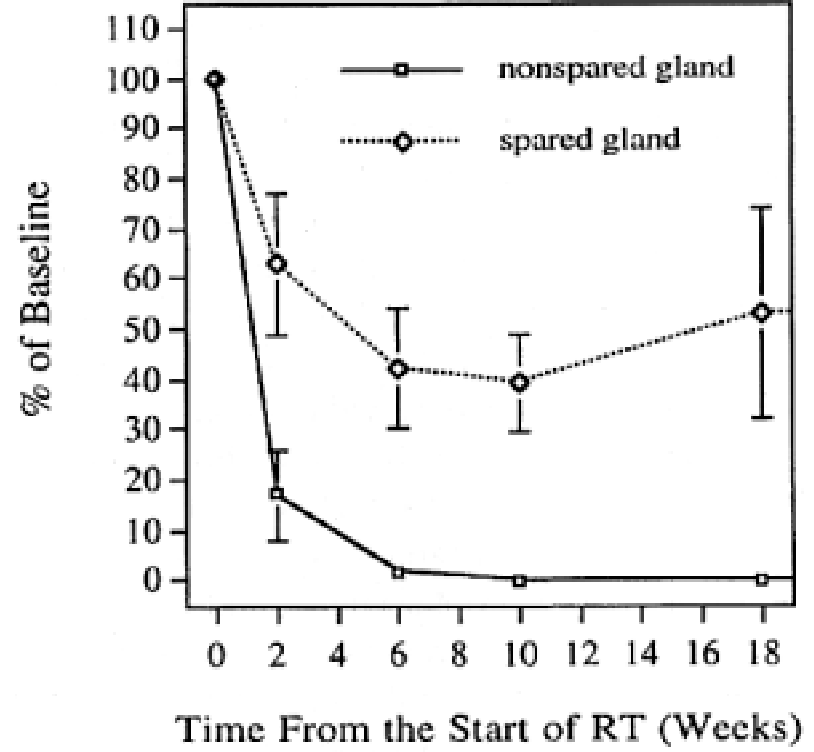
Parotid gland sparing in IMRT



Salivary flow rate in unstimulated gland



Salivary flow rate in stimulated gland

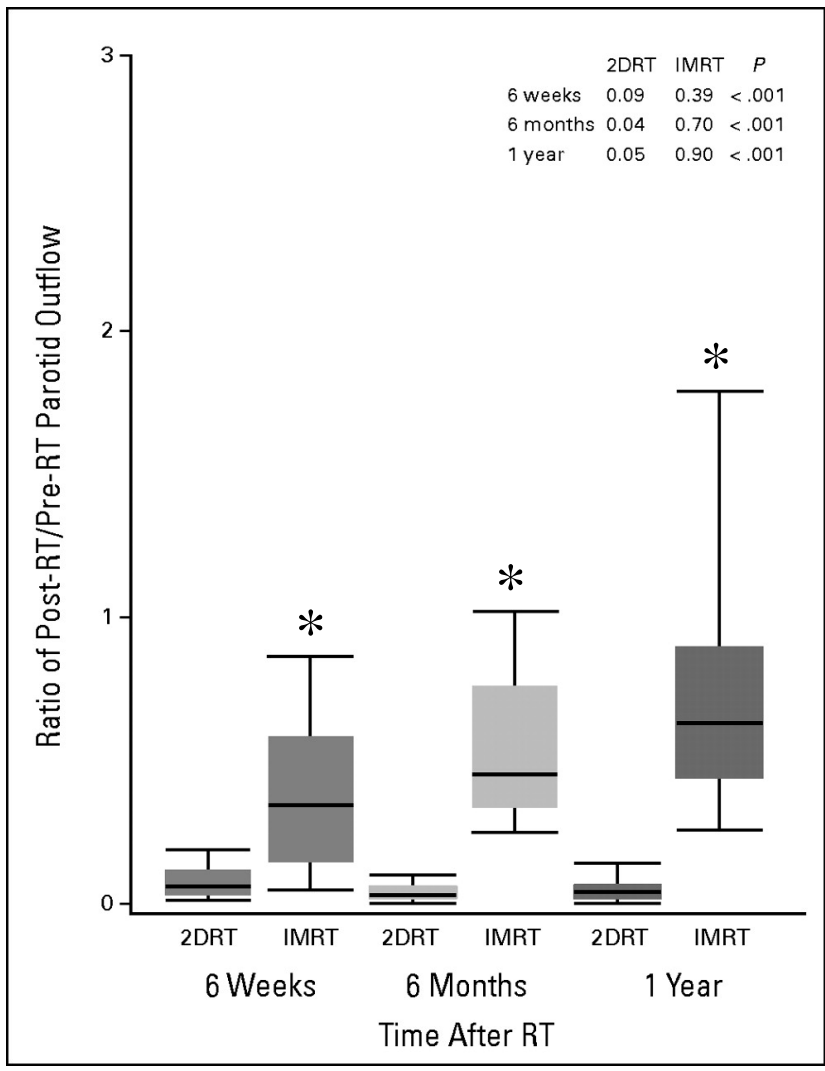
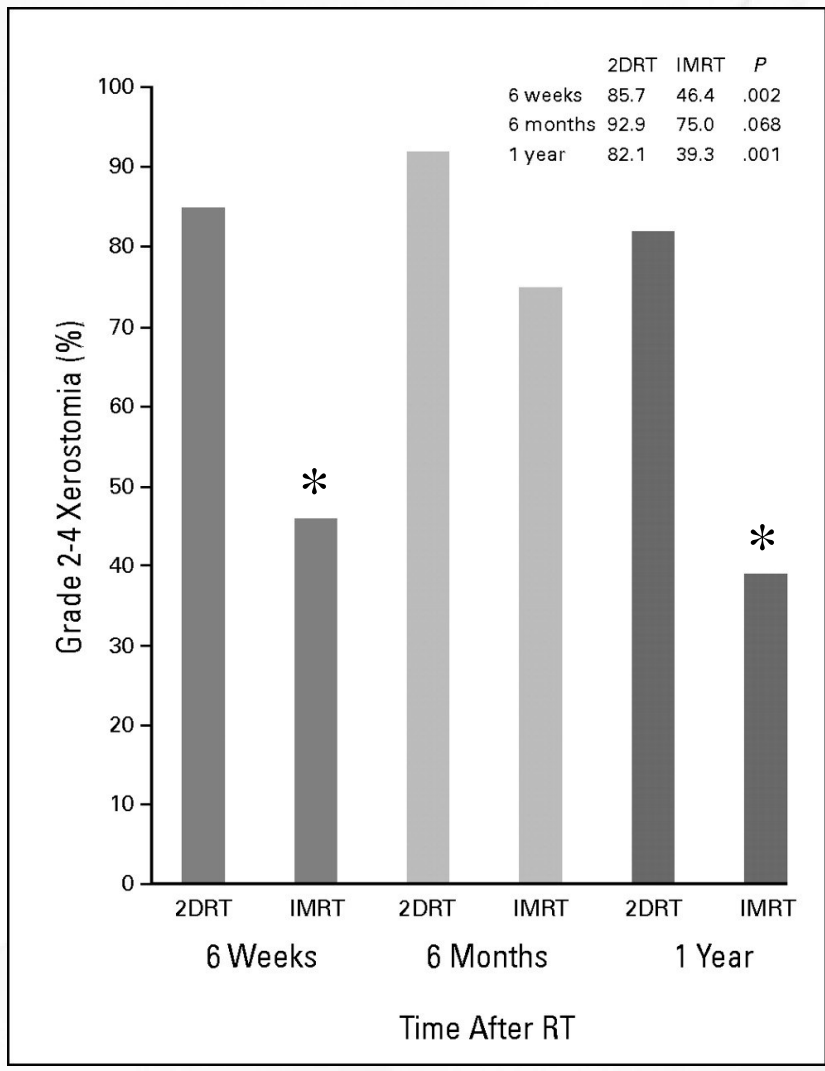




