Assessment and management of uncertainties in Head & Neck IMRT

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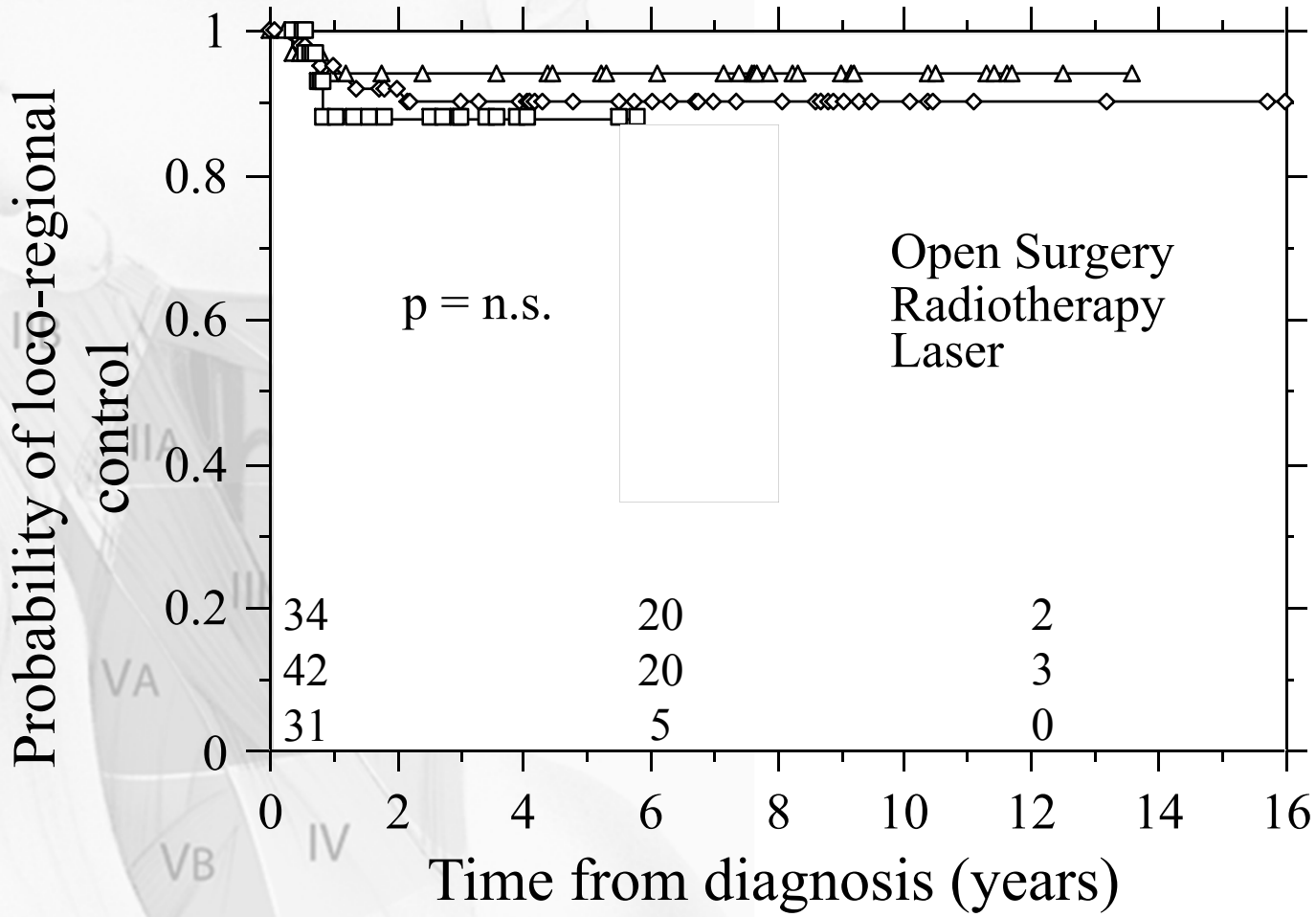
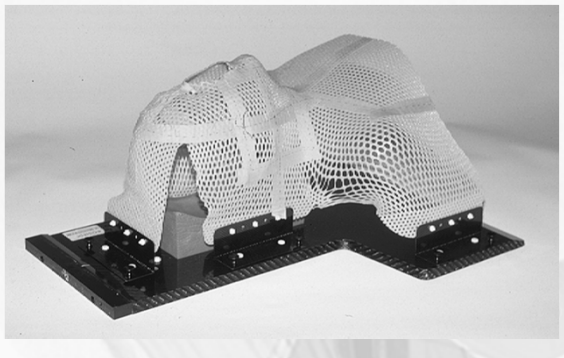
AAPM
Aug. 2011

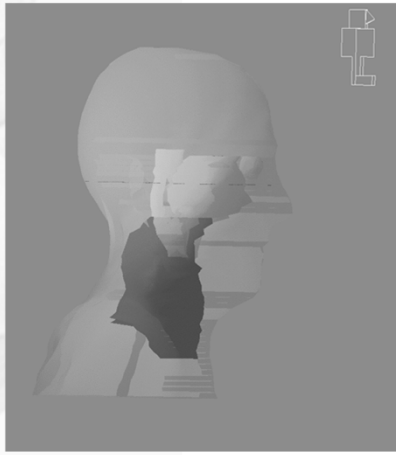
Evidence-based management of T1N0 glottic carcinomas: level 3

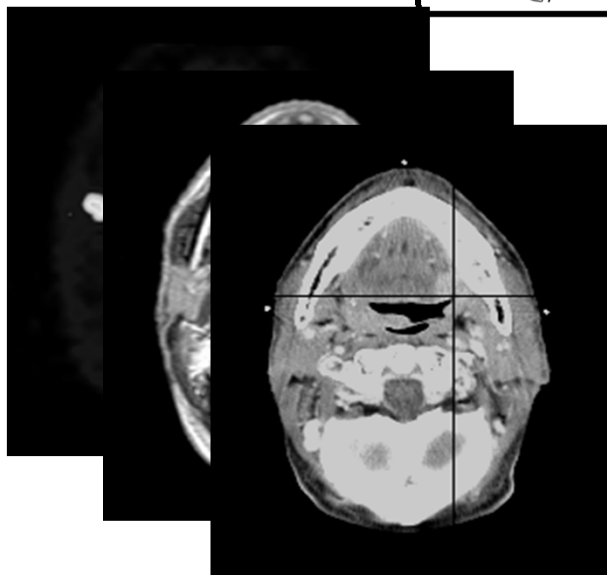


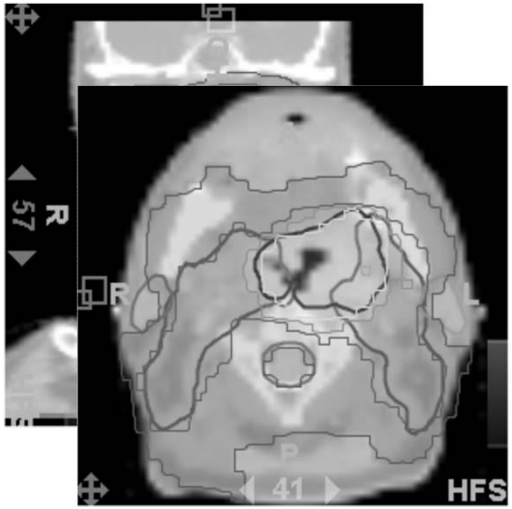
Rosier, *R&O*, 1998

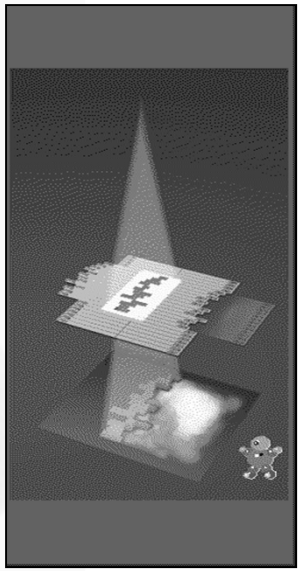
IMRT in Head and Neck Tumors











IMRT in Head and Neck Tumors

Where uncertainties could come from?

- selection and delineation of TVs and OARs
- choice of the optimal imaging modality
- patient positioning
- dose optimization
- treatment adaptation

IMRT in Head and Neck Tumors

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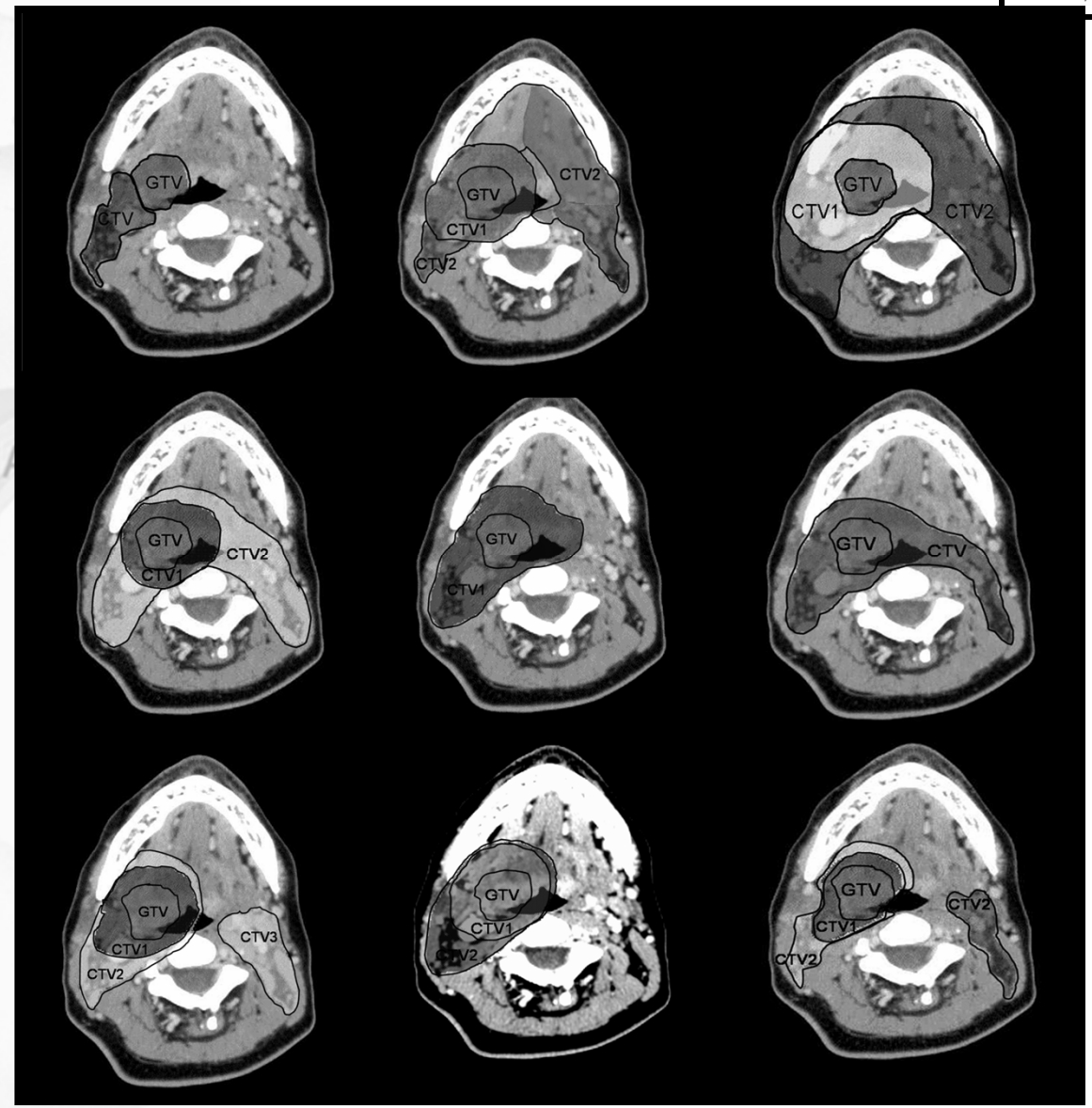
Heterogeneity in H&N TV delineation



Harari et al., 2004

Study design

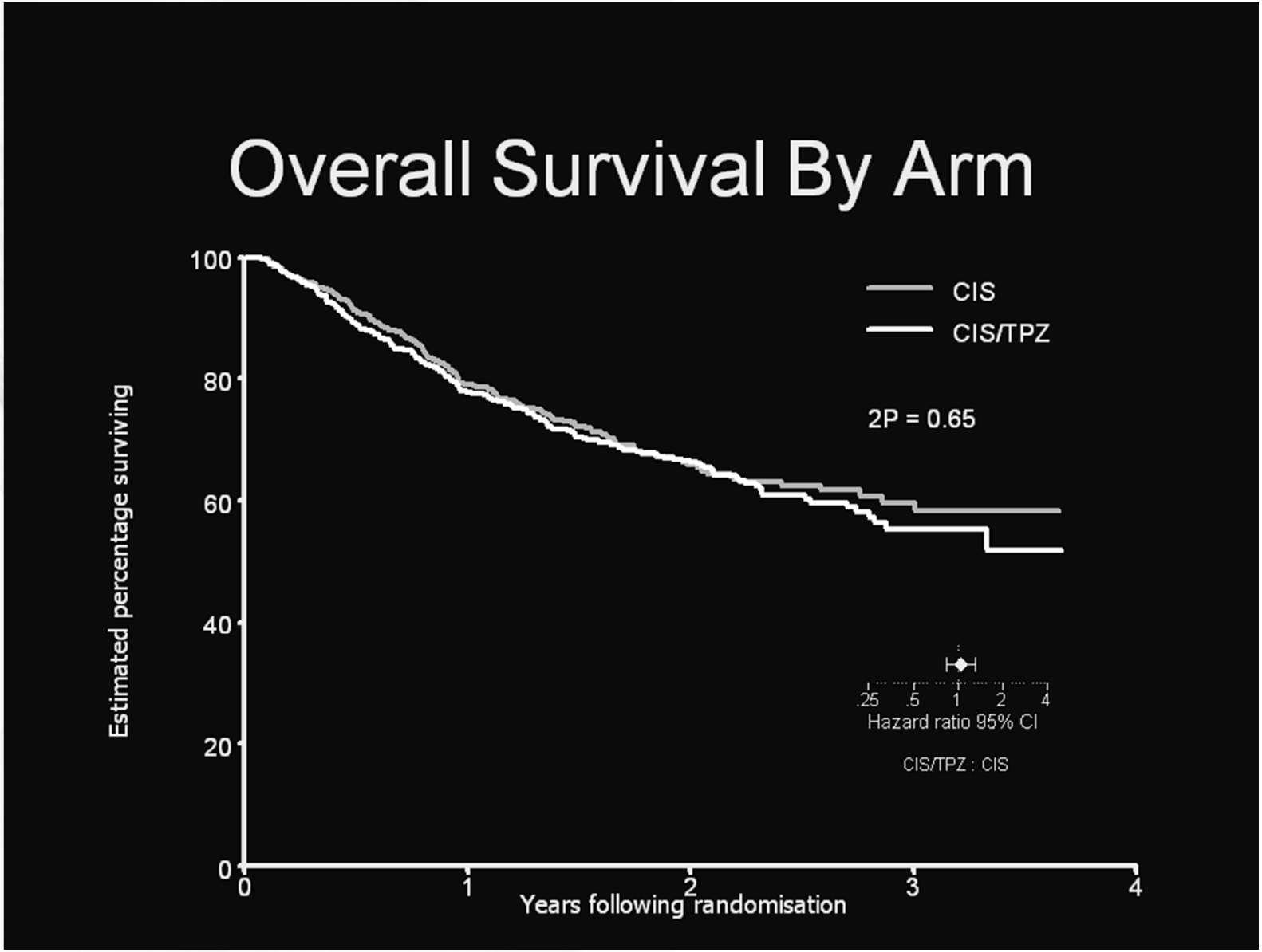
Patients with Stage III or IV SCCHN
(stratified by stage, site, hemoglobin)

Randomization

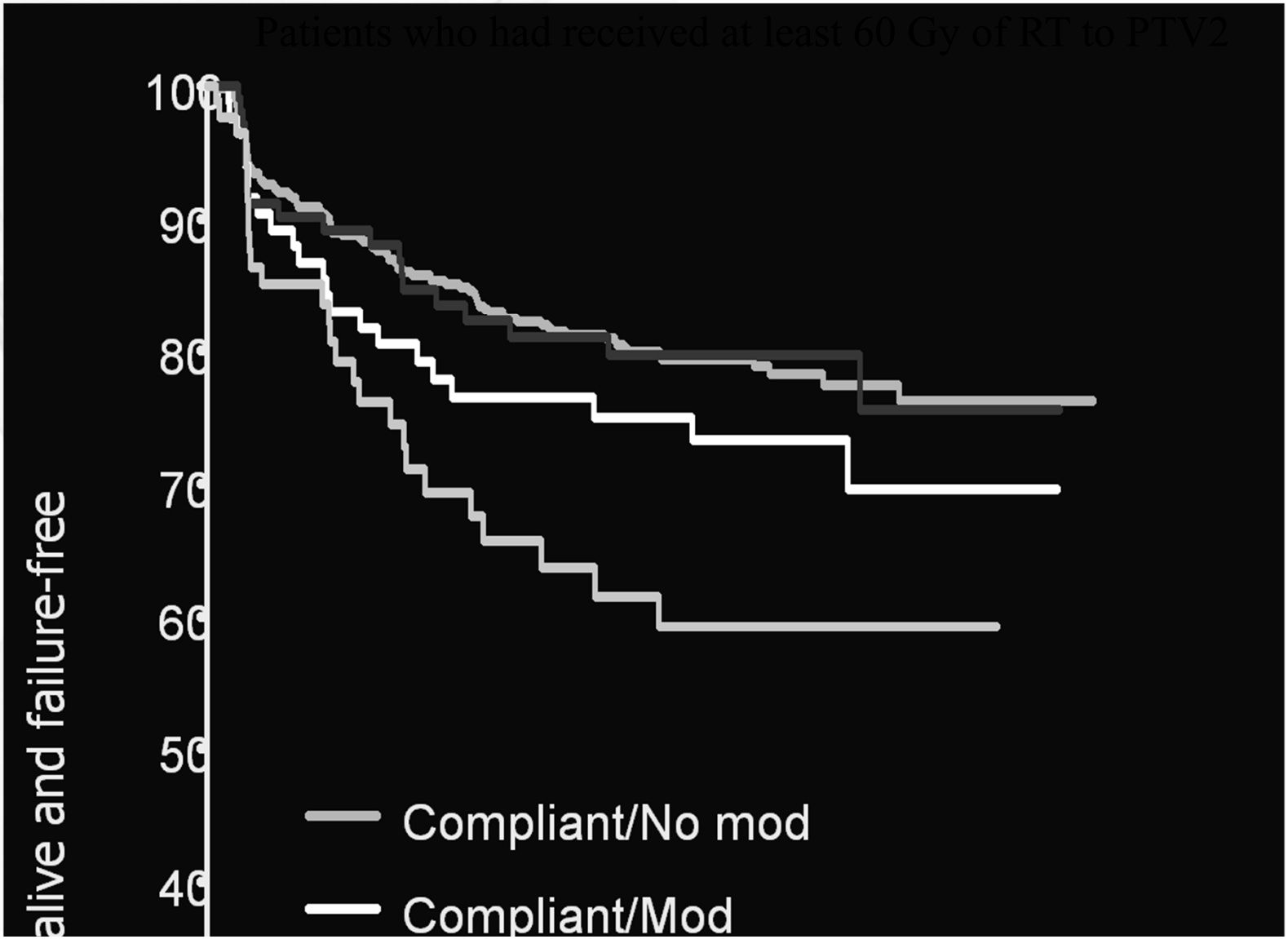
Cisplatin, RT

Tirapazamine,
cisplatin, RT

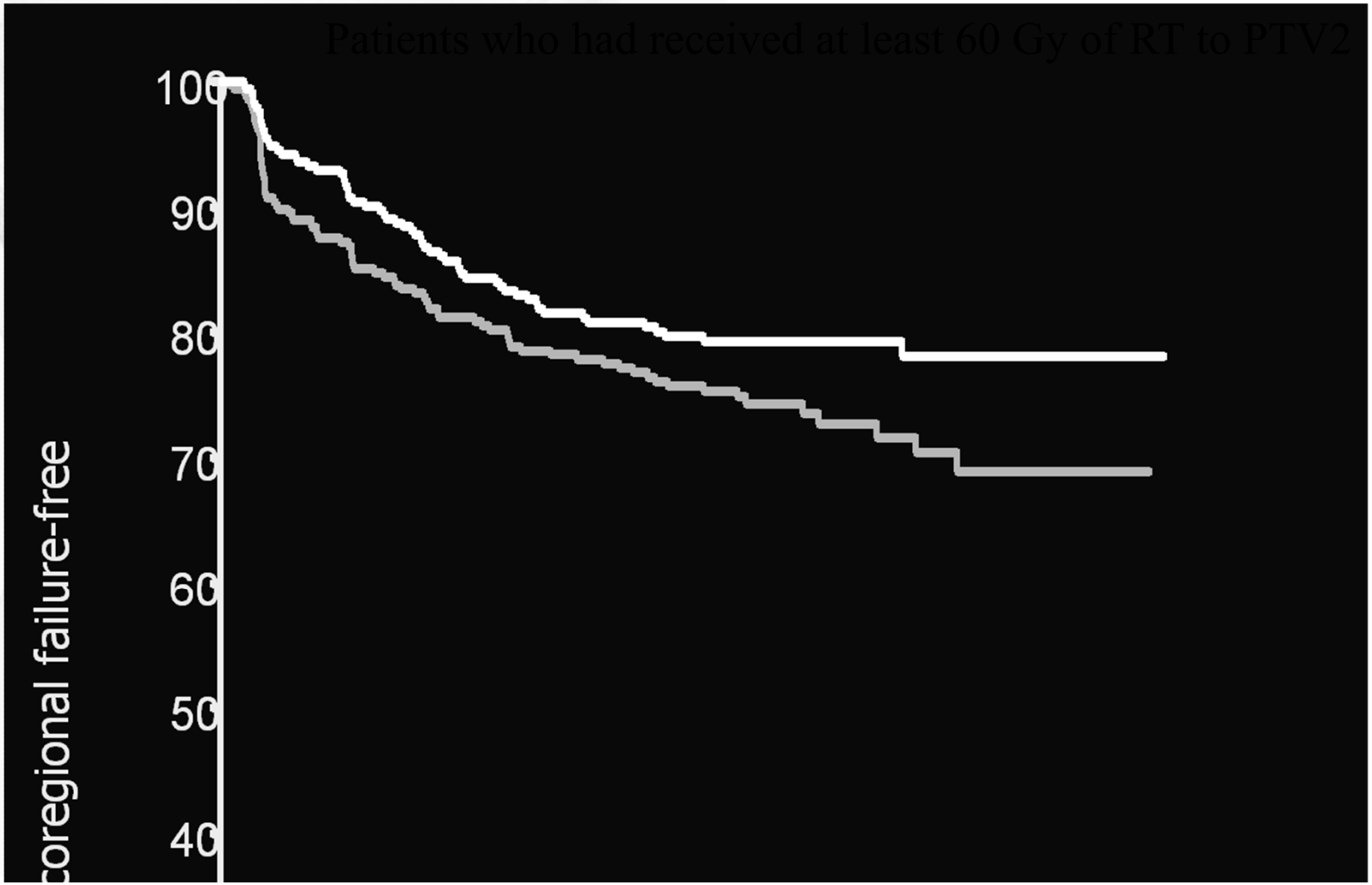
Results – Final analysis by ITT



Failure-free survival by deviation status



Time to LRF by treatment arm in patients without predicted adverse impact on TCP



Factors analysed for adverse impact on TCP after secondary review: Investigator factors