Parotid gland sparing in IMRT for NPC

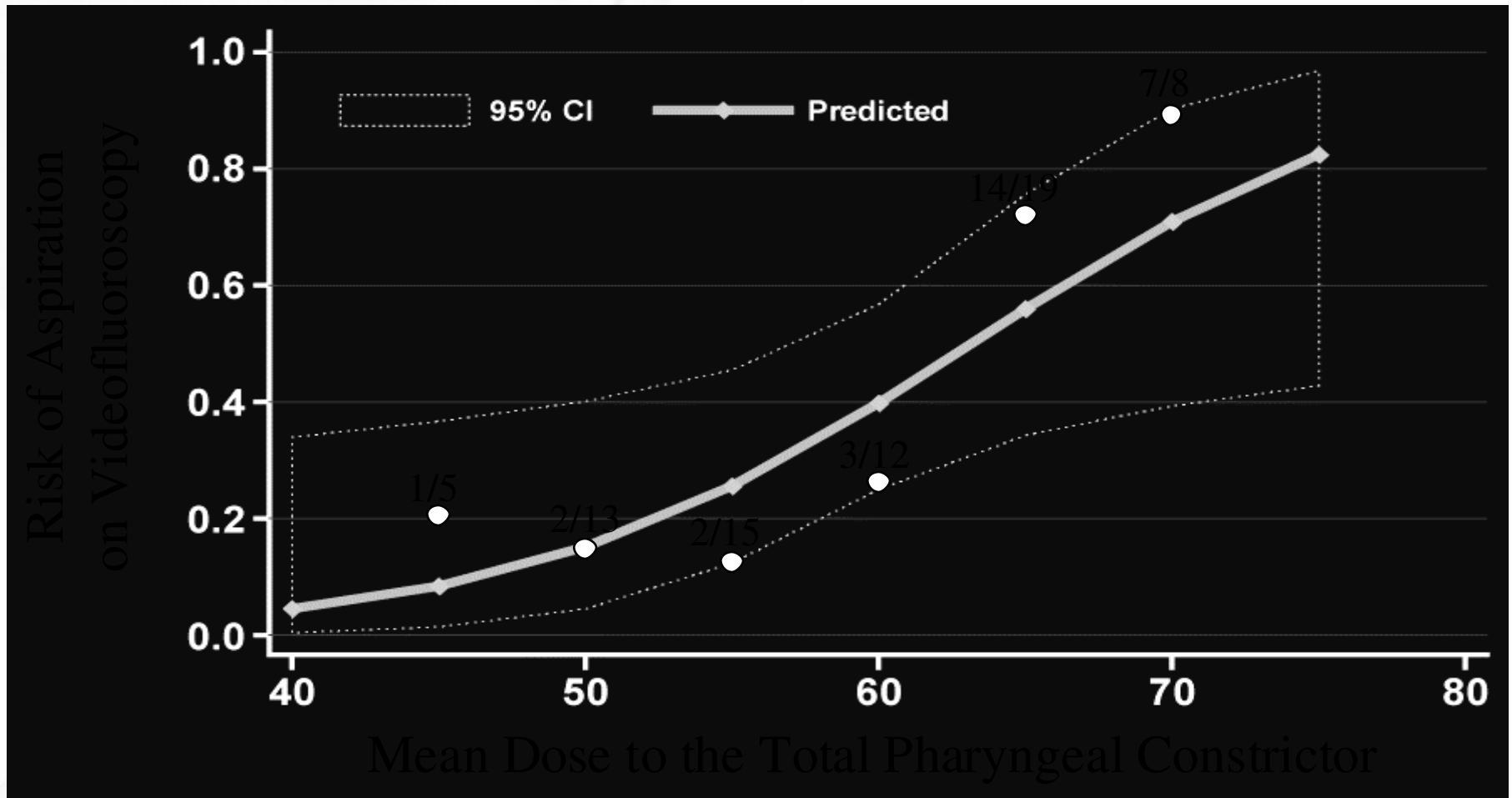


Stage I-II; 2DRT (66 Gy) >< IMRT (66 Gy); brachytherapy boost; no chemotherapy



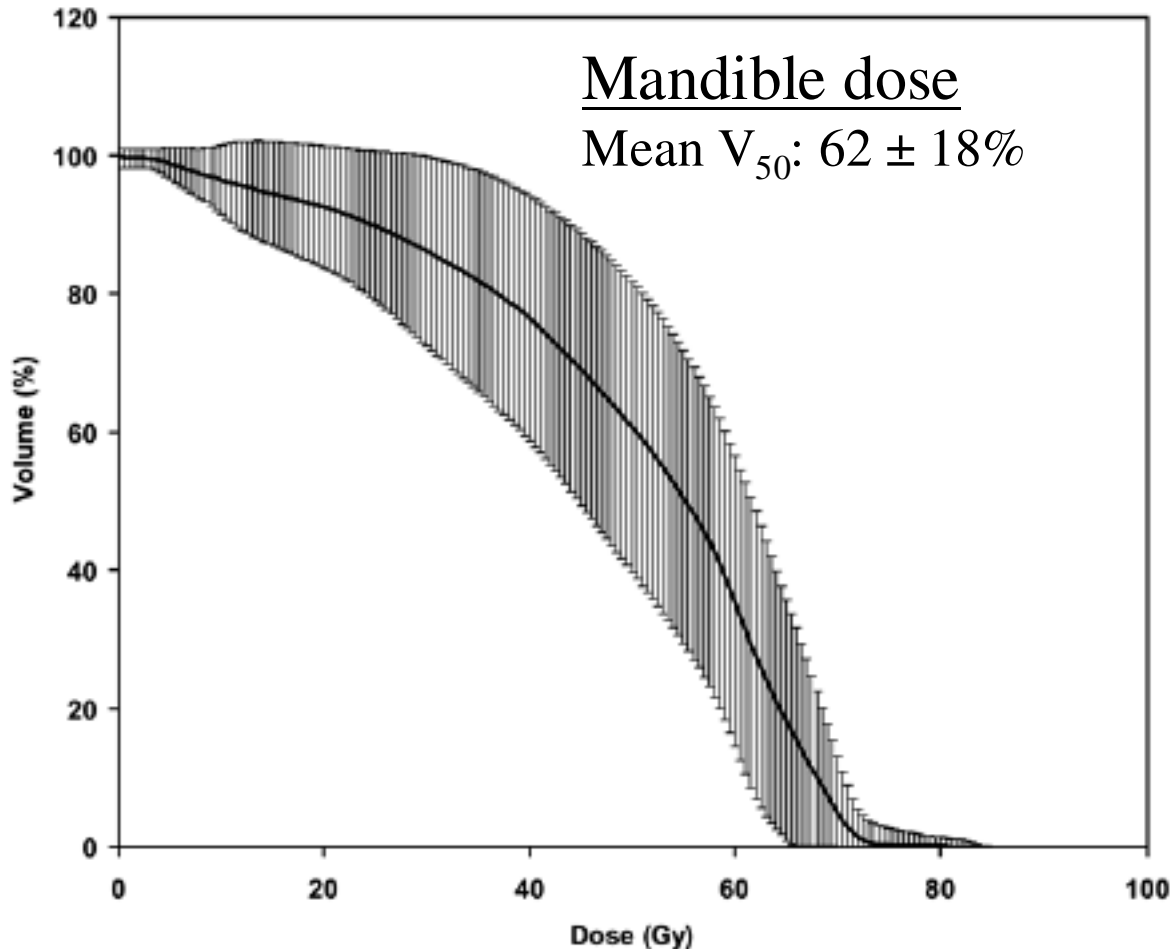


Relationship between radiation dose to the pharyngeal constrictors and aspiration





Osteoradionecrosis with “modern” radiotherapy techniques



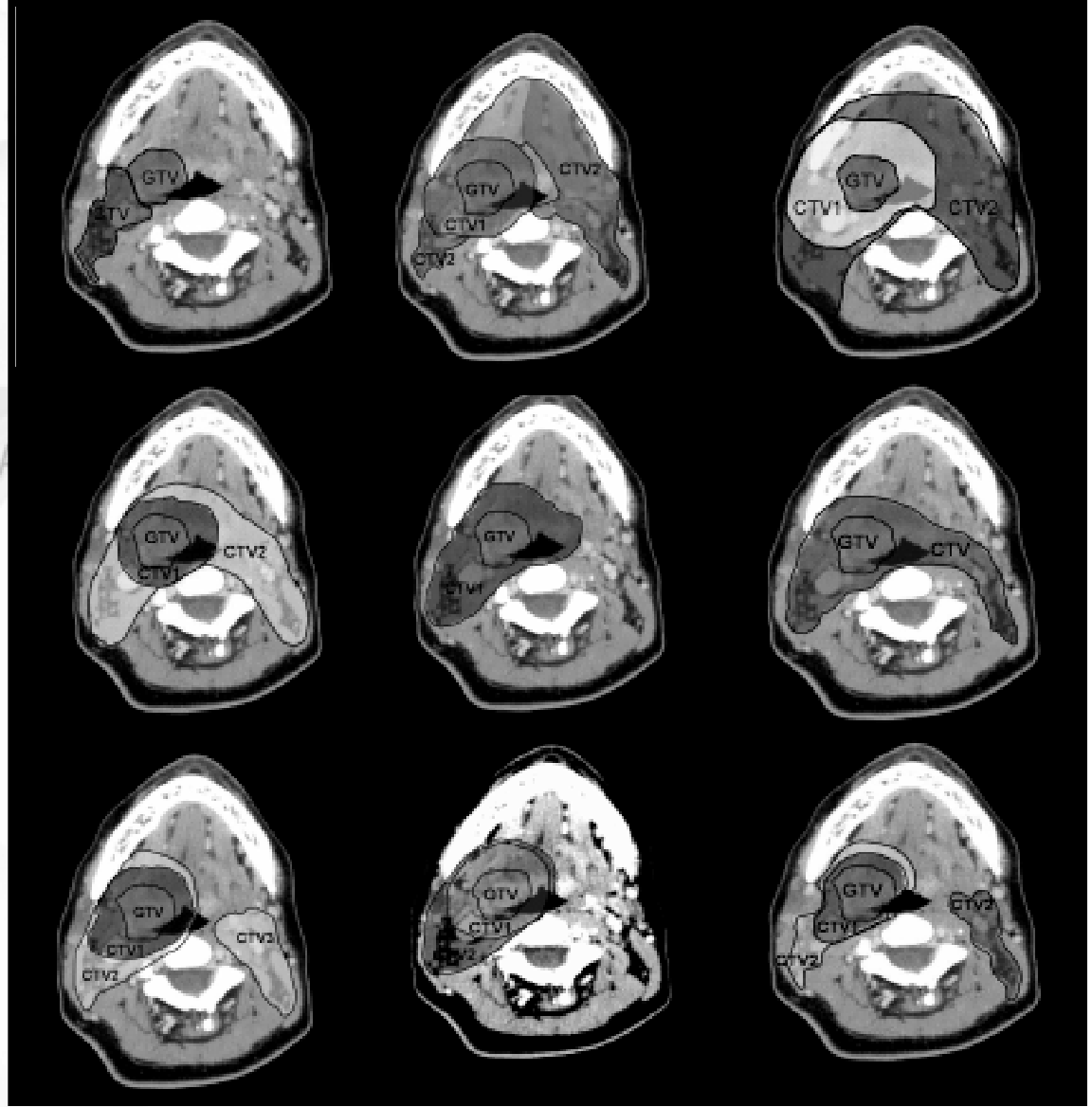
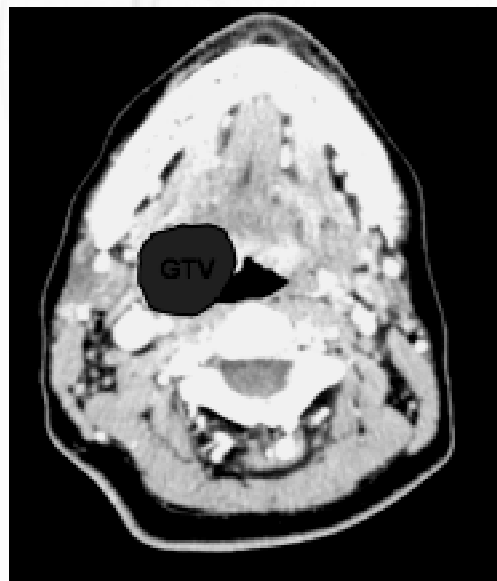
- n= 176 (86% ORO/OC)
- IMRT ± CH
- Primary RT + post-op RT
- Median FU of 35 months

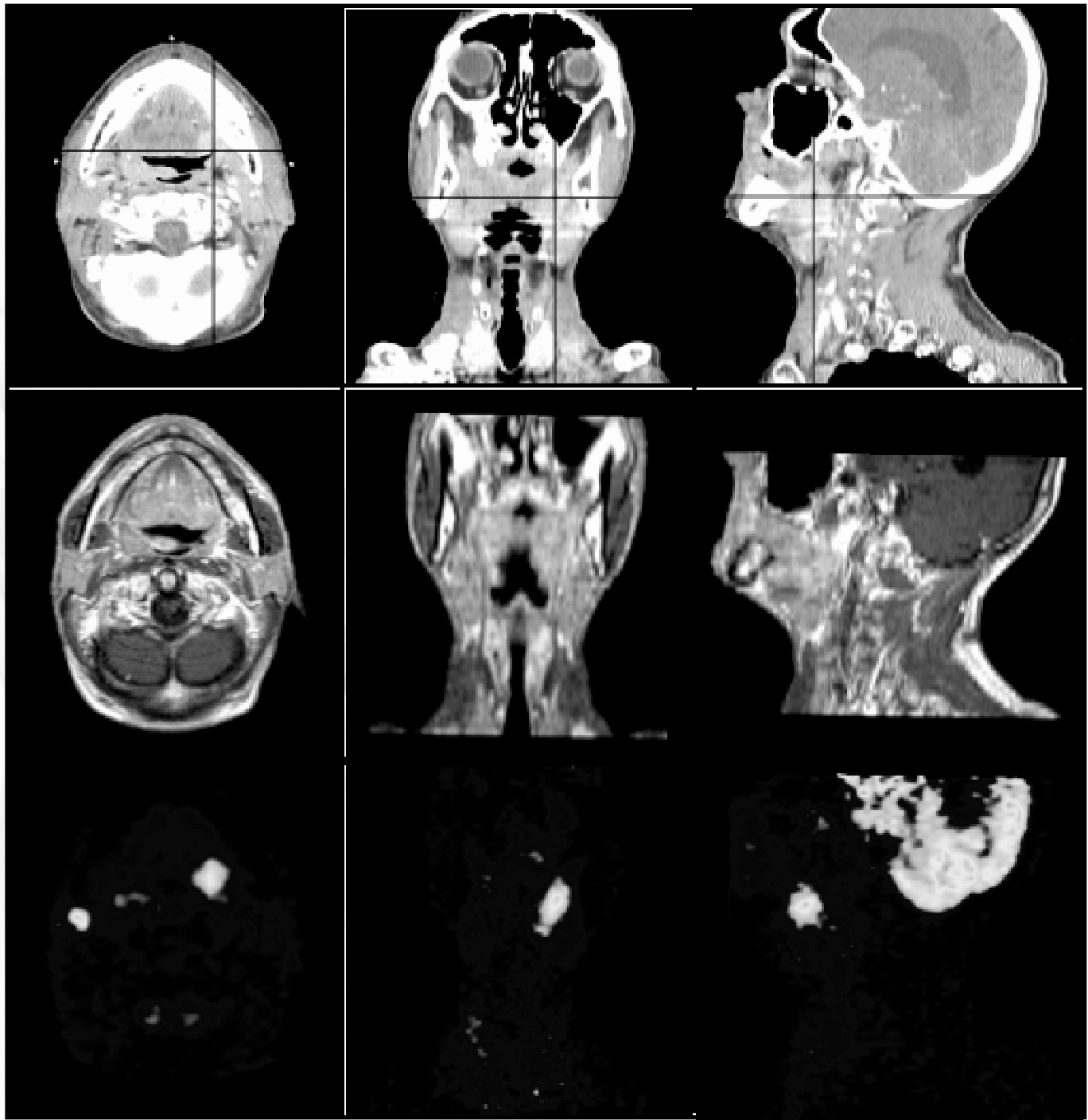
No case of ORN

- Pre-IMRT dental care
- Daily fluorination
- Dental protective stent
- Post-RT prophylactic dental care



Challenges in H&N IMRT





CAT Scan

NMR (T1)

^{18}F -FDG
PET

How far are we from the truth ?

TABLE 3
GTVs in Patients with Laryngeal or Hypopharyngeal Tumors

Patient No.	Tumor Site	T Stage	GTV (cm ³)			Surgical Specimen
			CT	MR Imaging	FDG PET	
1	PS	T4	47.7	36.3	19.3	NA
2	GL	T3	18.0	9.9	6.0	NA
3	GL	T3	41.1	30.2	9.2	NA
4	RC	T3	7.1	10.6	7.3	NA
5	PS	T2	4.1	9.1	2.3	NA
6	SGL	T2	3.7	1.4	1.2	NA
7	SubGL	T3	5.8	7.0	3.2	NA
8	PS	T3	17.3	17.6	12.6	NA
9	PS	T4	13.1	30.7	11.4	NA
10	PS	T4	55.6	53.4	34.2	NA
11	SubGL	T2	1.9	2.4	3.4	2.2
12	GL	T4	6.2	9.8	8.5	5.1
13	LAR	T4	41.0	58.4	30.2	30.9
14	LAR	T4	11.1	6.6	8.0	4.1
15	LAR	T4	14.6	22.0	10.2	5.6
16	LAR	T4	18.4	22.0	11.4	8.6
17	LAR	T4	28.1	32.3	26.6	17.3
18	LAR	T4	25.0	23.5	20.0	15.4
19	LAR	T4	40.4	37.3	28.7	24.3
Mean						
All patients (n = 19)	21.4	21.4	13.4*	NA
Patients with specimen available (n = 9)	20.8	23.8	16.3	12.6†

Note.—GL = glottic larynx, LAR = larynx without other specification, NA = not applicable, PS = pyriform sinus, RC = retro cricoid area, SGL = supraglottic larynx, SubGL = subglottic larynx.

* In the comparison with CT and MR imaging, $P < .01$ (for both).