Number of patients enrolled

Enrolment bracket	Number of patients	Number with major adverse impact	Percent
1-4 (26 centres)	57	17	29.8%
5-9 (22 centres)	130	28	21.5%
10-19 (22 centres)	279	33	11.8%
$\geq$ 20 (11 centres)	352	19	5.4%

2P<0.0001

IMRT in Head and Neck Tumors

ELSEVIER

Radiotherapy and Oncology 56 (2000) 135–150

RADIOTHERAPY & ONCOLOGY
JOURNAL OF THE EUROPEAN SOCIETY FOR THERAPEUTIC RADIOLOGY AND ONCOLOGY

www.elsevier.com/locate/radonline

Review article

Selection and delineation of lymph node target volumes in head and neck conformal radiotherapy. Proposal for standardizing terminology and procedure based on the surgical experience

Vincent Grégoire[a,*], Emmanuel Coche[b], Guy Cosnard[b], Marc Hamoir[c], Hervé Reychler[d]

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IMRT in Head and Neck Tumors

ELSEVIER

Radiotherapy and Oncology 69 (2003) 227–236

RADIOTHERAPY & ONCOLOGY
JOURNAL OF THE EUROPEAN SOCIETY FOR THERAPEUTIC RADIOLOGY AND ONCOLOGY

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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]

DAHANCA: http://www.dshho.suite.dk/dahanca/guidelines.html
EORTC: http://www.eortc.be/home/ Radio/EDUCATION.htm
RTOG: http://www.rtog.org/hnatlas/main.htm

Which CTV for the node positive and the post-operative neck?

Radiotherapy and Oncology 79 (2006) 15–20
www.thegreenjournal.com

Target volume delineation

Proposal for the delineation of the nodal CTV in the node-positive and the post-operative neck

Vincent Grégoire[a,*], Avraham Eisbruch[b], Marc Hamoir[c], Peter Levendag[d]

[a]Department of Radiation Oncology, Head and Neck Oncology Program and Center for Molecular Imaging and Experimental Radiation Oncology, Université Catholique de Louvain, Brussels, Belgium, [b]Department of Radiation Oncology, University of Michigan, Ann Arbor, MI, USA, [c]Department of Head and Neck Surgery and Head and Neck Oncology Program, Université Catholique de Louvain, Brussels, Belgium, [d]Department of Radiation Oncology, Rotterdam, The Netherlands

Which CTV for the neck?

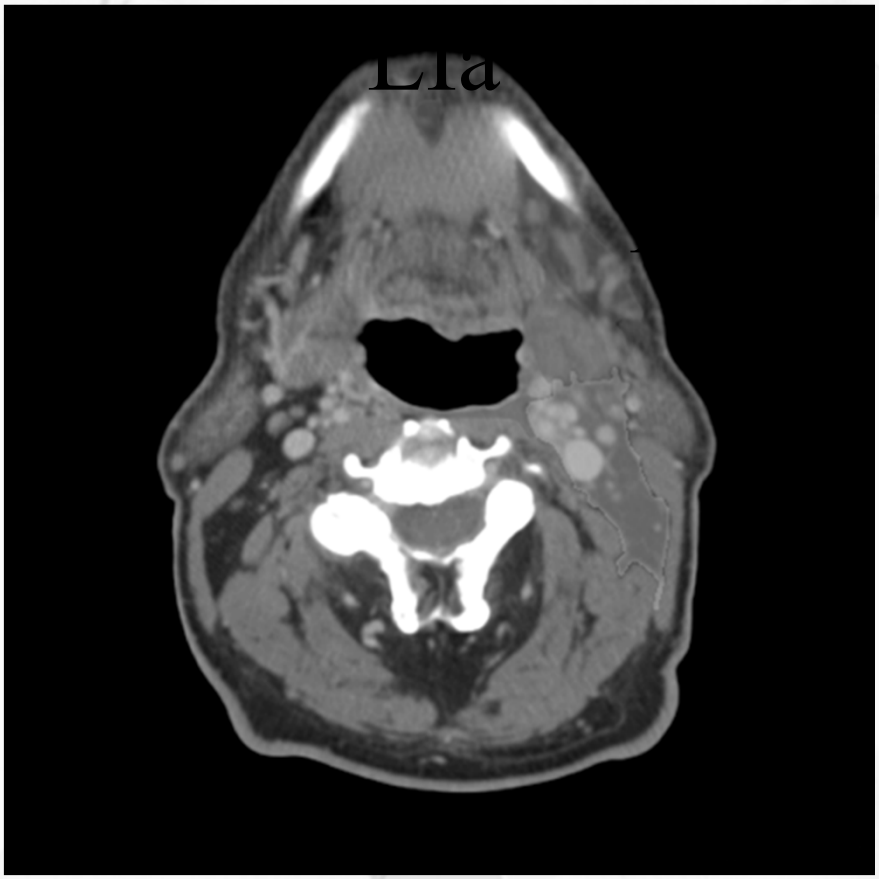
Oropharyngeal Carcinoma

Nodal stage (AJCC 1997)	Levels to be included in the CTV	
	Ipsilateral neck	Contralateral neck
N0 - N1 (in level II, III or IV)	II-III-IV + RP[1] for post. pharyngeal wall tumor	II-III-IV + RP[1] for post. pharyngeal wall tumor
N2a - N2b	Ib, II, III, IV, V + RP	II-III-IV + RP[1] for post. pharyngeal wall tumor
N2c	According to N stage on each side of the neck	According to N stage on each side of the neck
N3	I, II, III, IV, V + RP ± adjacent structures according to clinical and radiological data	II-III-IV + RP[1] for post. pharyngeal wall tumor

[1]retropharyngeal nodes

Grégoire et al., 2000

CT-based delineation of lymph node levels in the neck: international consensus guidelines

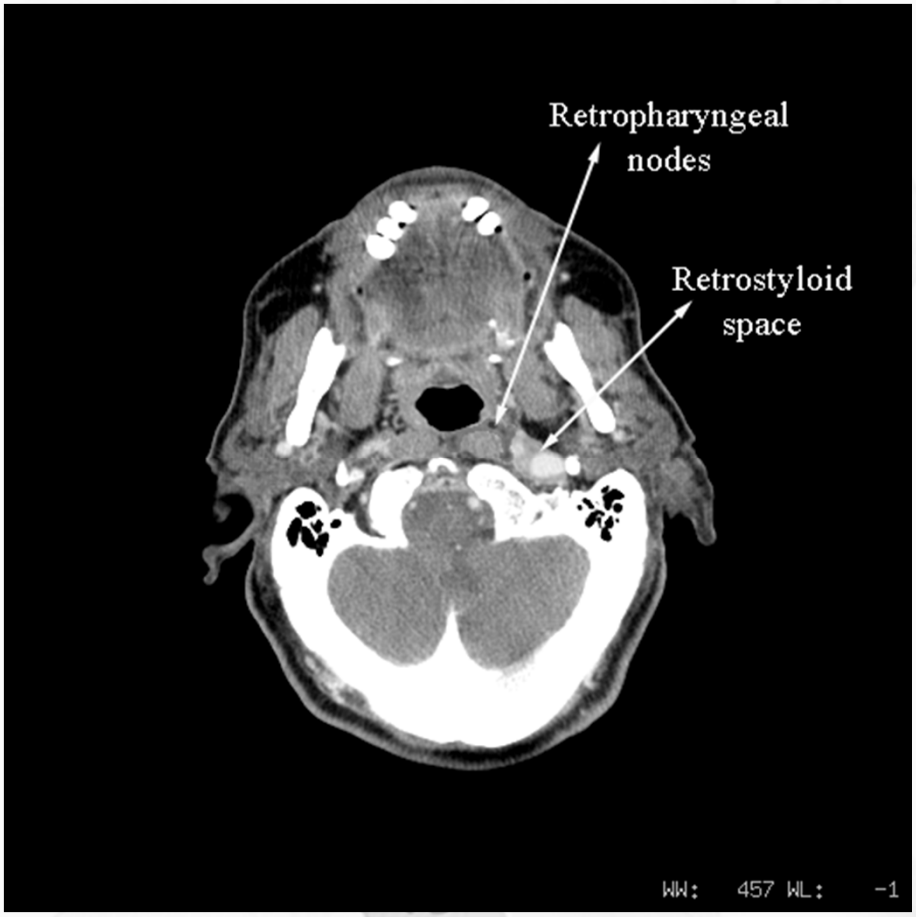


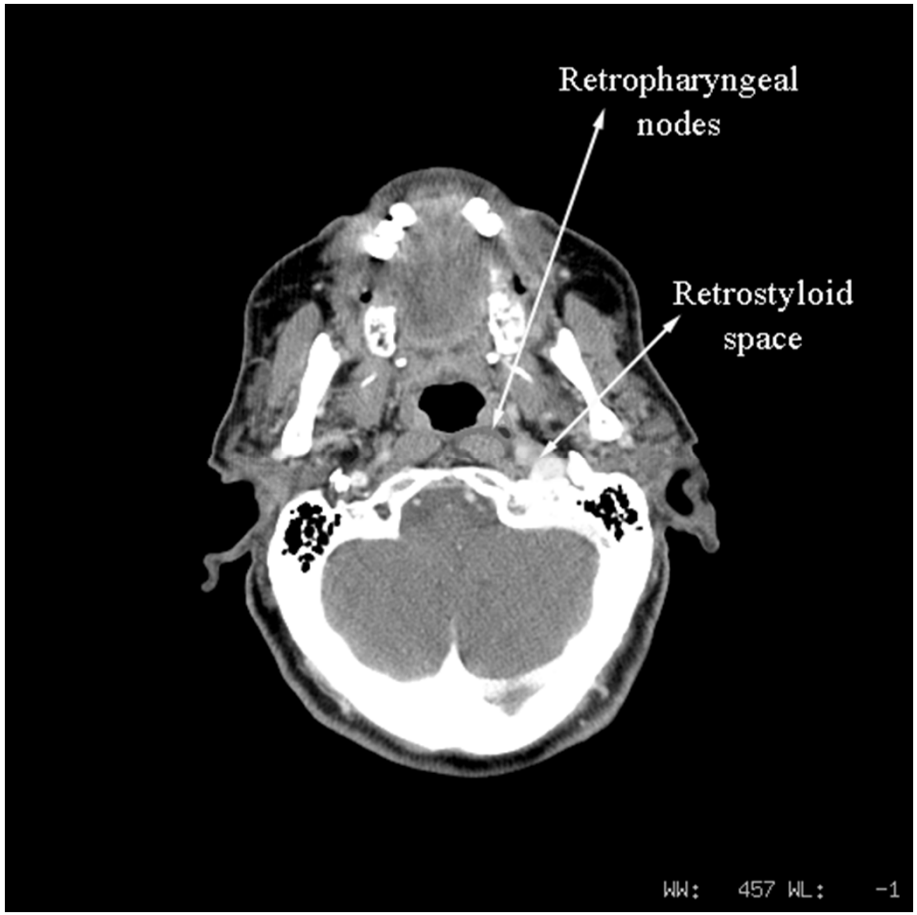
Level Ia and Ib

Ant.	symphysis menti / platysma
Post.	hyoid bone / submandibular gland
Lat.	ant. belly of digastric m. (Ia) mandible / platysma (Ib)
Med.	ant. belly of digastric m. (Ib)
Cra.	geniohyoid m./mandible (Ia) mylohyoid m, submandibular gland (Ib)
Cau.	hyoid bone