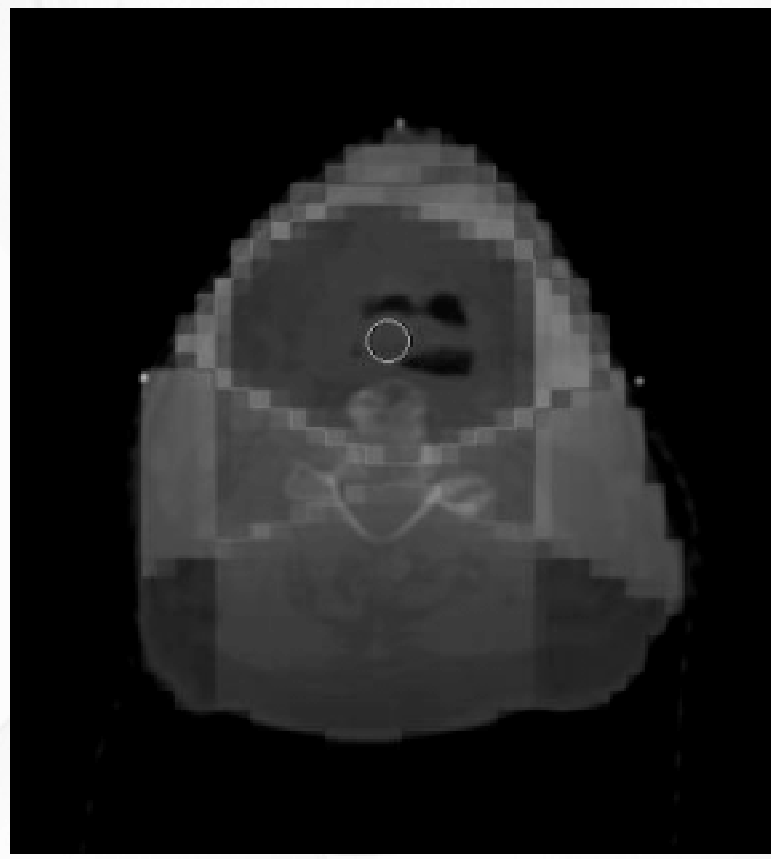
† In the comparison with CT, MR imaging, and PET, $P = .003, .001, \text{ and } .06$, respectively.



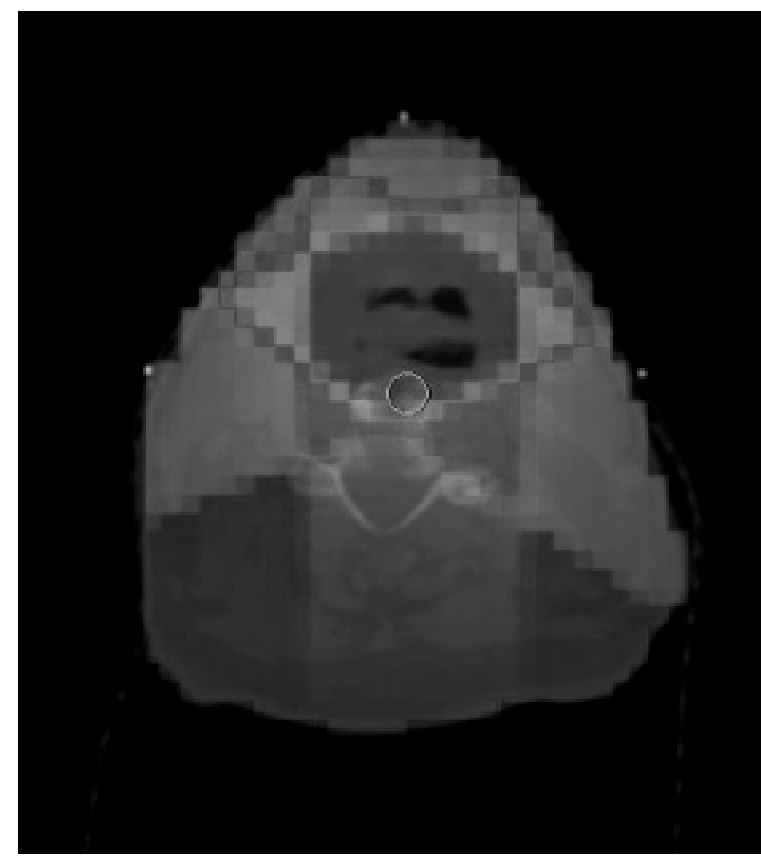
Image-Guided Radiation Therapy in HNSCC

Impact of imaging modality on dose distribution

CT-based target volume



FDG PET-based target volume





Validation protocol in locally advanced HNSCC



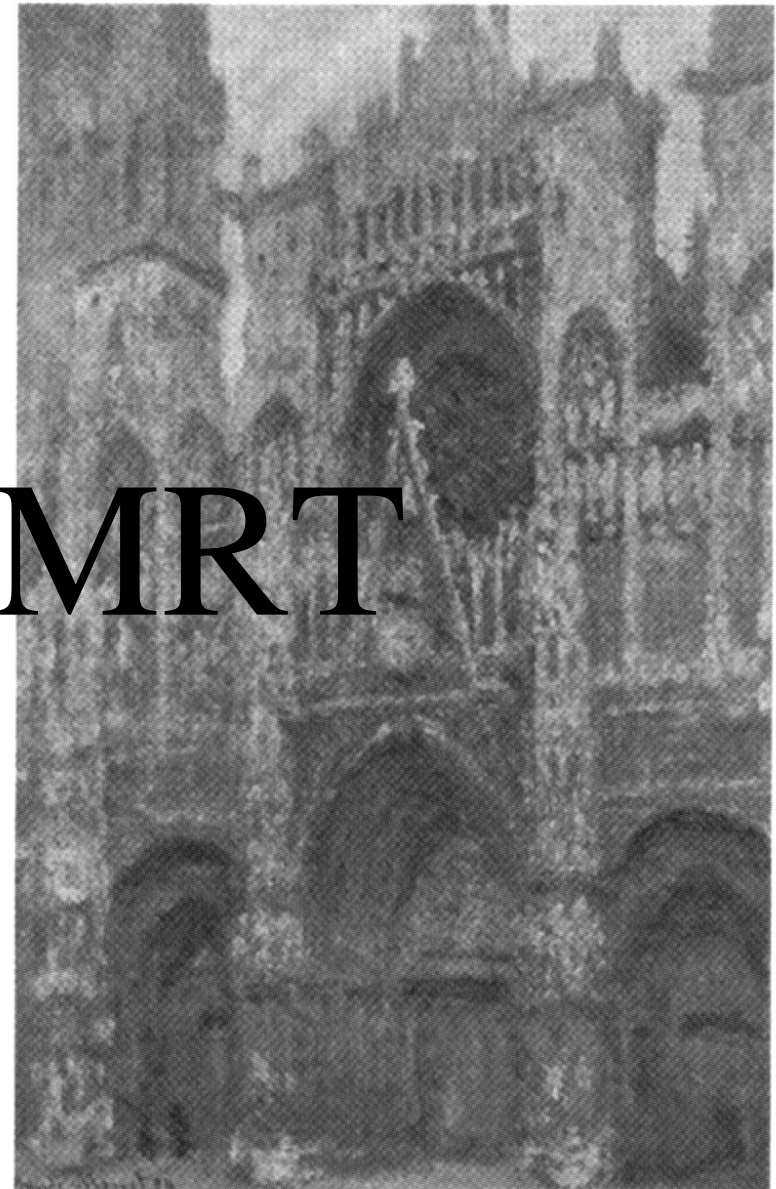
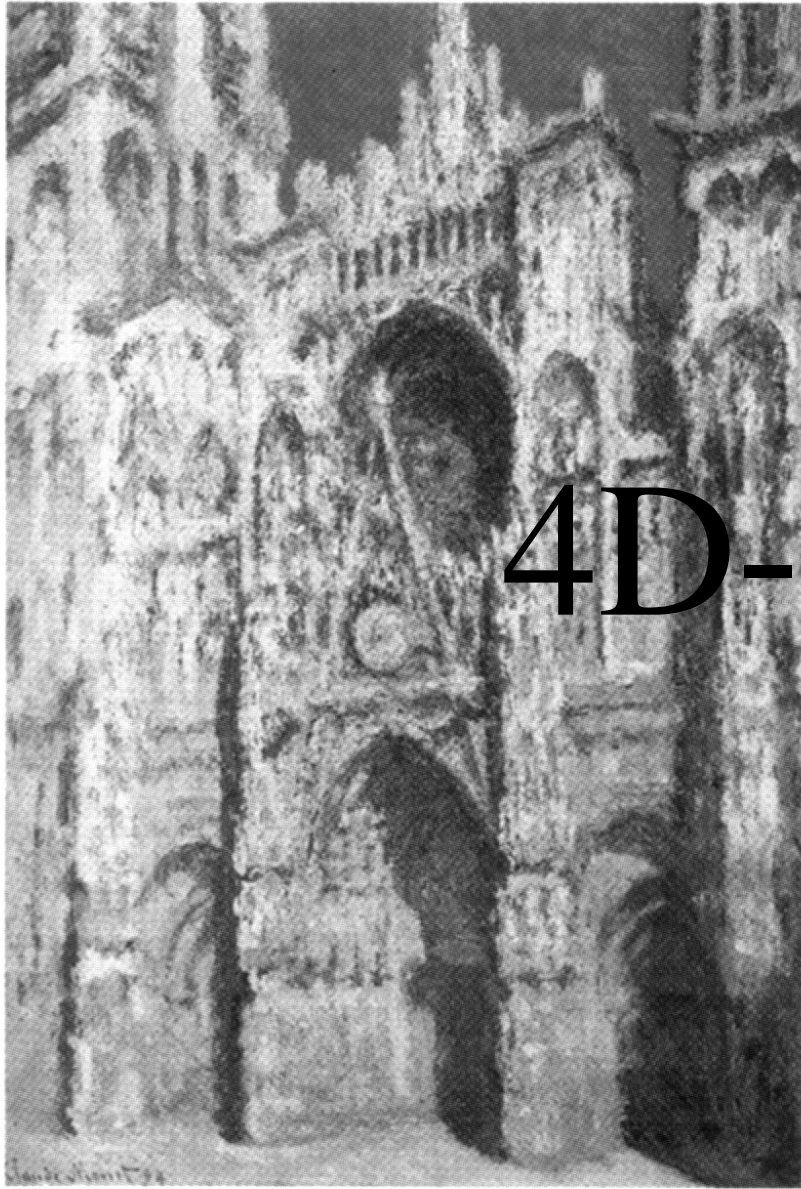
Apport de l'imagerie fonctionnelle par Tomographie par Emission de Positrons (TEP) dans le ciblage biologique par radiothérapie de conformation (3D-CRT) et par modulation d'intensité (IMRT) de tumeurs ORL

Use of functional imaging with PET for target volume delineation in 3D-CRT/IMRT for head and neck tumors

Prof. V. Grégoire, UCL St-Luc, Brussels, Belgium

Prof. E. Lartigau, COL, Lille, France

Dr. JF Daisnes, Cliniques St-Elisabeth, Namur, Belgium



4D-IMRT

The Cathedral of Rouen

C. Monet, 1894



Geometric 4D-IMRT



Tomotherapy Operator Station -- Cliniques universitaires Saint-Luc

User: Milan Tomsej

DOB: [redacted] Sex: M Plan: Plan_01
 ID: A21023J Plan status: Approved
 Plan date: Dec 12, 2005 8:33:53 AM DQA plan:
 Oncologist: Patient position: HFS
 Disease: 1: plan1

What's Next
Start Registration
 Click **Start Auto** OR **Start Manual**, or click **Accept** if finished.
 For automatic registration, select calculation parameters.

Scan Register Treat Calibrate

Bone and Tis Adjust patient position prior to beginning treatment

Automatic Calculation **Manual Control** Coarse Fine

Translational Adjustments (mm)
 Lateral (IEC Tx) 0
 Longitudinal (IEC Ty) 0
 Vertical (IEC Tz) 0
 [Reset]

Rotational Adjustments (degrees)
 Pitch 0
 Roll 0
 Yaw 0
 [Reset]

Accept
 Store Export

TomolImage **Correlated Images**

Orientation
 Transverse
 Coronal
 Sagittal
 [Switch]

TomolImage Component
 Color [redacted]

Composition
 Balance [slider]
 Checker [slider]

Reference Image Component
 ROIs
 Lasers
 Dose 46.0 Gy
 Isodose
 49.22
 46
 43.7
 41.4
 36.8
 32.2
 23

Auto-registration calculation canceled.

Monday, December 12, 2005 16:24:33

4:24 PM

MVCT

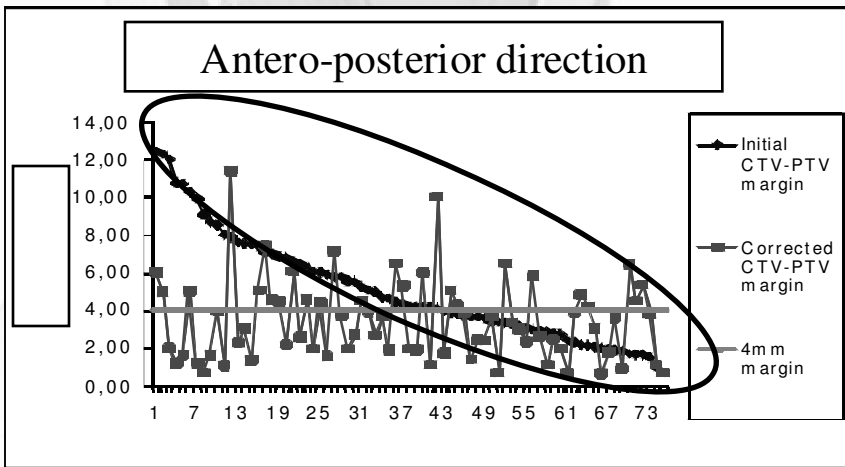
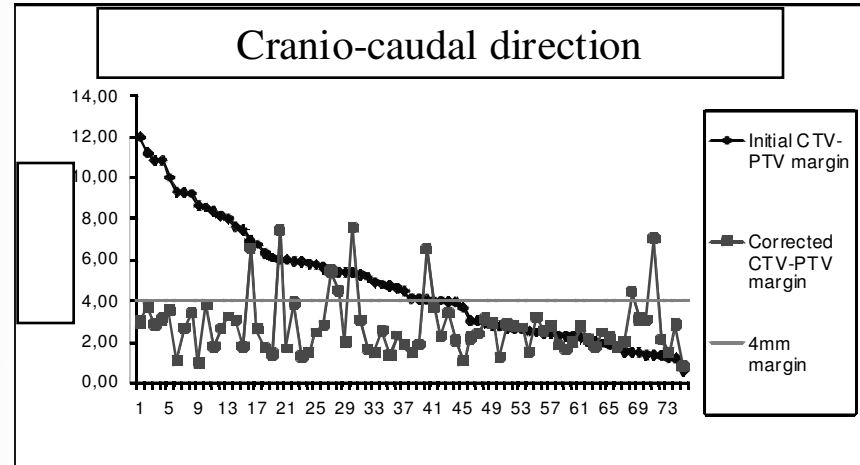
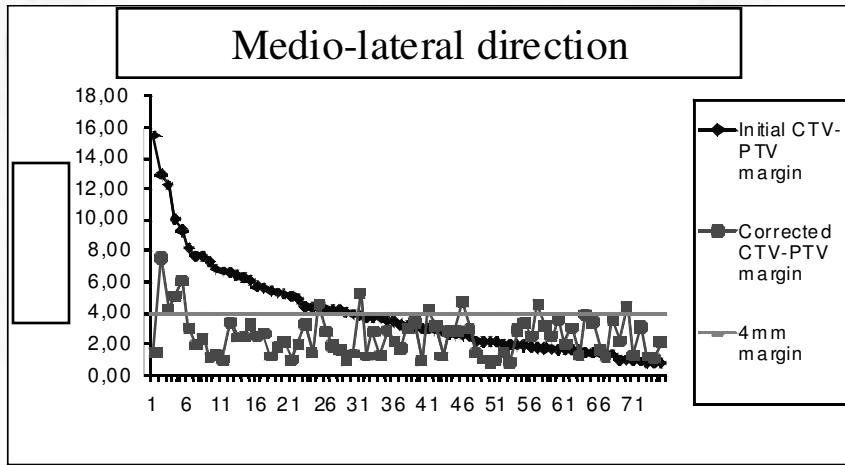
kVCT



Geometric 4D-IMRT

First five MVCTs: CTV to PTV margins

CTV to PTV margin



- 75 patients
- total of 1481 MVCT
- CTV-PTV: $(2 * \Sigma + 0.7s)$

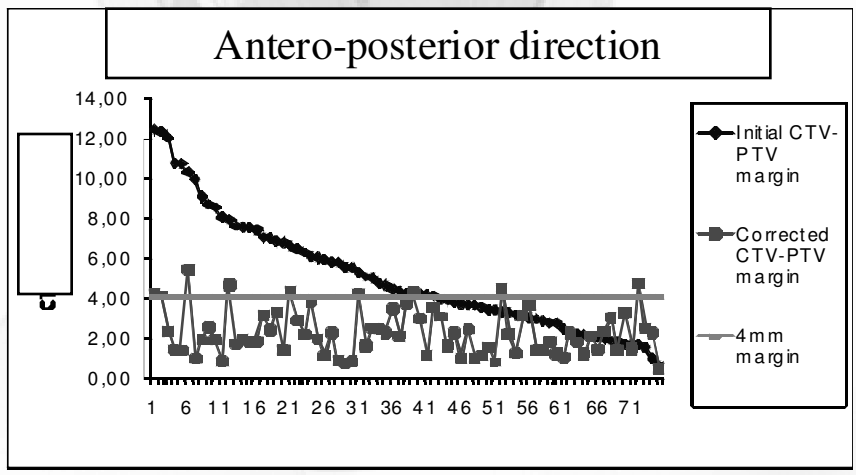
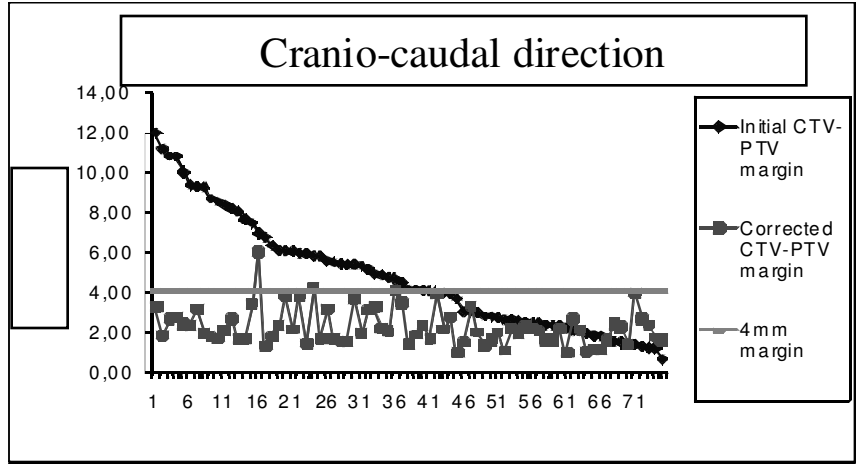
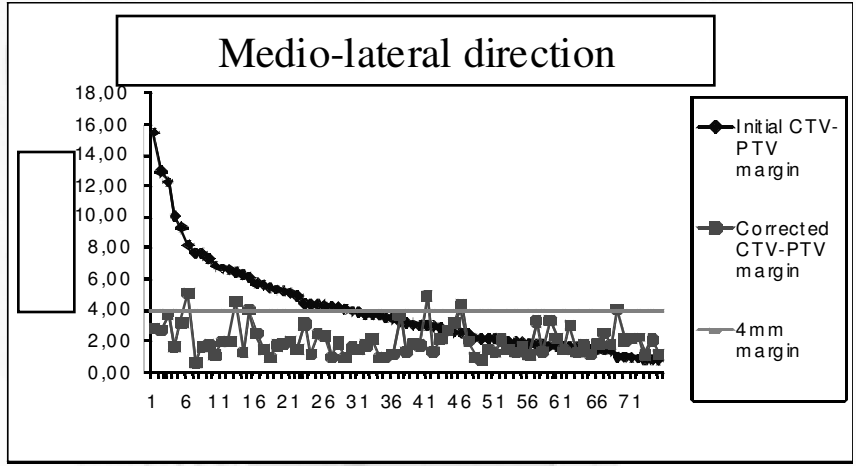


Geometric 4D-IMRT



Alternate week MVCTs: CTV-PTV margins

CTV to PTV margin

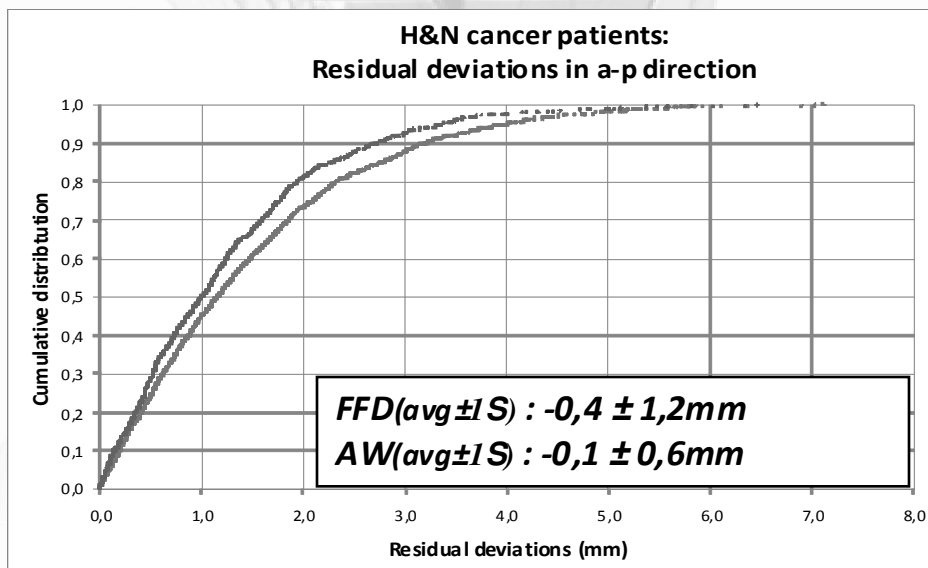
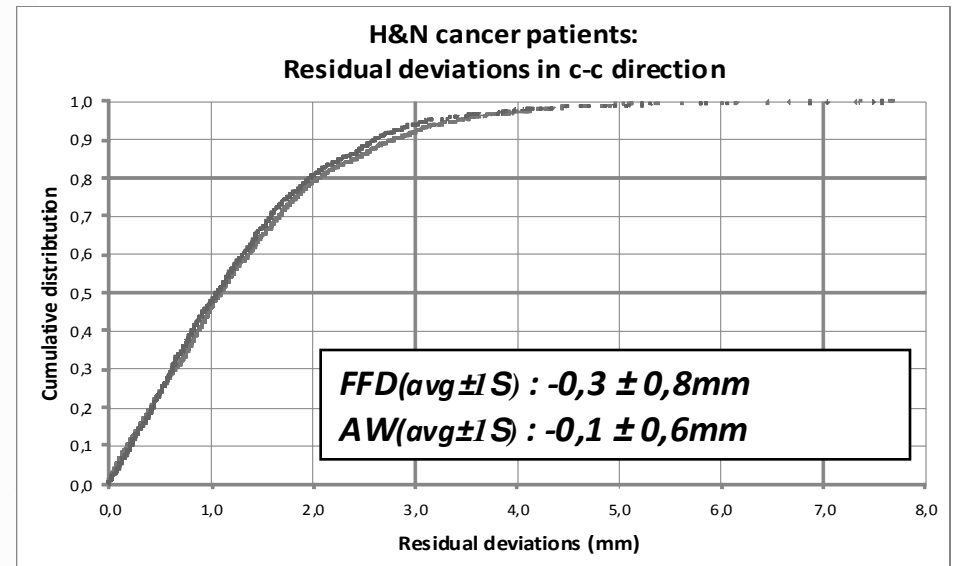
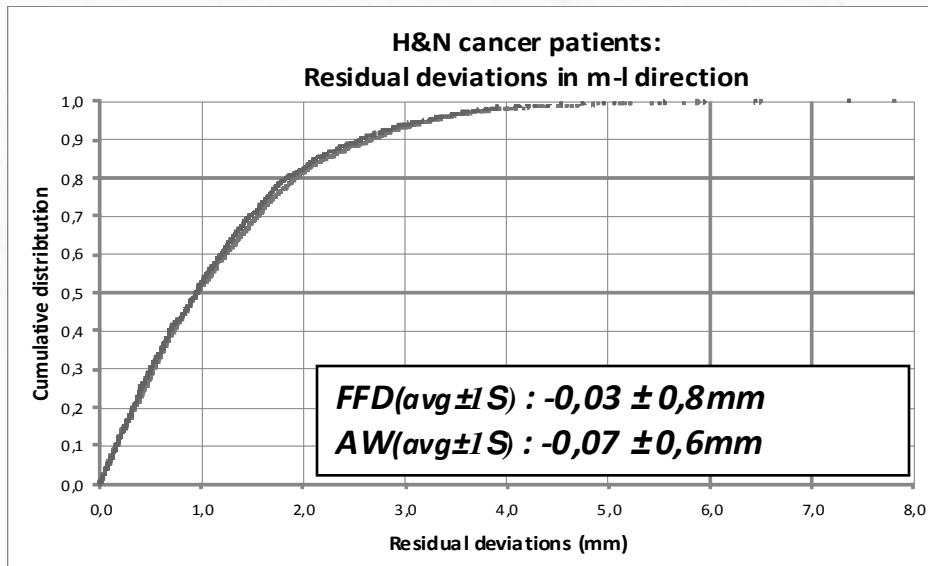