Grégoire et al., 2003

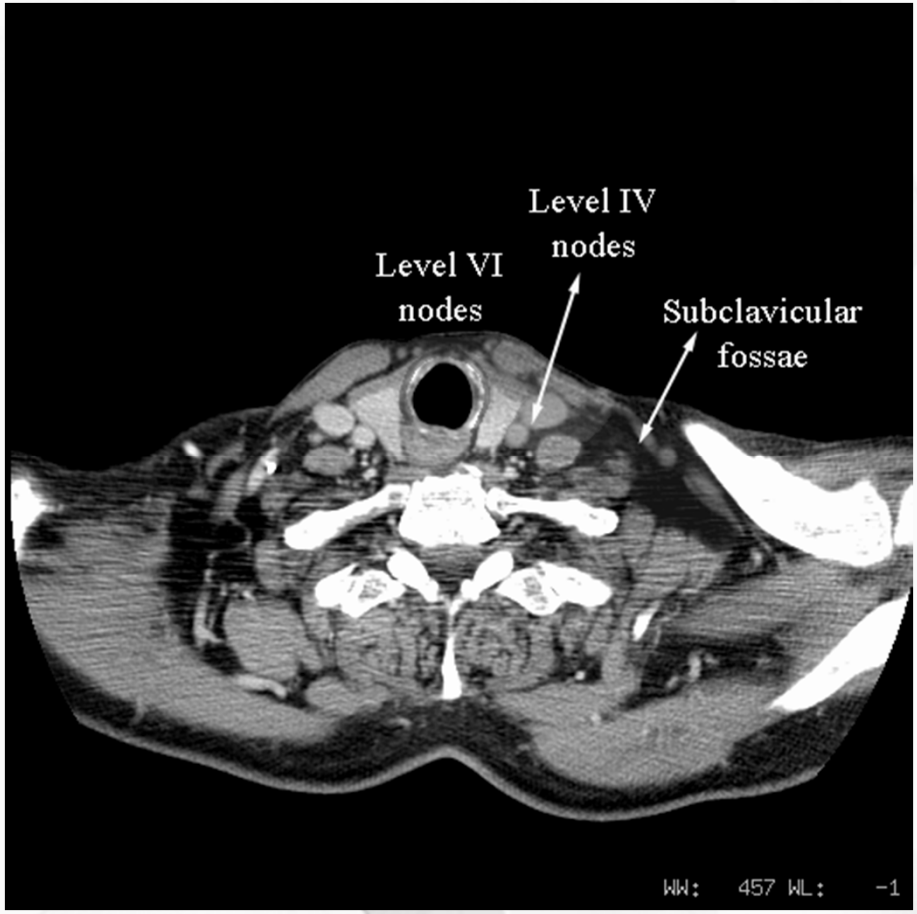
CT-based delineation of lymph node levels in the neck: retrostyloid space

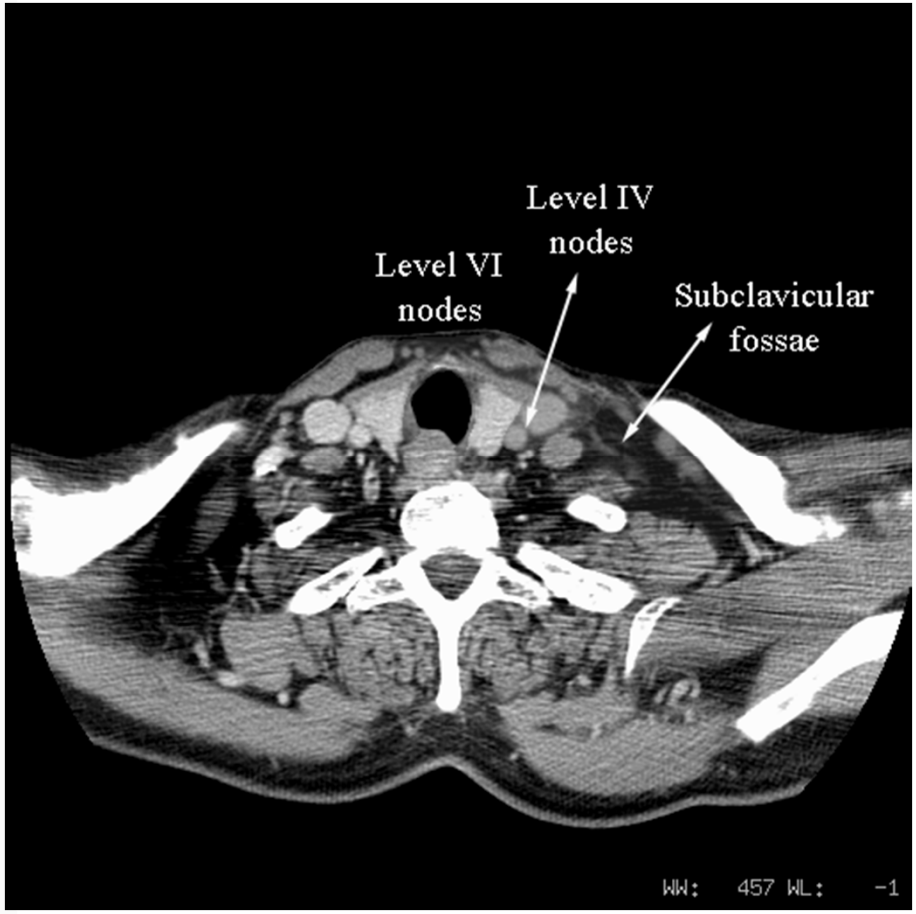




Grégoire et al., 2006

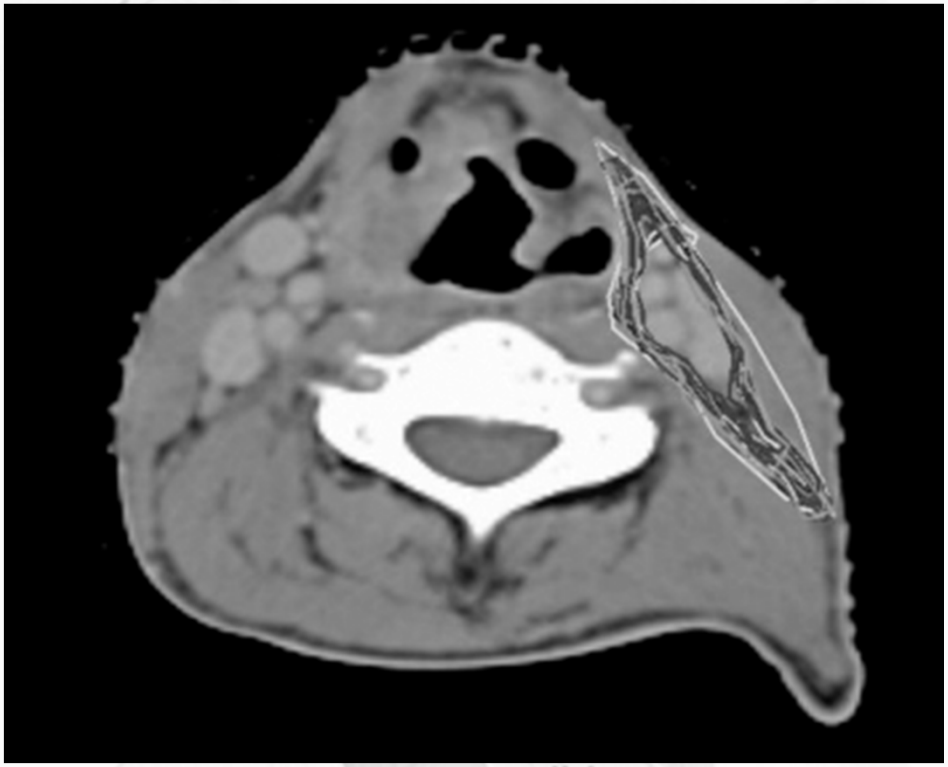
CT-based delineation of lymph node levels in the neck: subclavicular fossae