- 75 patients
- total of 1481 MVCT
- CTV-PTV: $(2 * \Sigma + 0.7s)$



Geometric 4D-IMRT

Residual deviations



Residual deviations analysis

-- *First five days protocol (FFD)*

-- *Alternate week protocol (AW)*

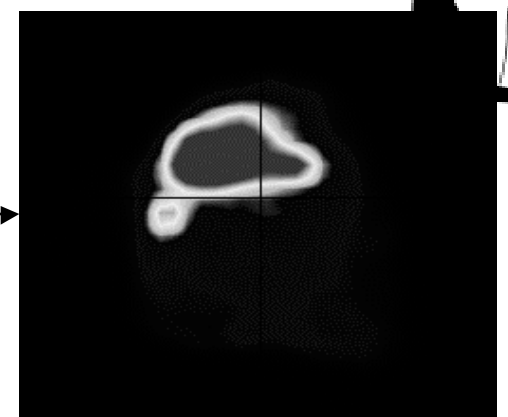
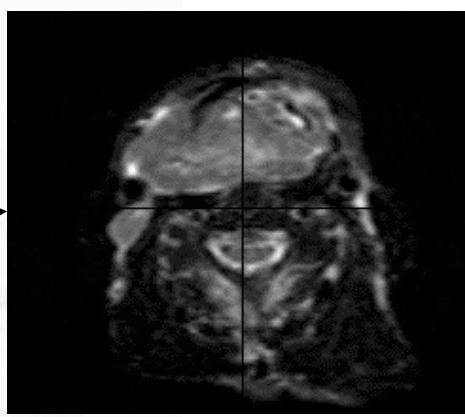
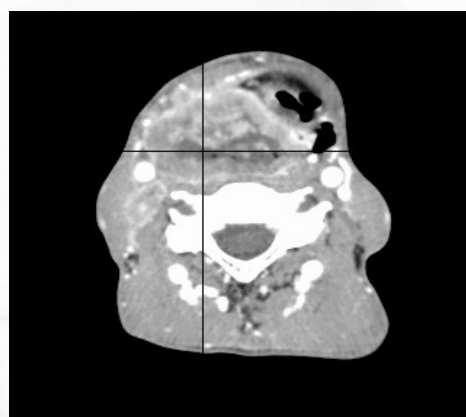


CT

MRI (T2)

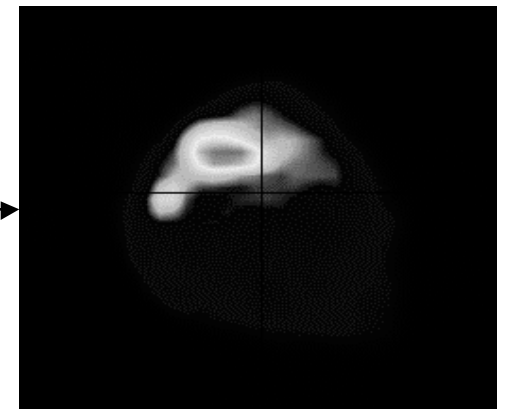
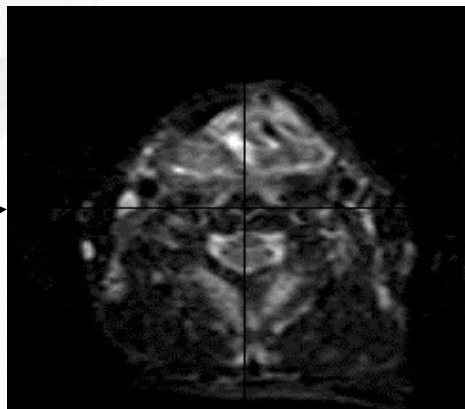
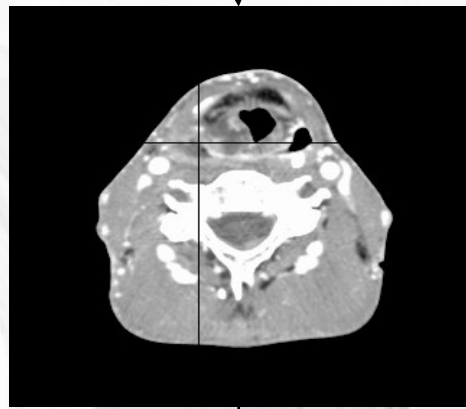
FDG-PET

PRE-R/
(Week 2)



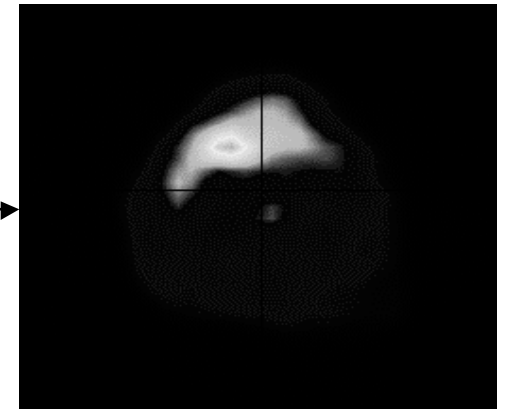
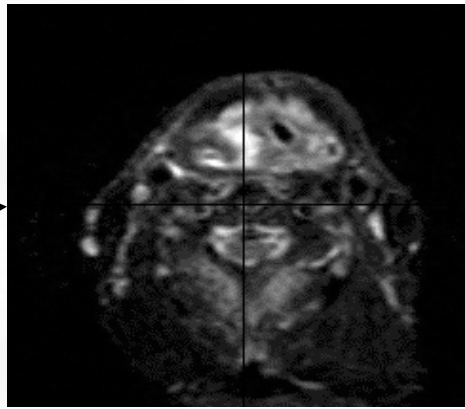
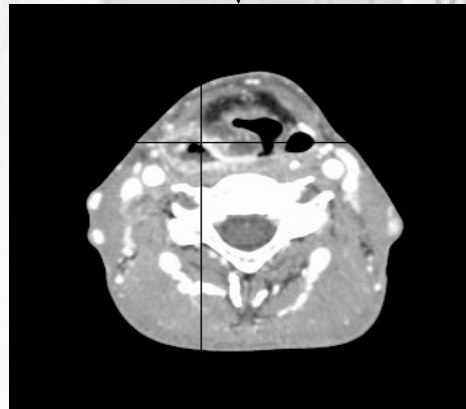
(Week 2)

WEEK 3
(Week 4)



(Week 4)

WEEK 5



IA



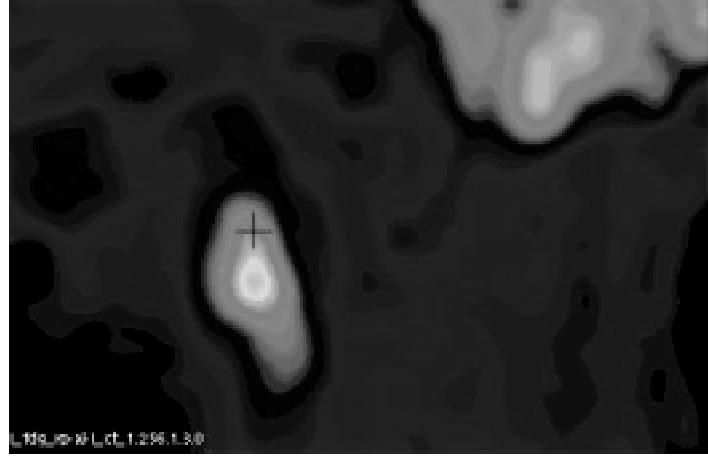
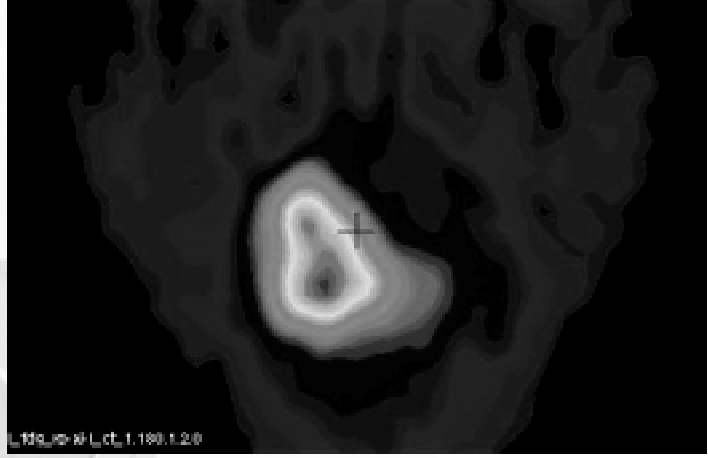
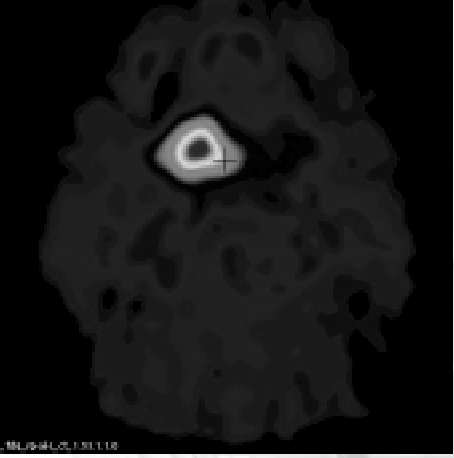
Image-Guided Radiation Therapy in HNSCC

The 4th dimension ...

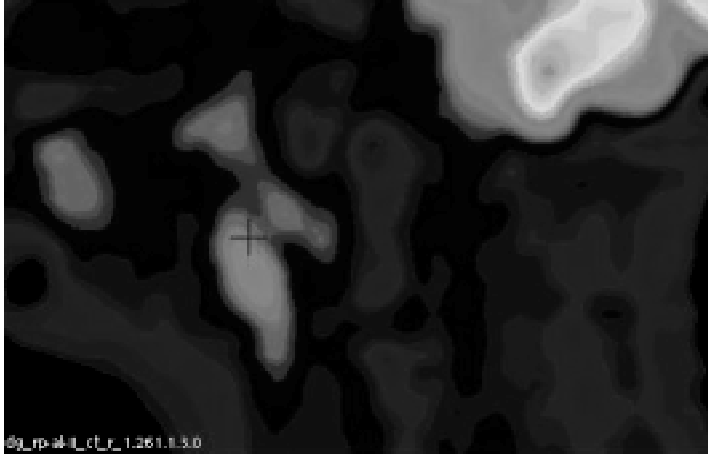
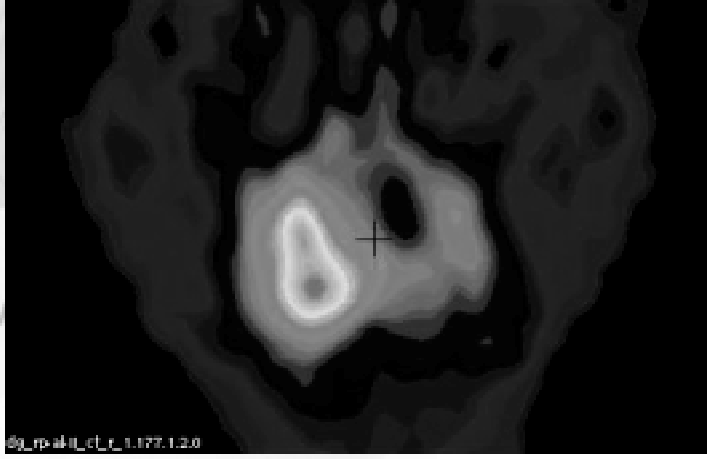
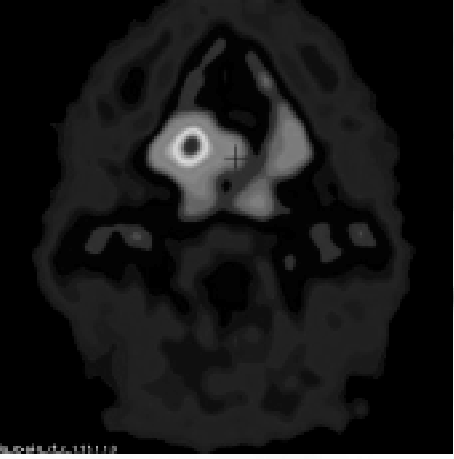