Grégoire et al., 2006

H&N IMRT practice heterogeneity among Dutch Radiation Oncologists

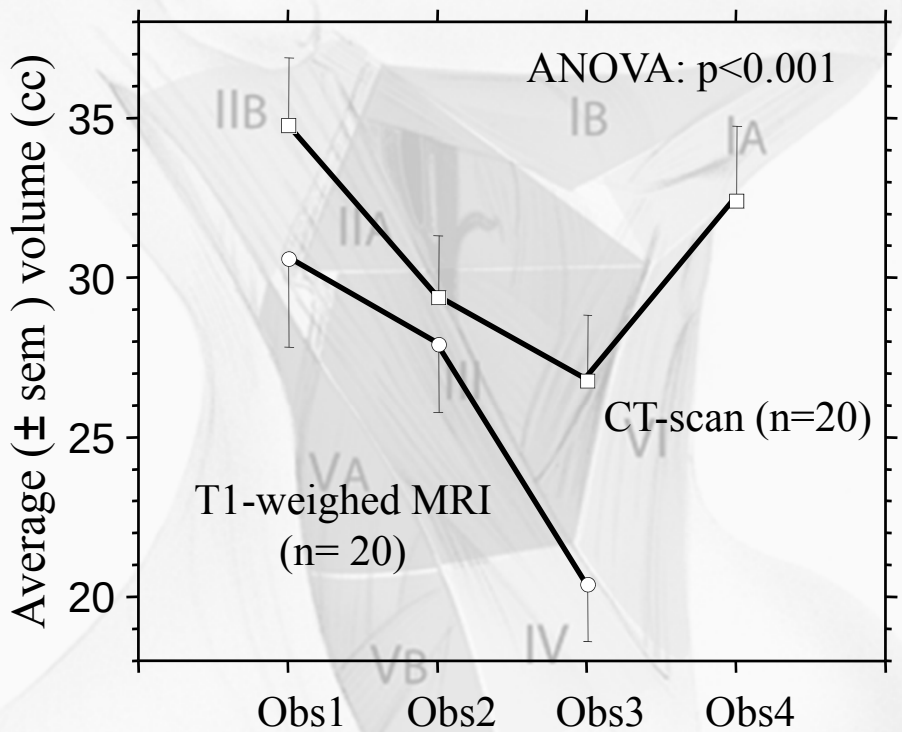


Rasch et al., 2007

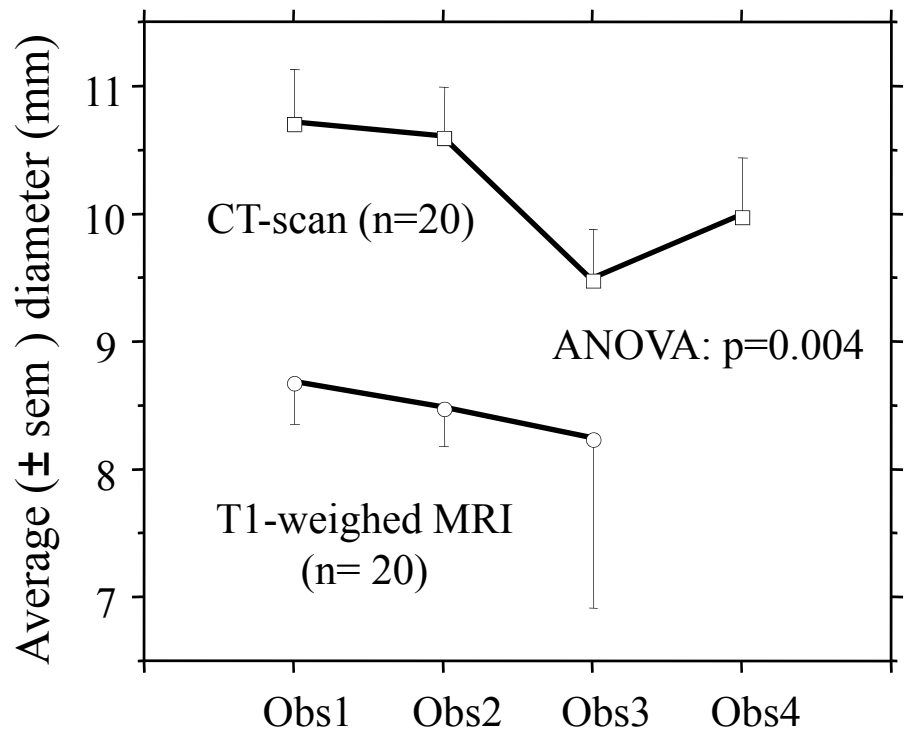
Inter-observer variability on OAR delineation with CT-scan and MRI

Organ At Risk (OAR)

Parotid glands



Spinal cord



Geets *et al*, 2005

IMRT in Head and Neck Tumors

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- patient positioning
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Target selection and delineation

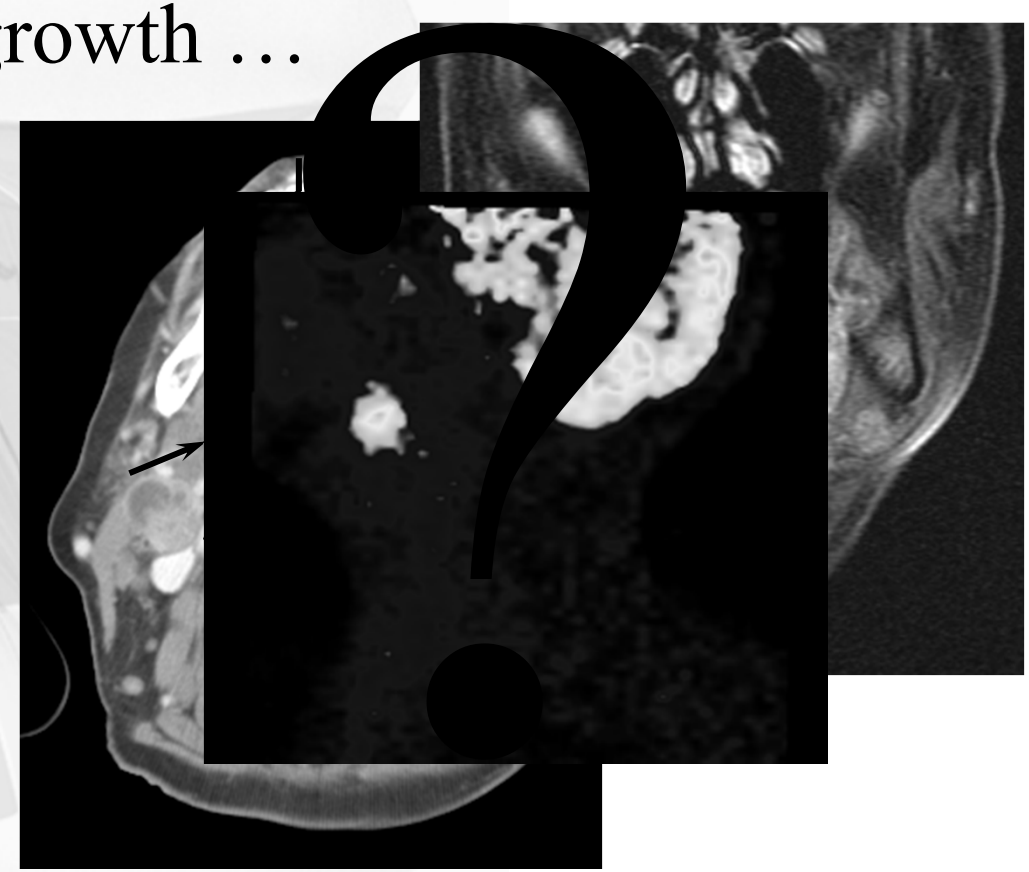
Betrayal of images

This is not an apple…

R. Magritte

Image-Guided Radiation Therapy in HNSCC

The Gross Target Volume (GTV) is the gross demonstrable extend and location of the malignant growth …



ICRU report 50, 1993

Detection of metastatic disease in the neck: Comparison between CT, MRI and FDG-PET

- Meta-analysis: n= 1236 patients (32 studies)
- HNSCC (all sites)
- Neck dissection for all patients

Diagnostic methods compared	No. of studies (references)	Independent estimates (95% CI)		Likelihood ratio (95% CI)	
		Sensitivity	Specificity	LR+	LR−
CT	16 (20,21,23,24,26,28,31,	0.74 (0.61 to 0.83)	0.76 (0.68 to 0.83)	3.12 (2.32 to 4.21)	0.35 (0.23 to 0.51)
^{18}F-FDG PET	32,36,40,43–47,49,50)	0.82 (0.72 to 0.89)	0.86 (0.78 to 0.91)	5.64 (3.61 to 8.83)	0.22 (0.14 to 0.34)
MRI	9 (20,21,24,31,40,43,	0.78 (0.54 to 0.92)	0.80 (0.67 to 0.88)	3.86 (2.01 to 7.38)	0.27 (0.10 to 0.70)
^{18}F-FDG PET	44,47,48,51)	0.78 (0.64 to 0.87)	0.85 (0.79 to 0.90)	5.07 (3.47 to 7.41)	0.27 (0.16 to 0.44)
CT + MRI	4 (19,27,34,47)	0.66 (0.44 to 0.82)	0.76 (0.53 to 0.90)	2.73 (1.43 to 5.19)	0.45 (0.28 to 0.72)
^{18}F-FDG PET		0.73 (0.58 to 0.84)	0.89 (0.84 to 0.93)	6.85 (4.50 to 10.42)	0.30 (0.18 to 0.49)
USFNA	4 (20,21,25,39)	0.42 (0.01 to 0.97)	0.96 (0.76 to 0.99)	10.87 (0.51 to 230.6)	0.61 (0.12 to 3.19)
^{18}F-FDG PET		0.45 (0.27 to 0.64)	0.88 (0.76 to 0.95)	3.79 (1.49 to 9.60)	0.63 (0.42 to 0.92)

* CI = confidence interval; LR+ = positive likelihood ratio; LR− = negative likelihood ratio; CT = computed tomography; ^{18}F-FDG PET = positron emission tomography using ^{18}F-fluorodeoxyglucose; MRI = magnetic resonance imaging; USFNA = ultrasound-guided fine-needle aspiration.

Kyzas et al., JNCI 2008

The Gross Tumor volume (GTV)

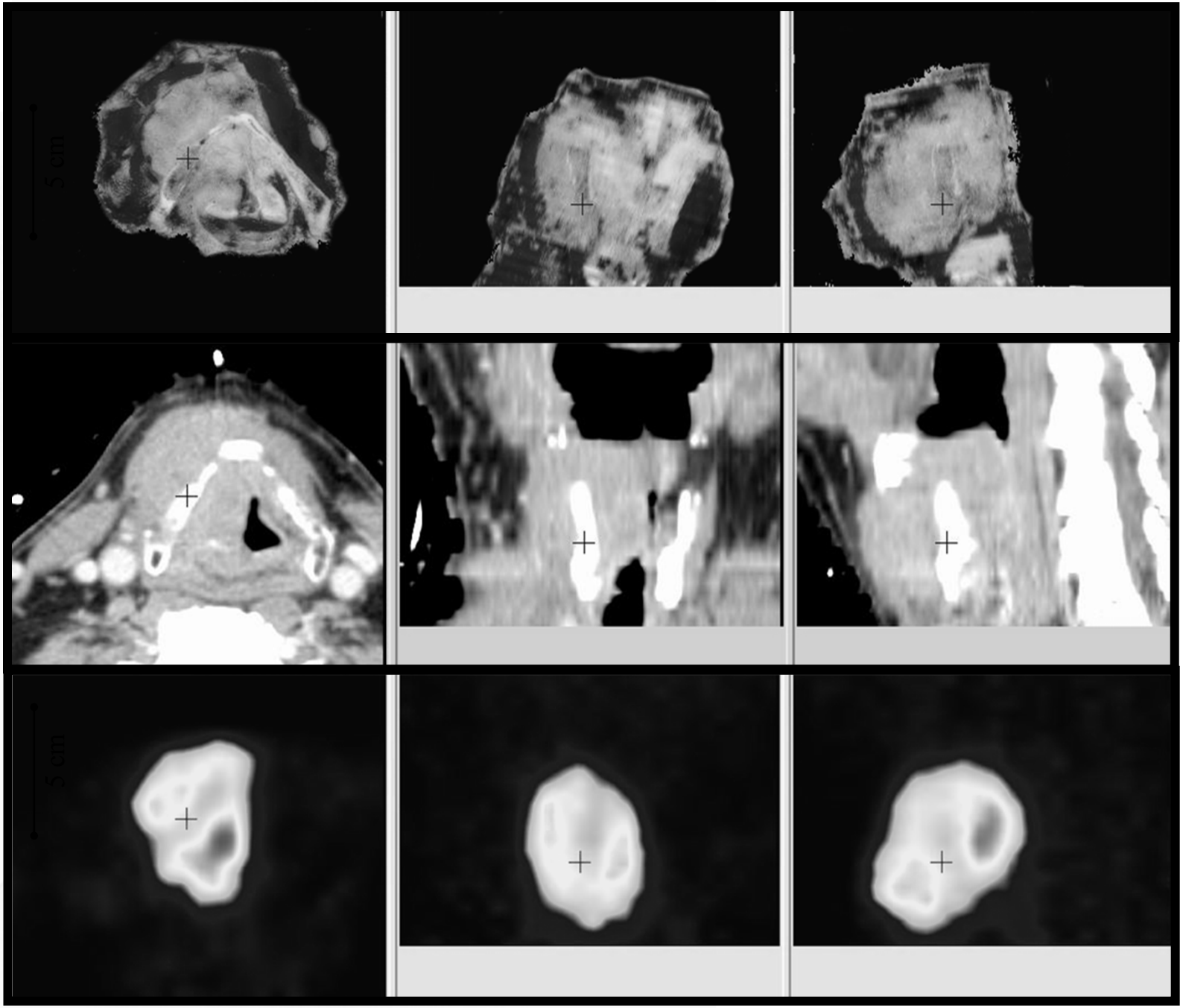
Radiology

Jean-François Daisne, MD
Thierry Duprez, MD
Birgit Weynand, MD
Max Lonneux, MD, PhD
Marc Hamoir, MD
Hervé Reychler, MD, DDS
Vincent Grégoire, MD, PhD

Index terms:
Head and neck neoplasms, CT, 26.1211, 27.1211
Head and neck neoplasms, MR,

Tumor Volume in Pharyngolaryngeal Squamous Cell Carcinoma: Comparison at CT, MR Imaging, and FDG PET and Validation with Surgical Specimen[1]

Daisne et al., *Radiology*, 233: 93-100, 2004



Macroscopy

CAT Scan

^{18}F-FDG PET

Daisne *et al*, 2003

How far are we from the truth ?