FDG-PET

0 Gy



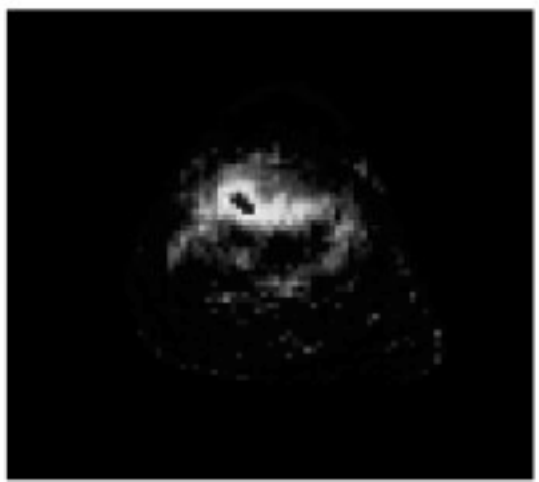
50 Gy





PET image segmentation during RxTh

Raw image



SBR

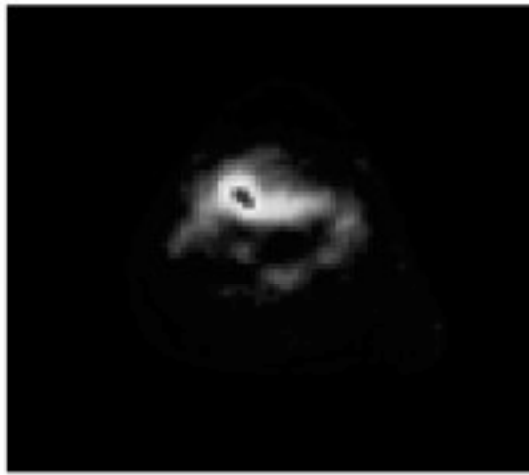


Image processing

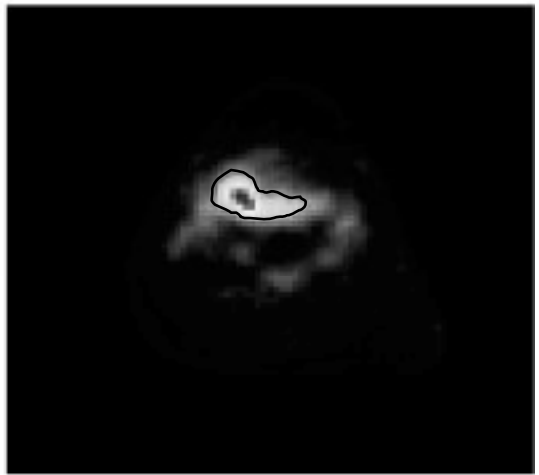


Image segmentation

W&C

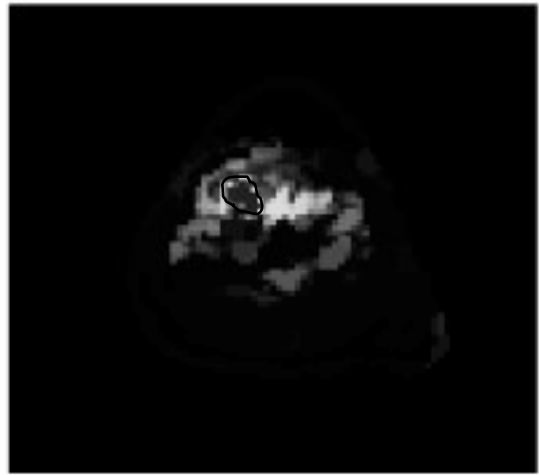
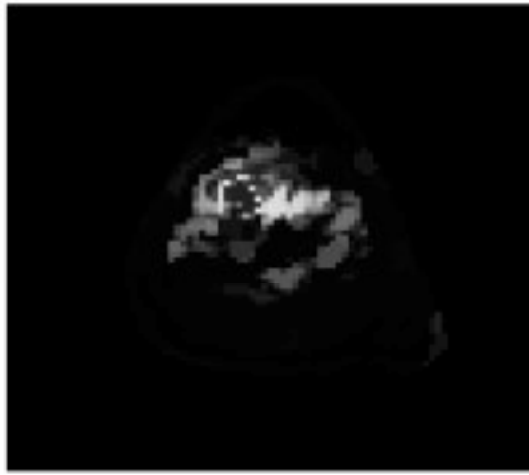
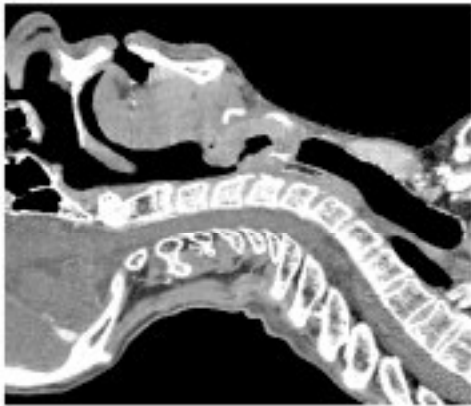




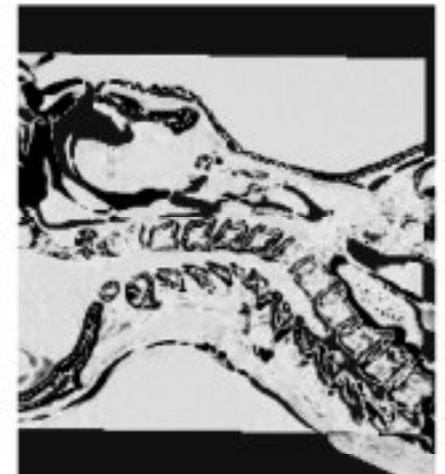
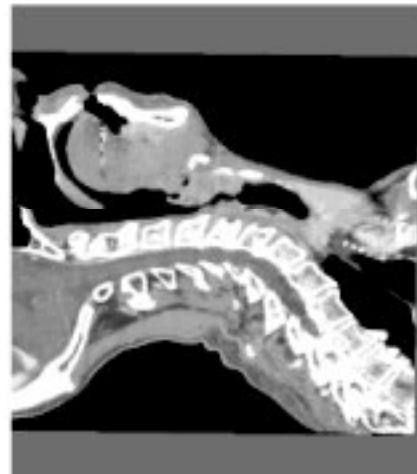
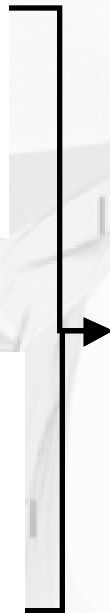
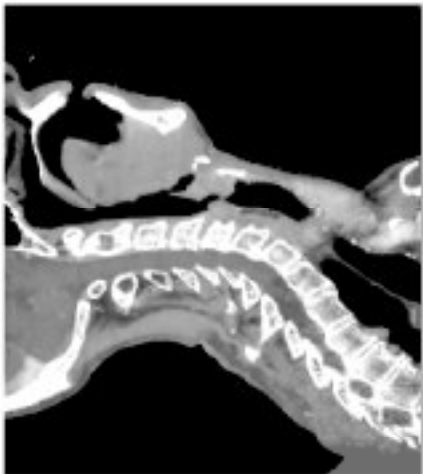
Image registration...

Rigid Registration (mutual information)

Week 0



Week 3

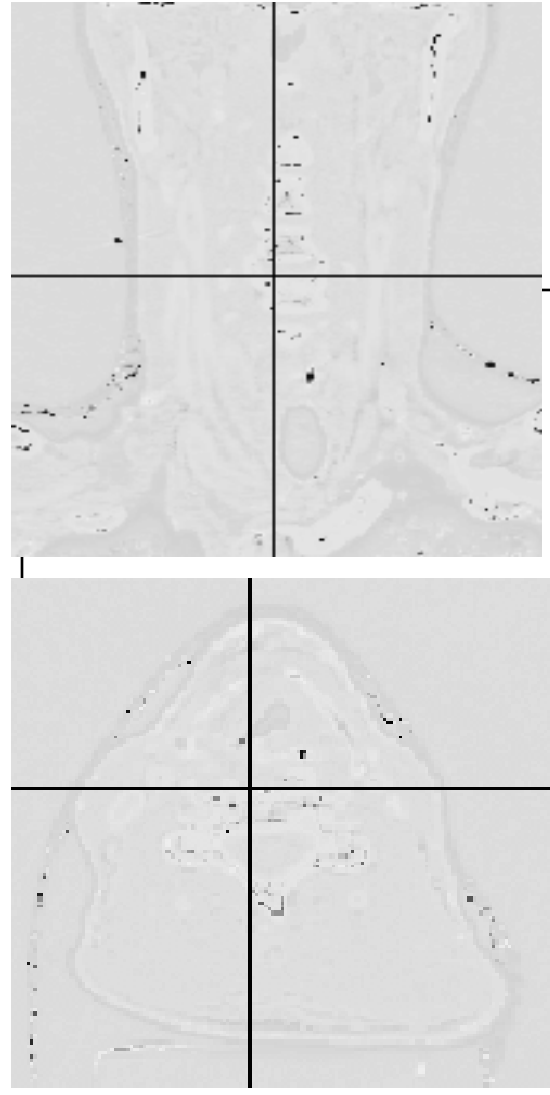
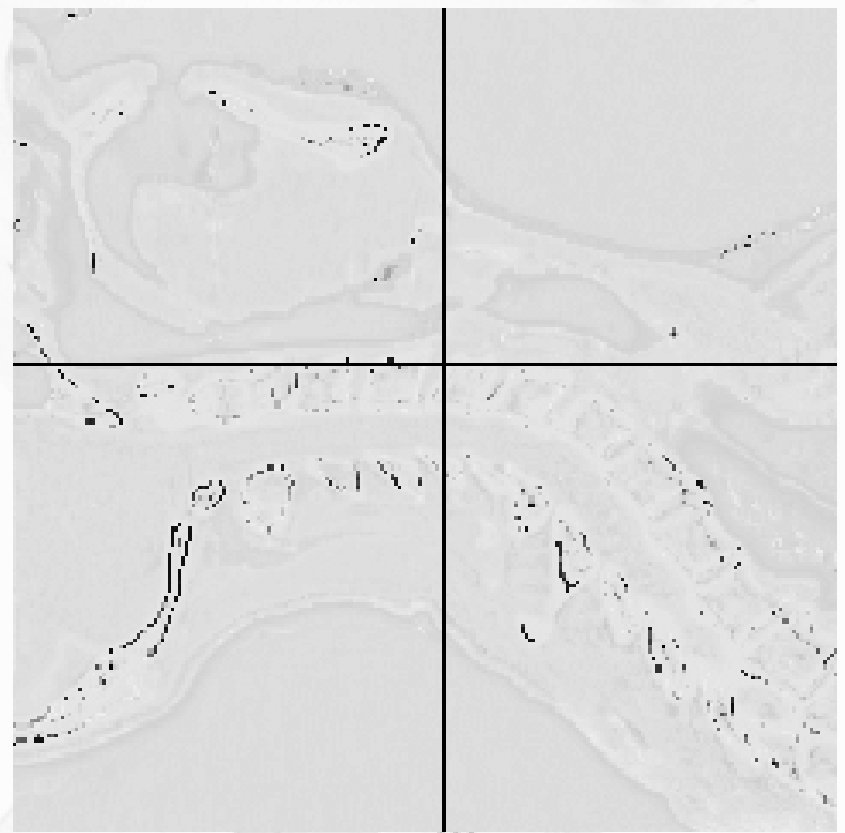


Differential display



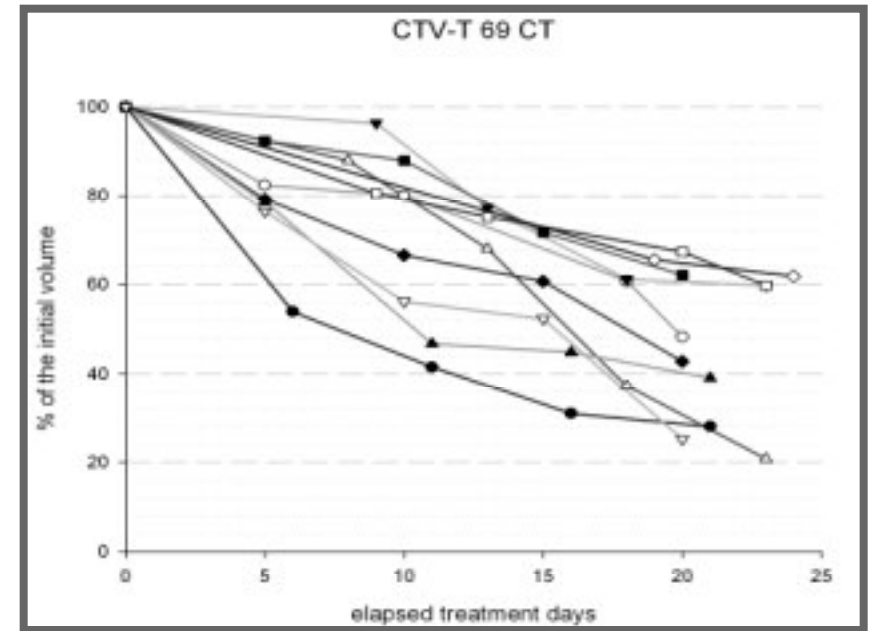
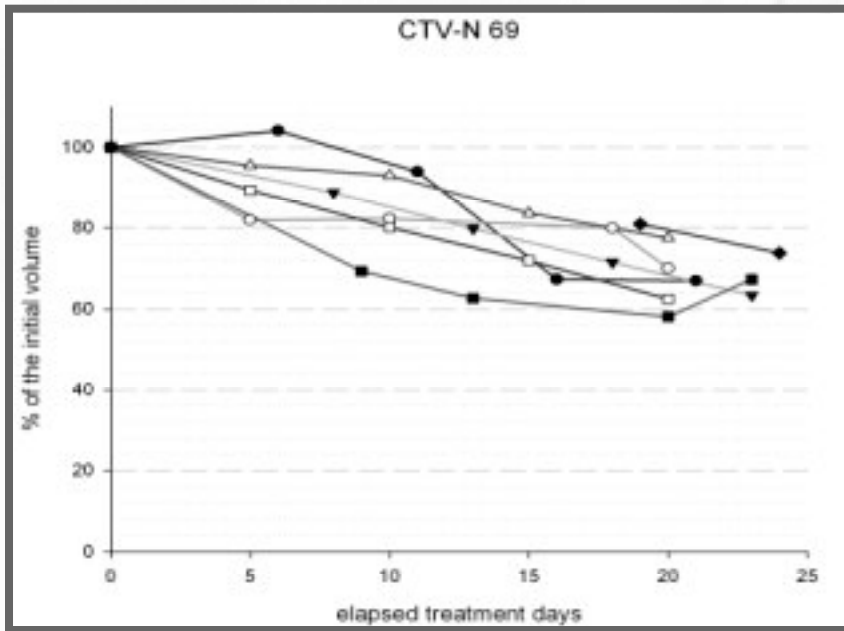
Image registration...