TABLE 3
GTVs in Patients with Laryngeal or Hypopharyngeal Tumors

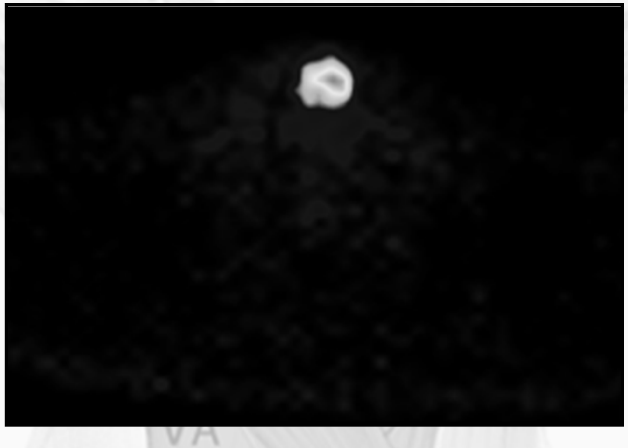
Patient No.	Tumor Site	T Stage	GTV (cm^3) CT	MR Imaging	FDG PET	Surgical Specimen
1	PS	T4	47.7	36.3	19.3	NA
2	GL	T3	18.0	9.9	6.0	NA
3	GL	T3	41.1	30.2	9.2	NA
4	RC	T3	7.1	10.6	7.3	NA
5	PS	T2	4.1	9.1	2.3	NA
6	SGL	T2	3.7	1.4	1.2	NA
7	SubGL	T3	5.8	7.0	3.2	NA
8	PS	T3	17.3	17.6	12.6	NA
9	PS	T4	13.1	30.7	11.4	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, and .06, respectively.

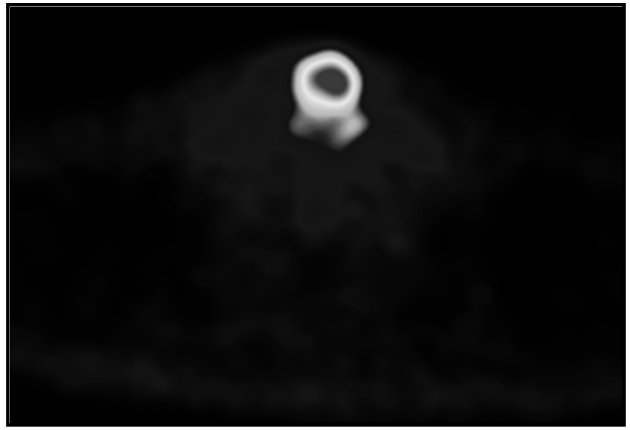
Daisne *et al*, 2004

PET image segmentation: an issue?

Volume delineation based on automatic thresholding with ^{18}F-FDG



OSEM (unsmoothed)
1.1 cm^3



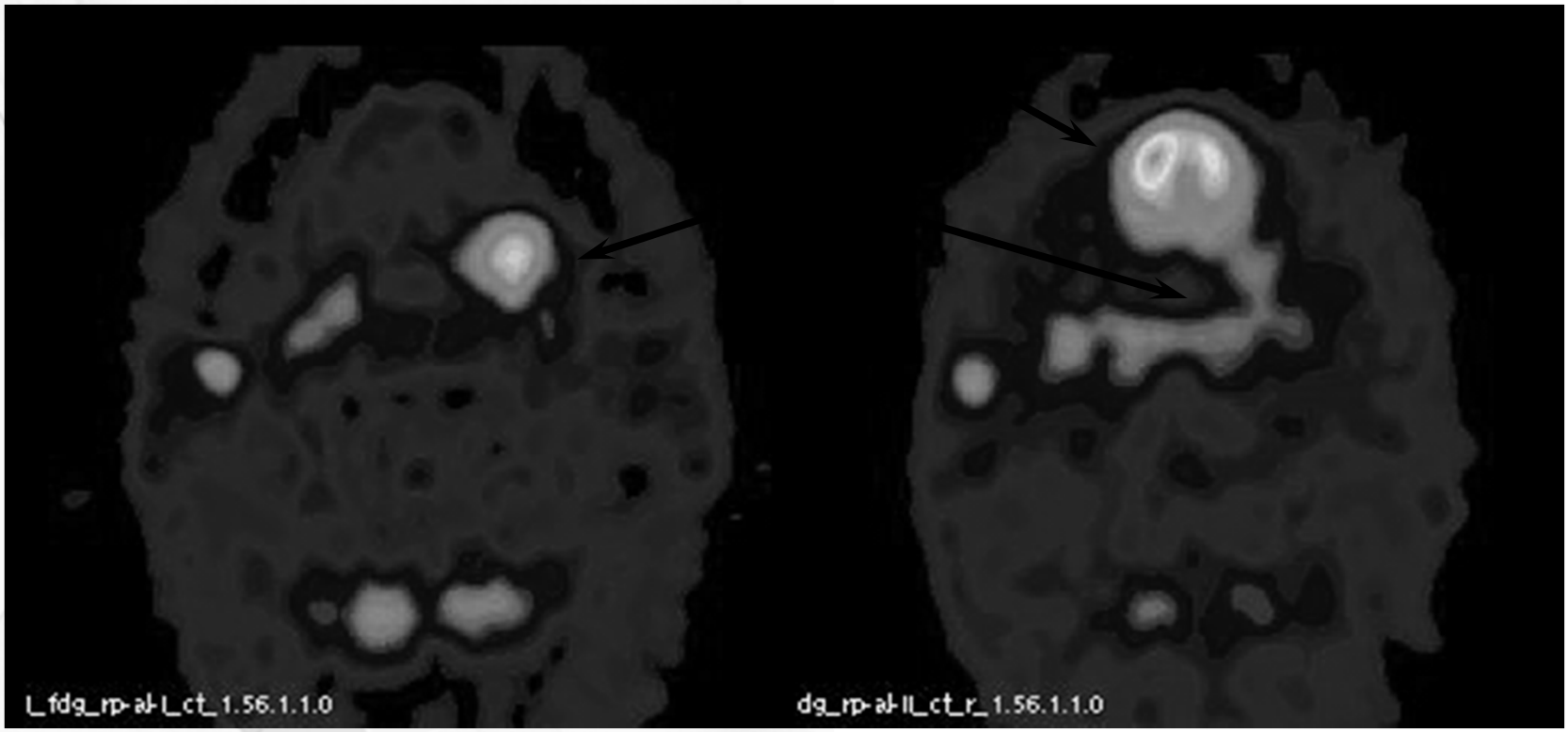
OSEM (smoothed at 6 mm)
1.6 cm^3

Image-Guided Radiation Therapy in HNSCC
The 4th dimension …

FDG-PET

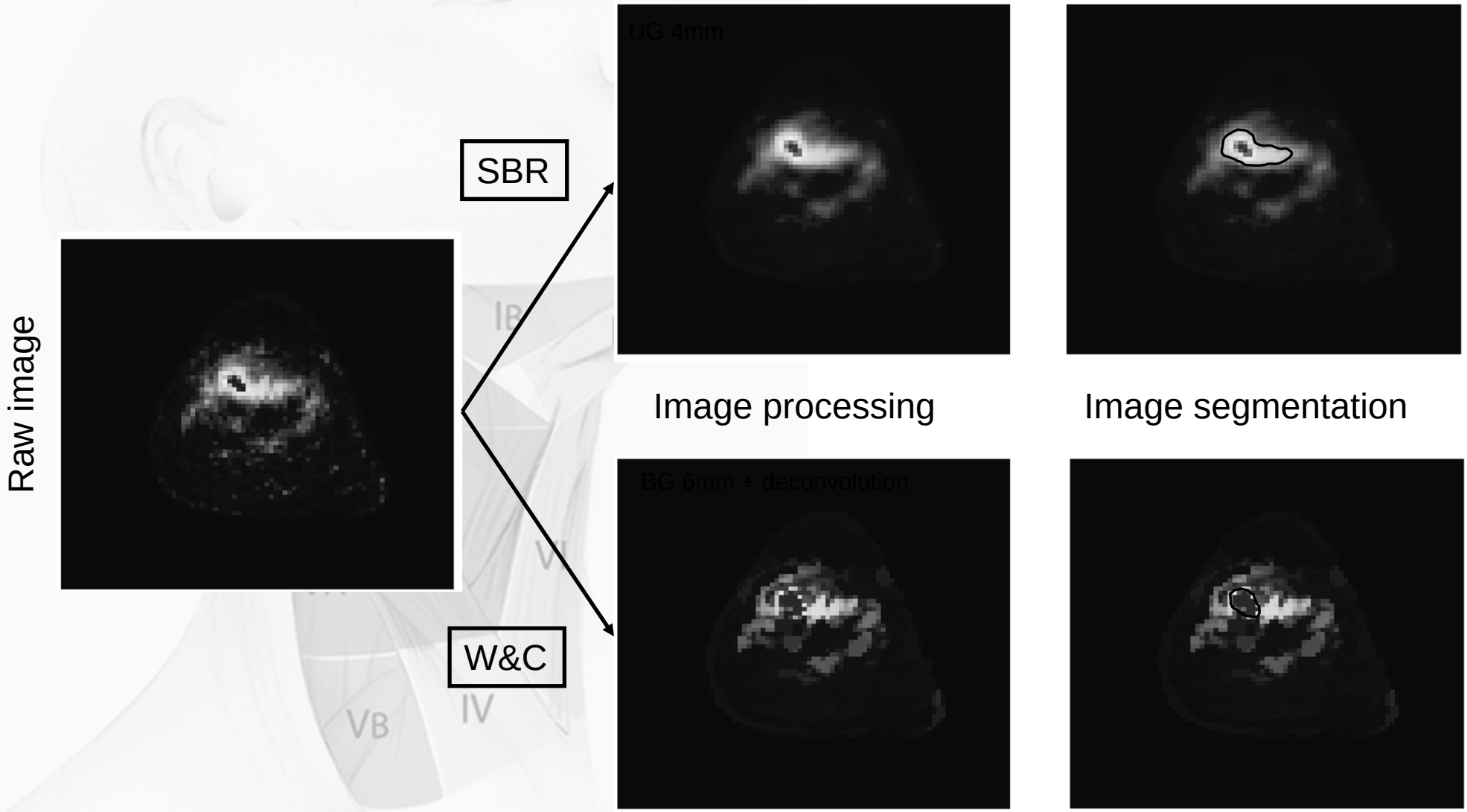
0 Gy

46 Gy



Geets *et al*, 2003

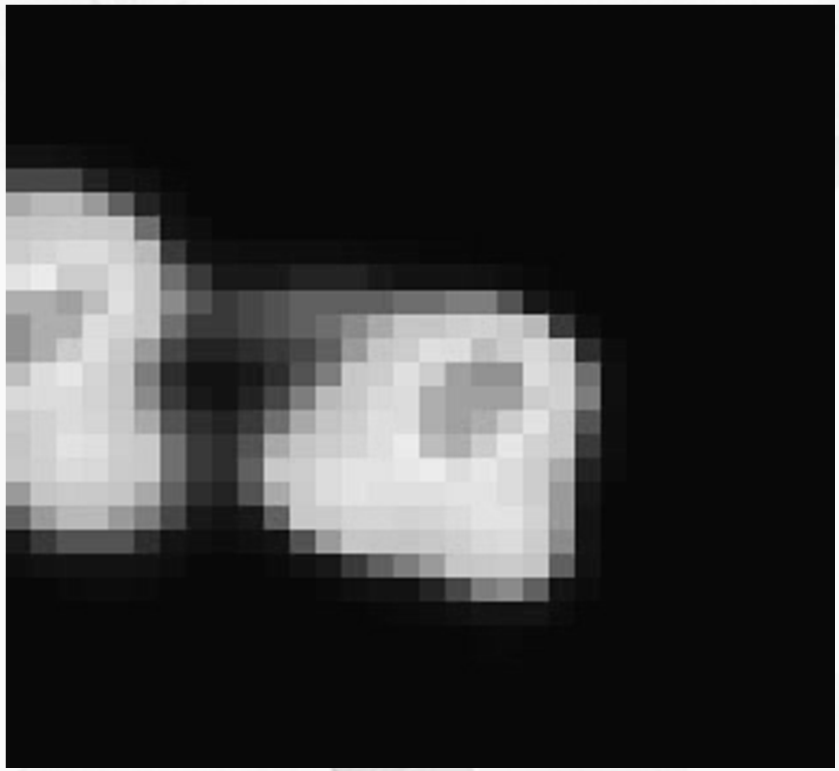
PET image segmentation during RxTh



J. Lee & X. Geets, 2005

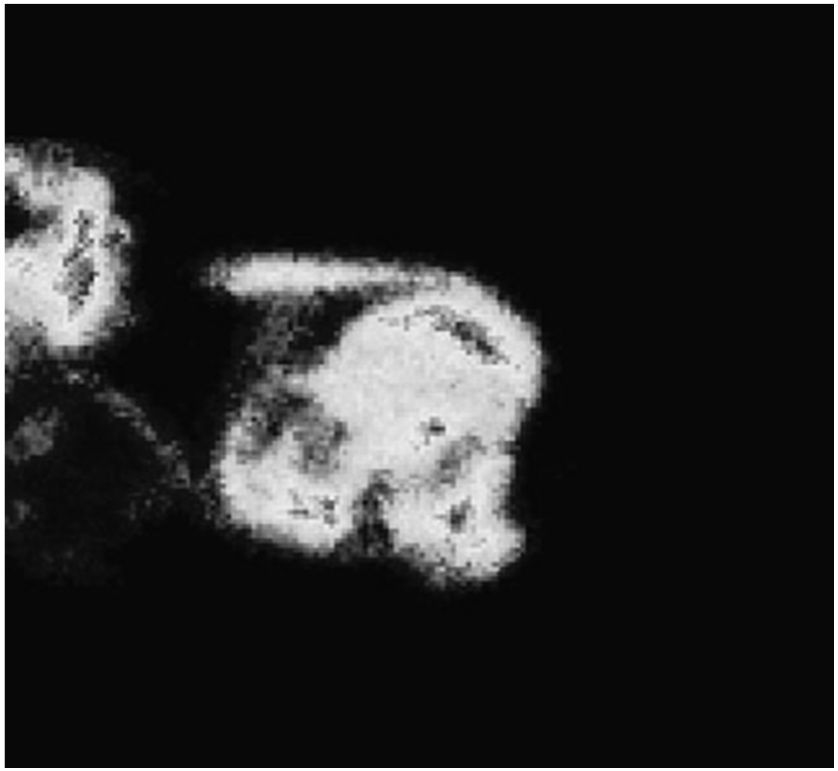
Imaging resolution and biological heterogeneity

[^{18}F]-FDG TEP



Resolution 2.3 mm

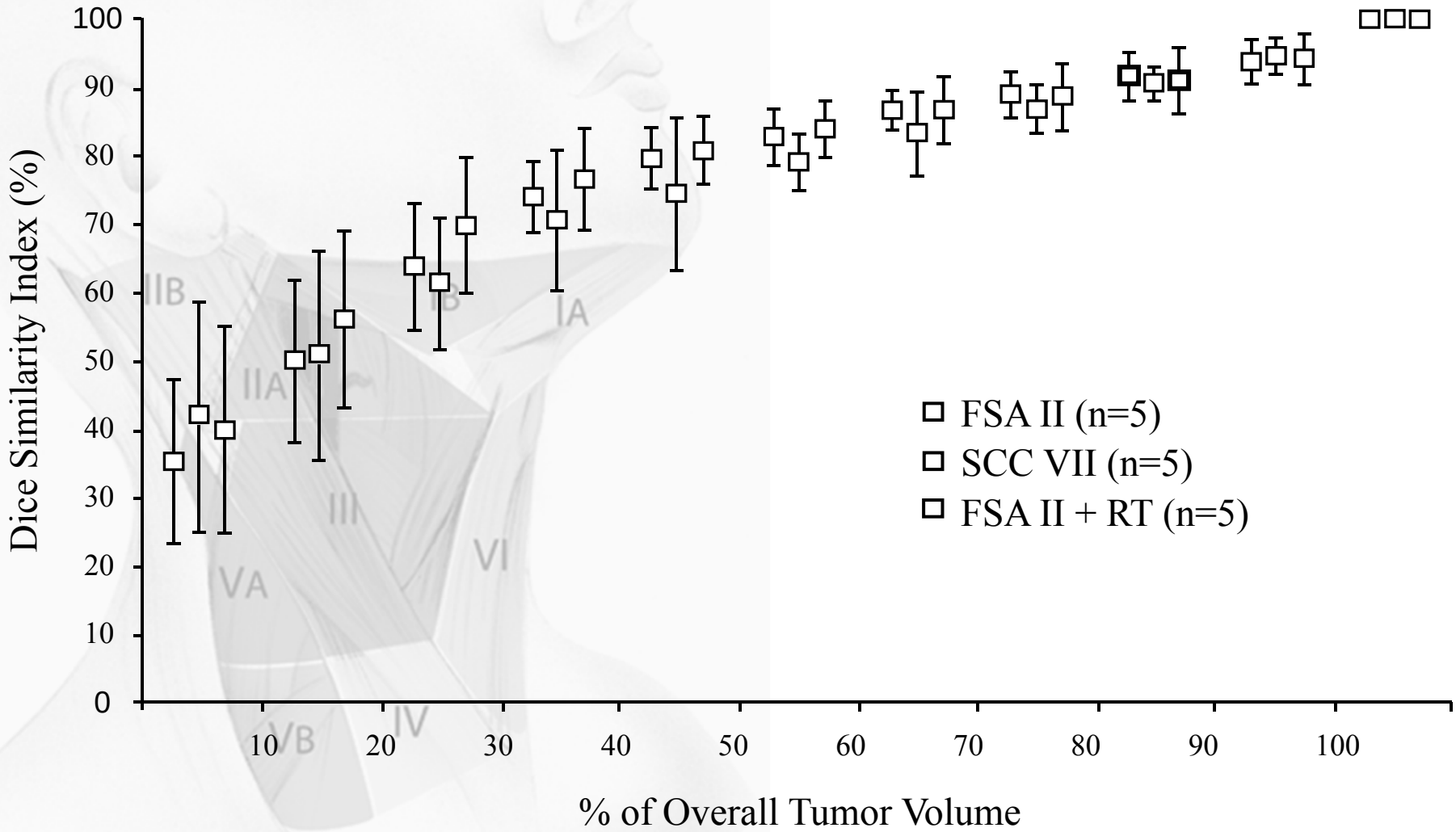
Registered autoradiography



Resolution 0.1 mm

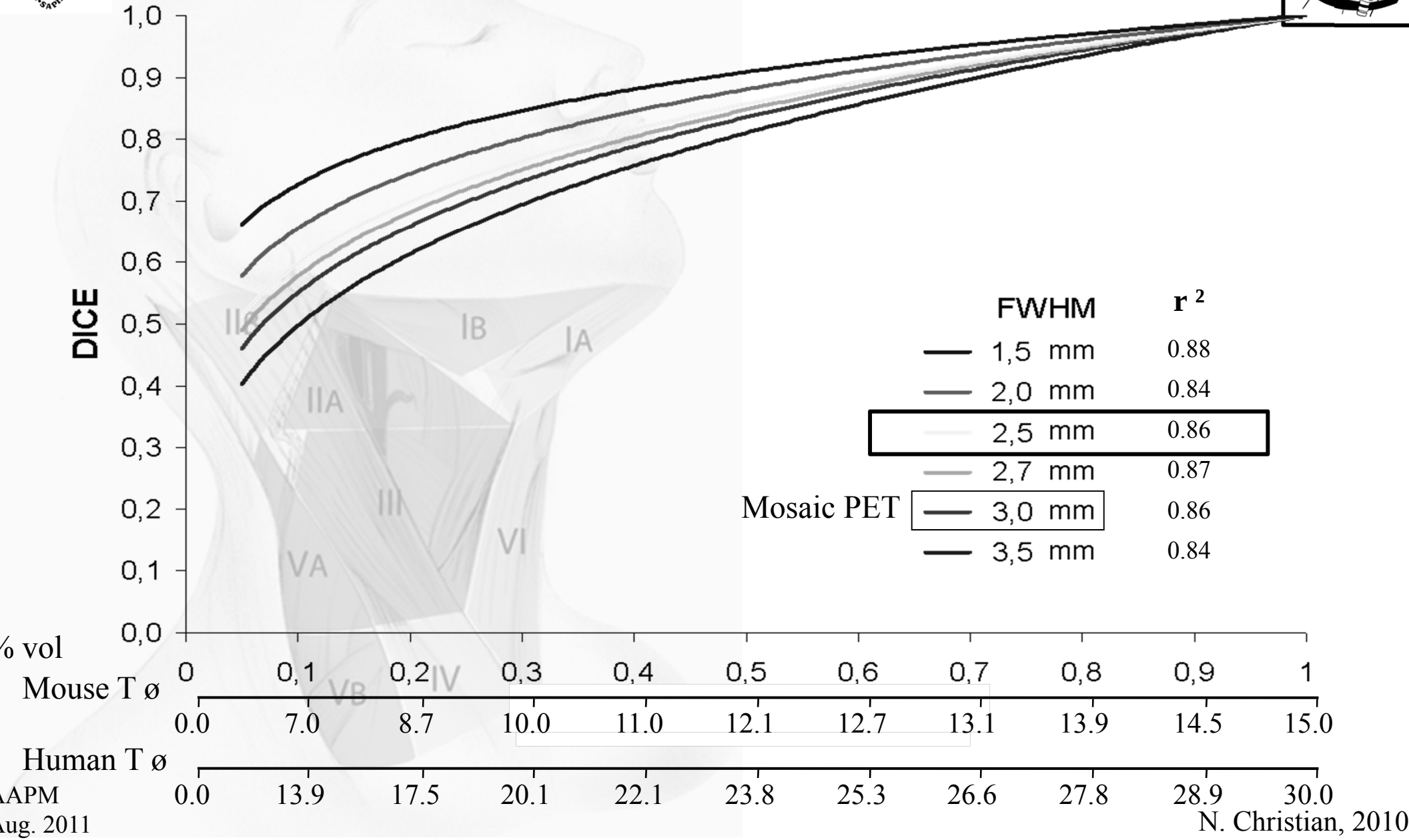
N. Christian, 2010

Imaging resolution and biological Heterogeneity: a scaling issue …



N. Christian, 2007

Effect of resolution



N. Christian, 2010

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

IMRT in Head and Neck Tumors

Where uncertainties could come from?