Differential display





Variation in therapeutic CTVs during RT-CH..



Mean slope: -1.46% / treat day ($p < 0.05$)

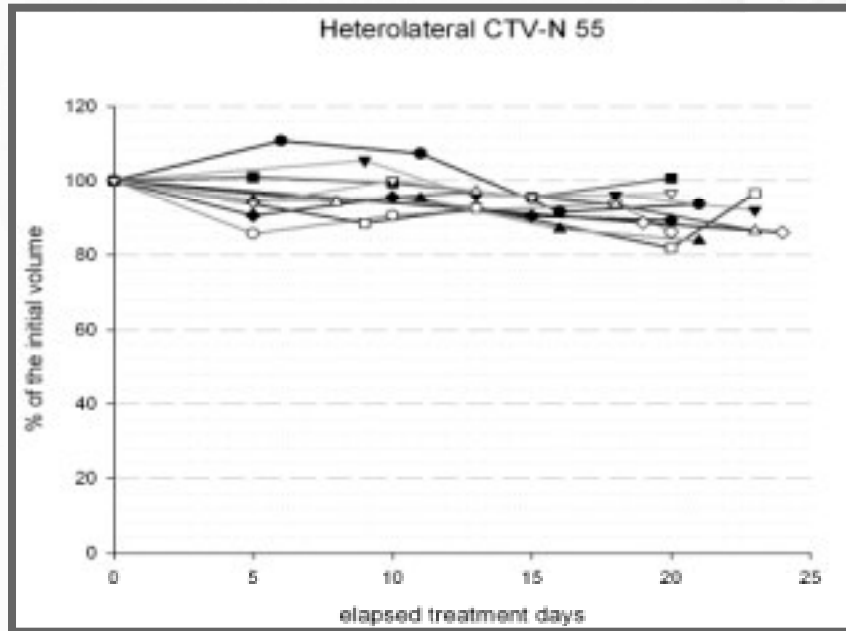
Medial shift: 0.91mm after 25# ($p < 0.05$)

Mean slope: -2.55% / treat day ($p < 0.05$)

Lateral shift: 1.52mm after 25# ($p < 0.05$)

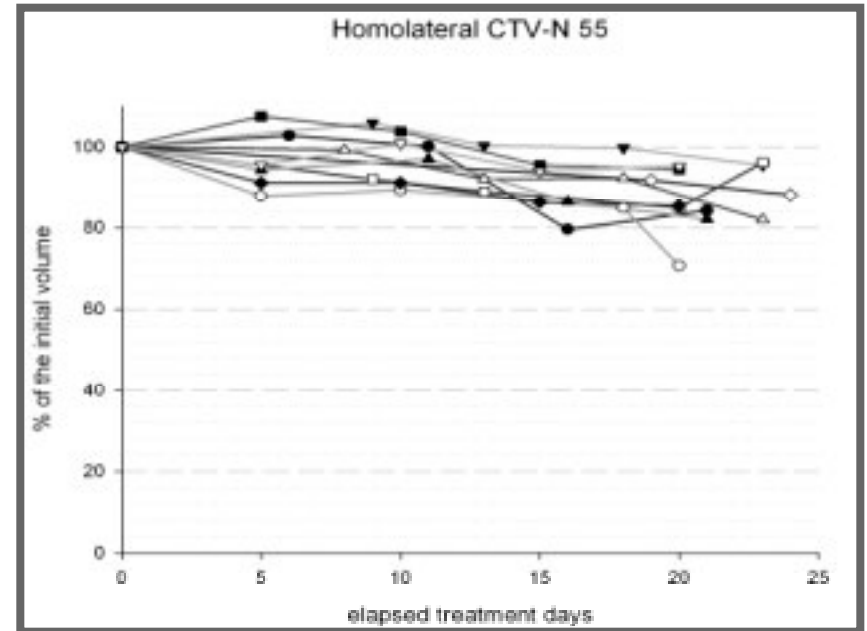


Variation in prophylactic CTVs during RT-CH...



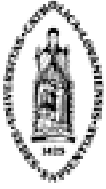
Mean slope: -0.47% / treat day ($p < 0.05$)

No shift

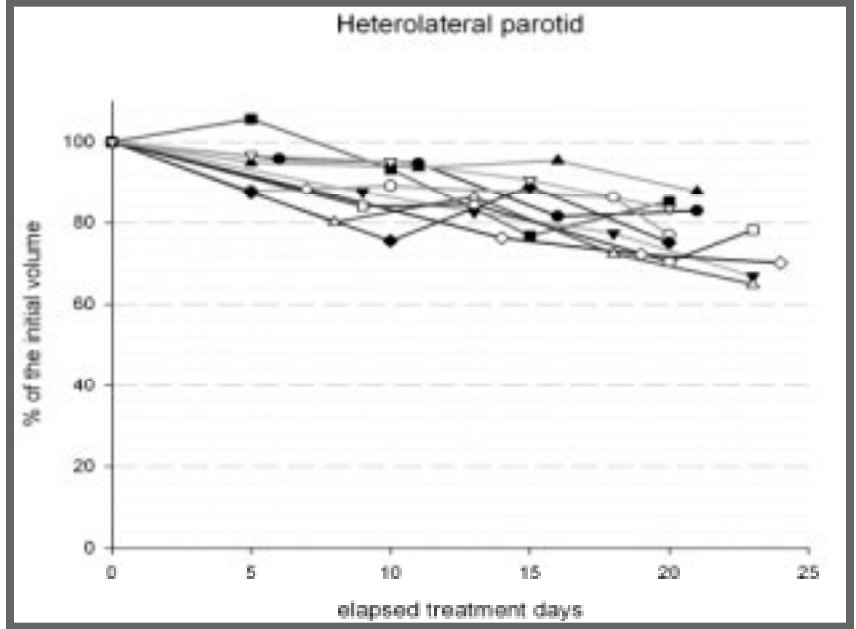
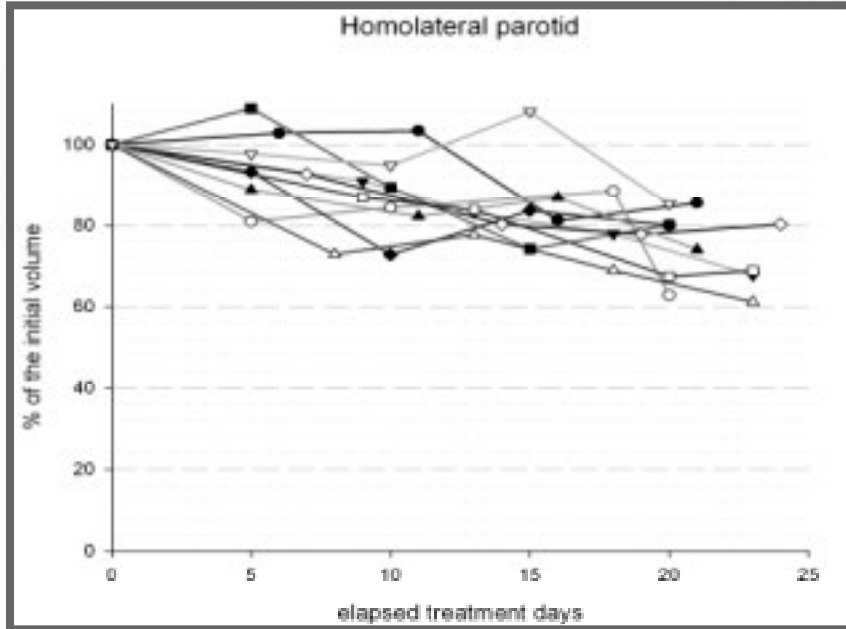


Mean slope: -0.41% / treat day ($p < 0.05$)

Medial shift: 1.76mm after 25# ($p < 0.05$)



Variation in parotid volumes during RT-CH...



Mean slope: -0.93% / treat day ($p < 0.05$)

Mean slope: -1.03% / treat day ($p < 0.05$)

Medial shift: 3.21mm after 25# ($p < 0.05$)

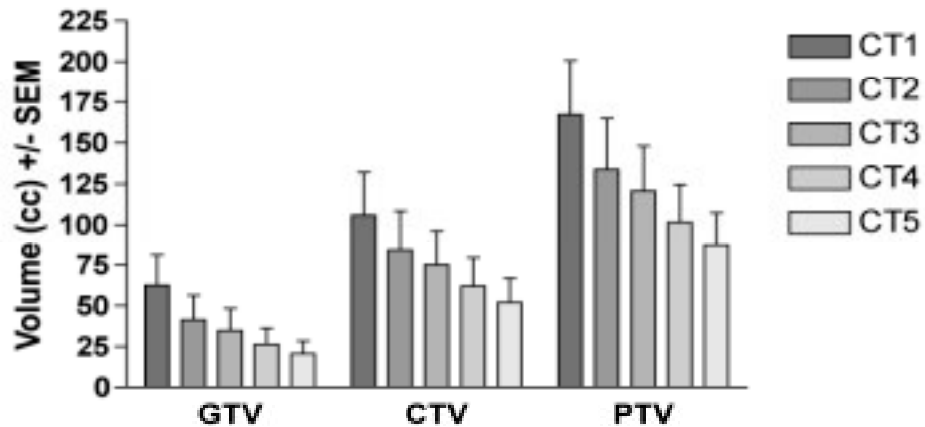
No shift



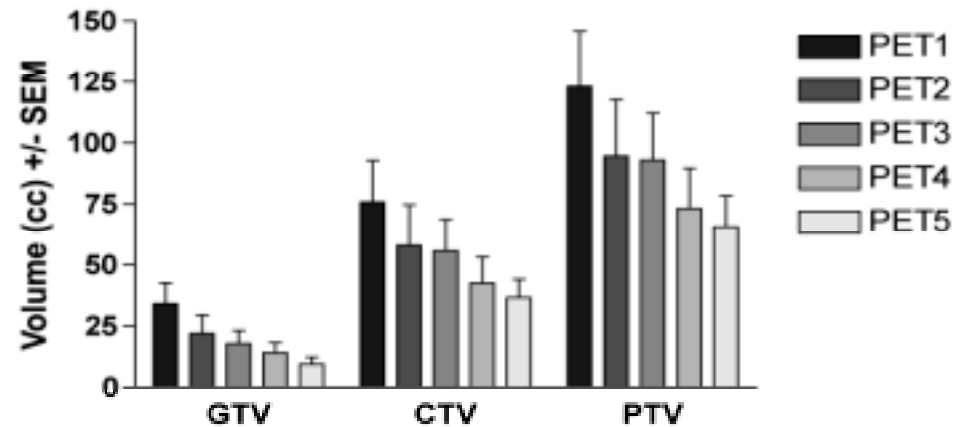
Impact on Target Volume delineation



Therapeutic CT-based Target Volumes

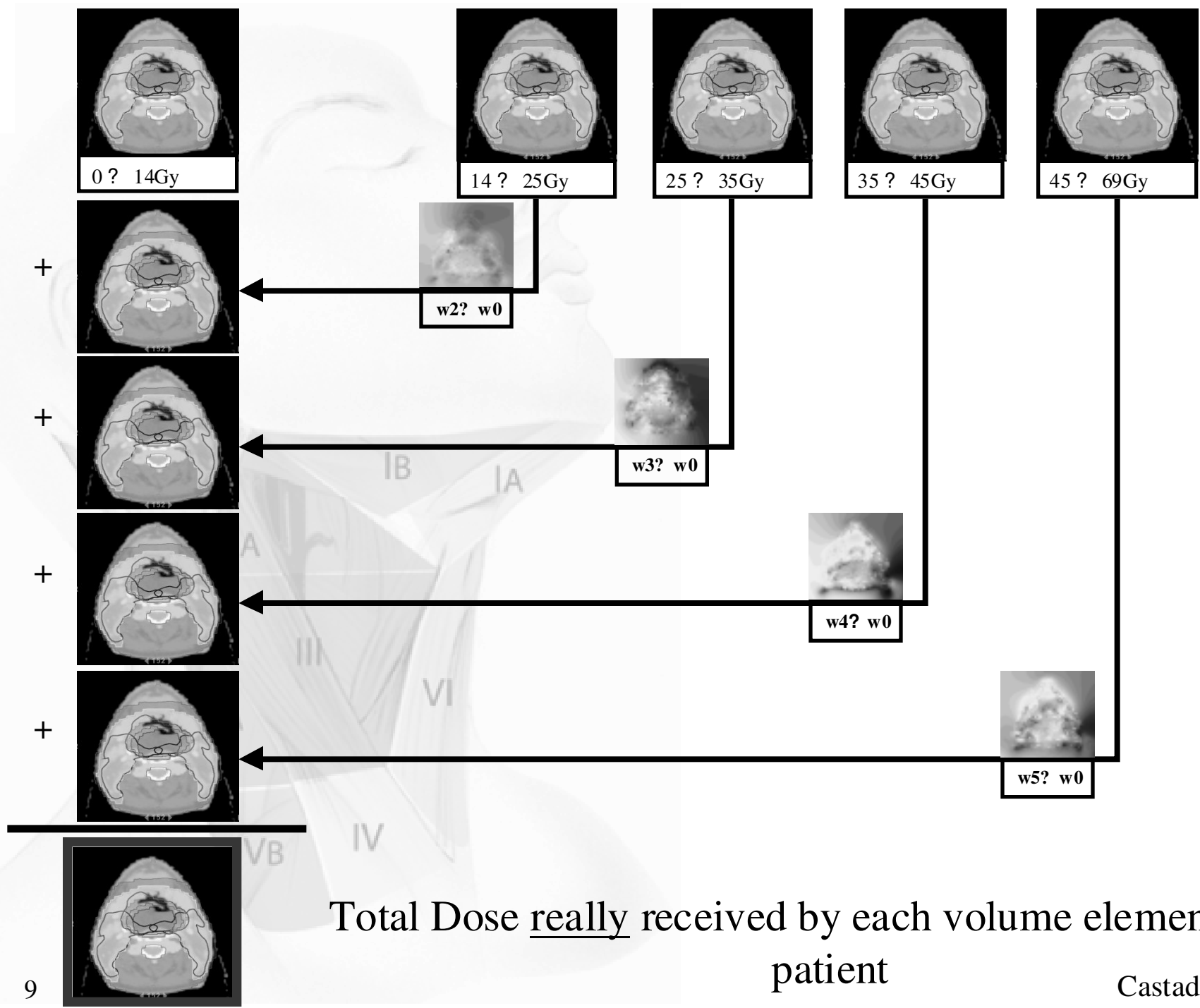


Therapeutic PET-based Target Volumes



$P < 0.001$

VB IV

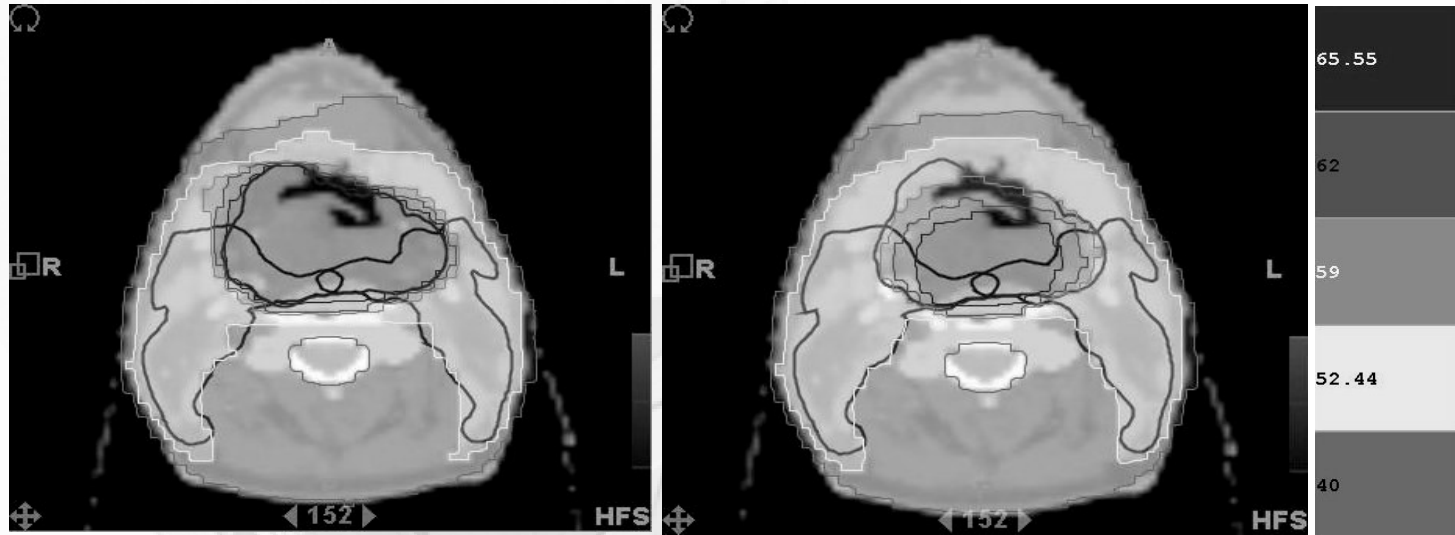




Impact on dose distribution

Classic CT-based planning

Adaptive PET-based planning



SIB-IMRT
 30x2.3 Gy
 30x1.85 Gy

P<0.001

Planning	V ₁₀	V ₅₀	V ₈₀	V ₉₀	V ₉₅	V ₁₀₀
<i>Classic CT-based</i>	100%	100%	100%	100%	100%	100%
<i>Adaptive CT-based</i>	99%	100%	100%	85%	80%	66%
<i>Classic PET-based</i>	99%	99%	98%	83%	82%	81%
<i>Adaptive PET-based</i>	99%	100%	98%	73%	67%	58%

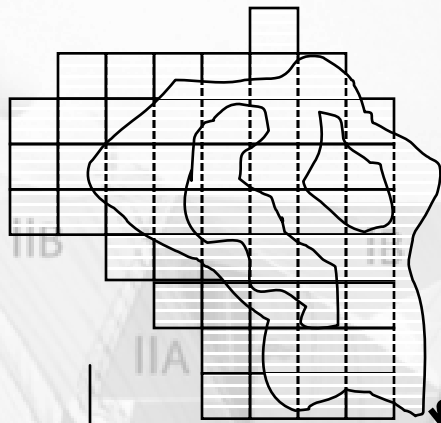
Dose distribution after adaptive RT-CH (n=5)

	« Classical » CI-based	« Classical » PIL-based	« Real » CI-based	« Real » PIL-based	Adaptive CI-based	Adaptive PIL-based
Homolat Parotid D_{mean} (Gy)	22.05	21.63	23.80	23.27	22.91	22.09
Heterolat Parotid D_{mean} (Gy)	18.15	20.00	18.52	19.34	18.57	18.40
SC D_2 (Gy)	39.49	39.76	41	42.04	37.90	38.26
Larynx D_5 (Gy)	65.63	66.33	65.37	66.35	65.57	65.37
Oral cavity D_{mean} (Gy)	37.80	35.18	38.79	36.16	36.01	33.35
Mandible D_2 (Gy)	60.59	57.51	59.52	56.77	58.30	57.27
Homolat Submax gl D_{mean} (Gy)	65.04	62.96	65.52	63.59	64.57	63.09
Heterolat Submax gl D_{mean} (Gy)	54.92	53.77	54.97	53.63	55.11	54.58
Skin V_{65Gy} (cc)	11.66	8.78	12.08	9.25	10.25	7.24
$V_{95\%}$ (cc)	308.89	297.00	400.11	327.56	311.39	254.40



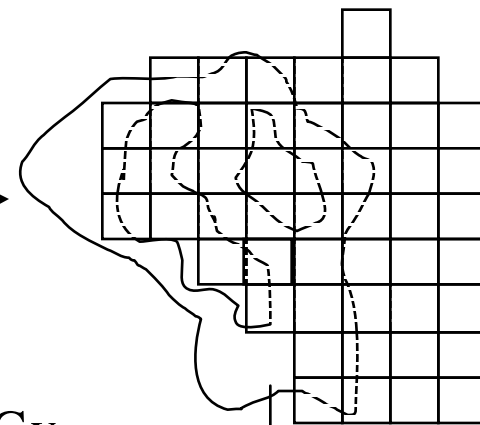
“Dose painting” by number...

Flat dose



Survival is non-flat
(higher in resistant areas)

Non-flat dose



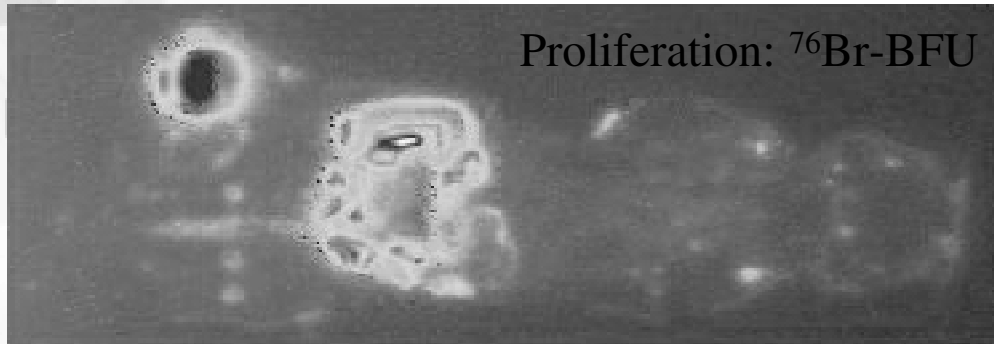
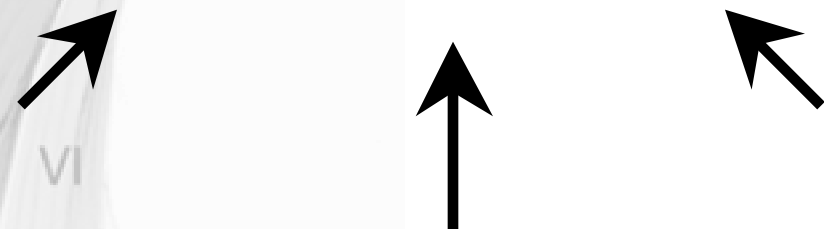
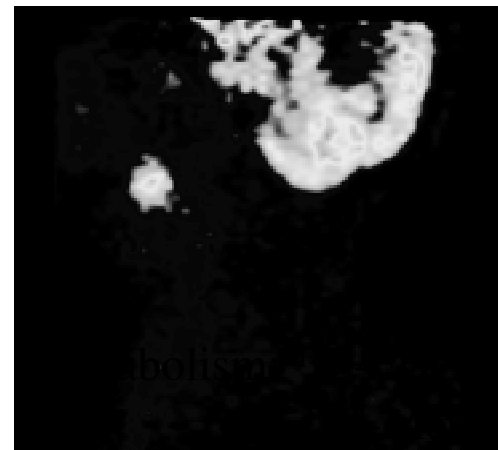
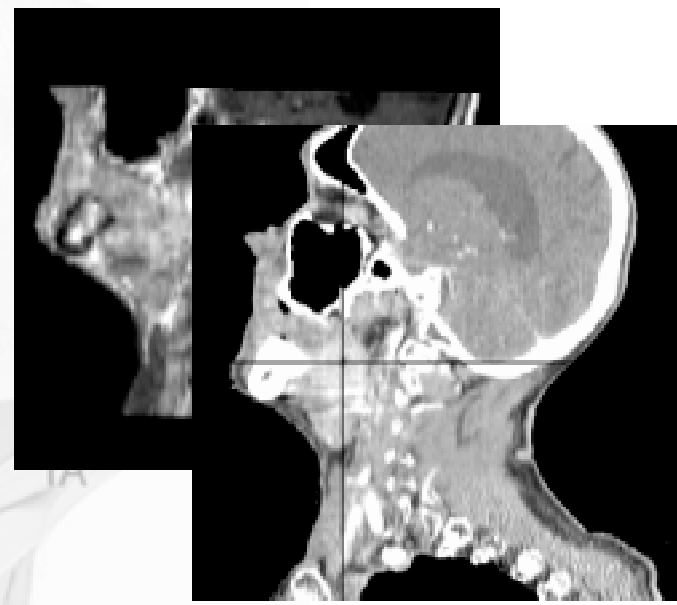
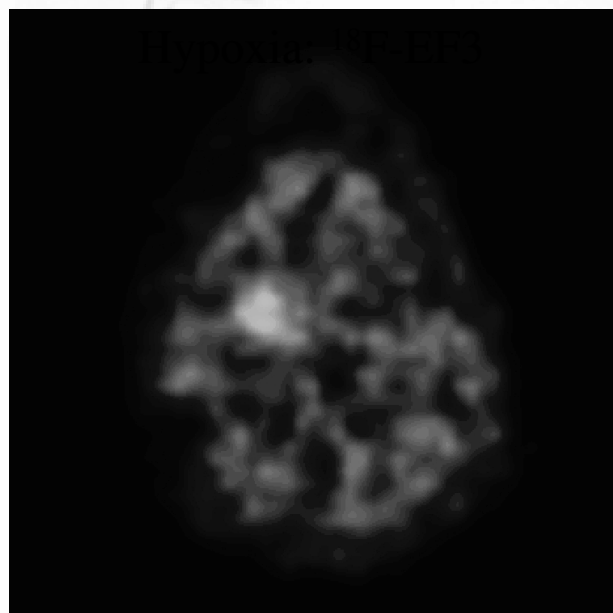
More similar survival
across entire tumor

Far more efficient use of dose

Mean Tumor Dose = 2 Gy



Which biological pathways? ...



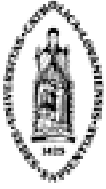


Challenges in Head & Neck loco-regional treatment



- Target selection and delineation
- Adaptive IMRT: geometrical, biological & dosimetrical
 - which imaging modalities??
 - which biological pathways??
 - which volume/dose registration algorithms??
 - how frequently??
- Concomitant association with drugs and/or “small molecules”

The Bridge
at
Argenteuil



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- Oral & Maxillo-Facial surgery
- Pathology
- PET laboratory
- Radiation Oncology

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