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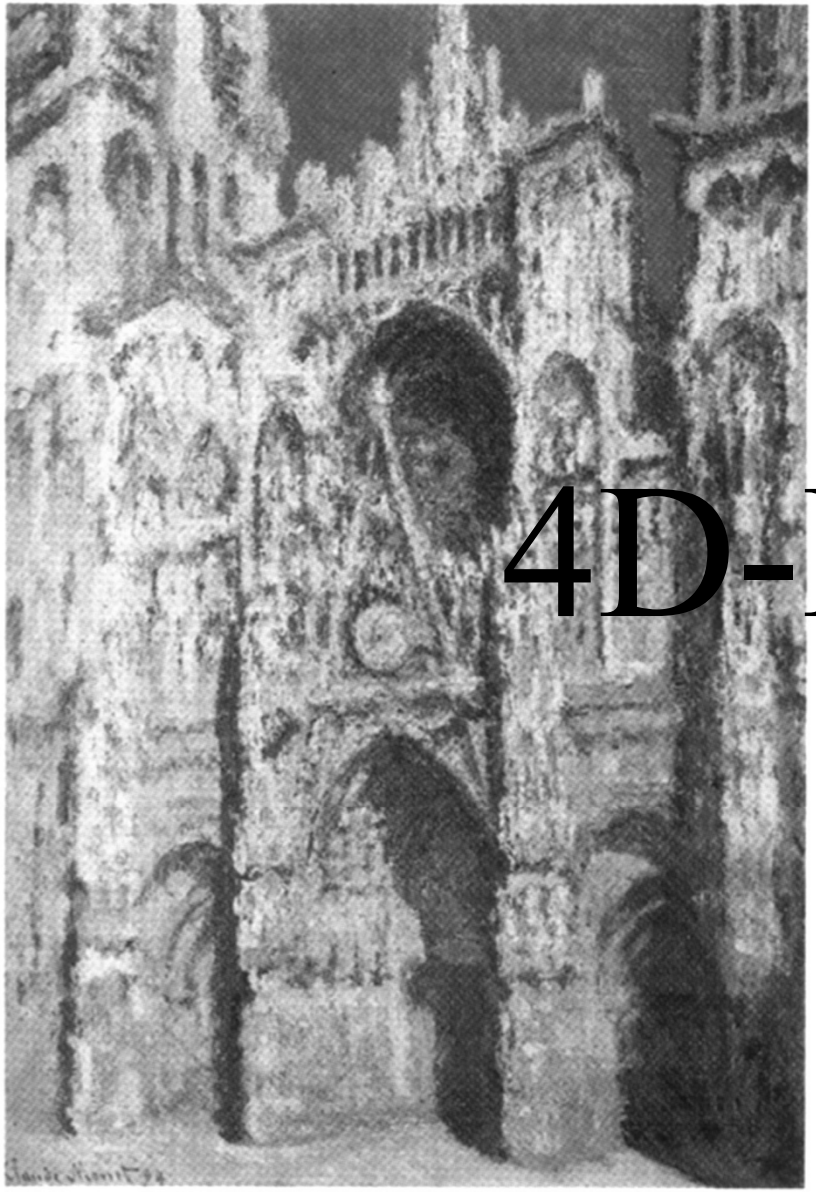
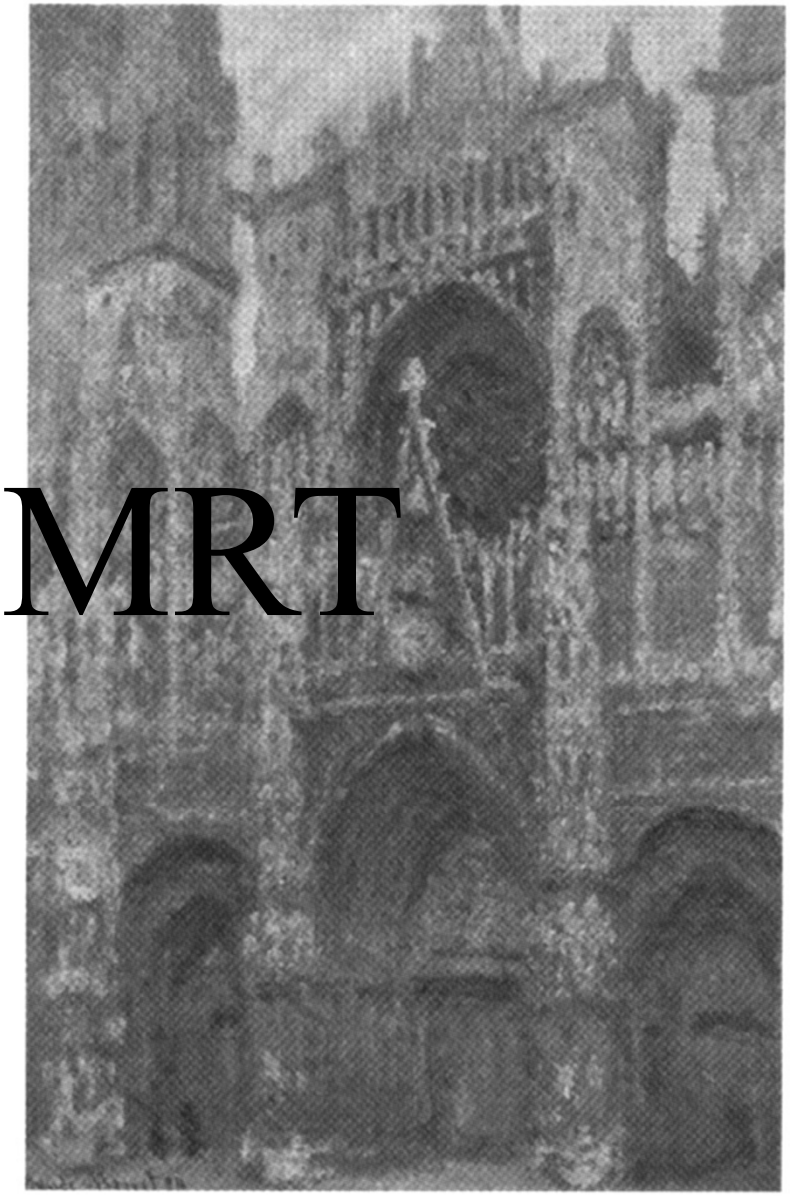
4D-IMRT





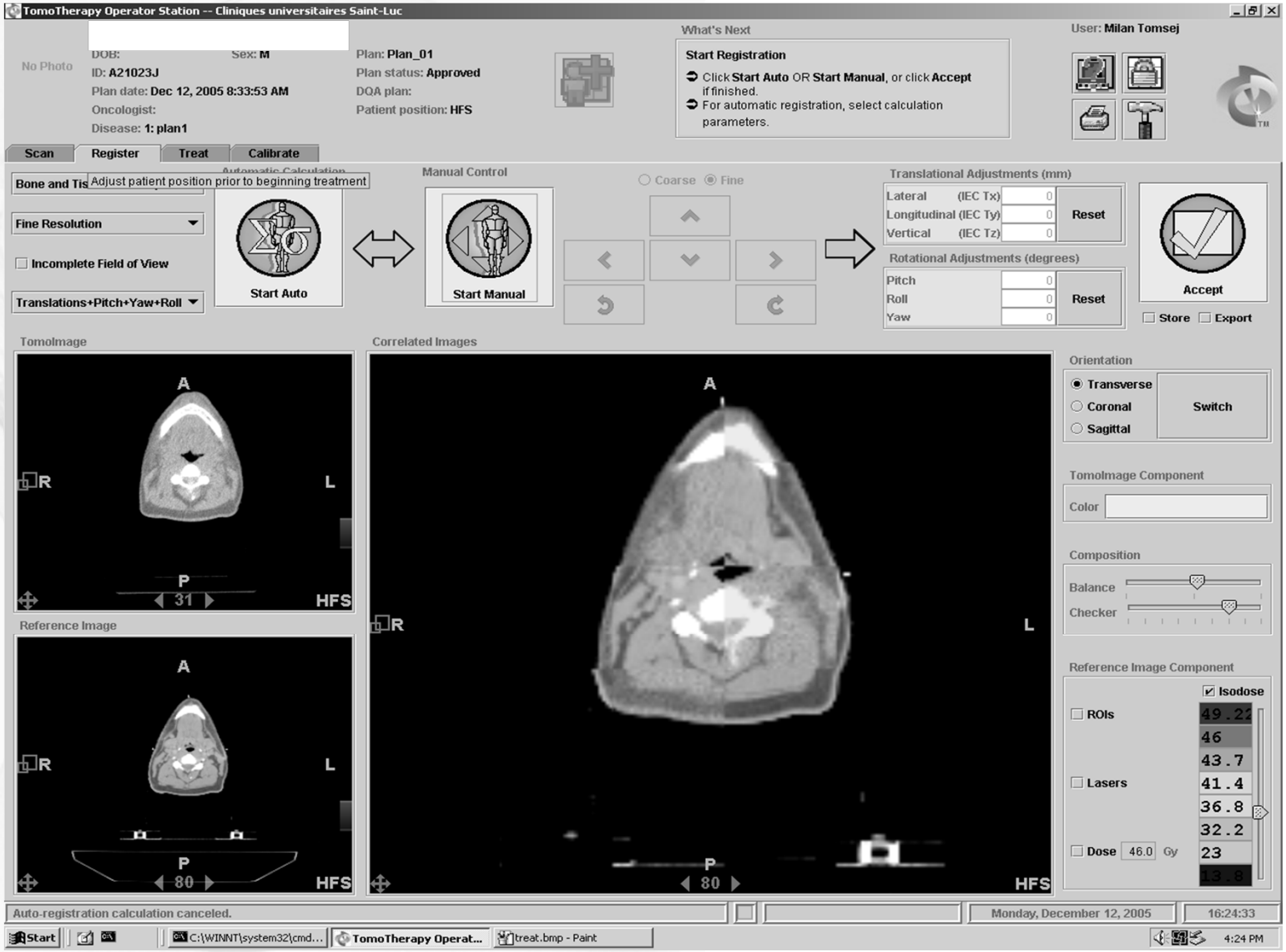
The Cathedral of Rouen

C. Monet, 1894

Geometric 4D-IMRT

MVCT

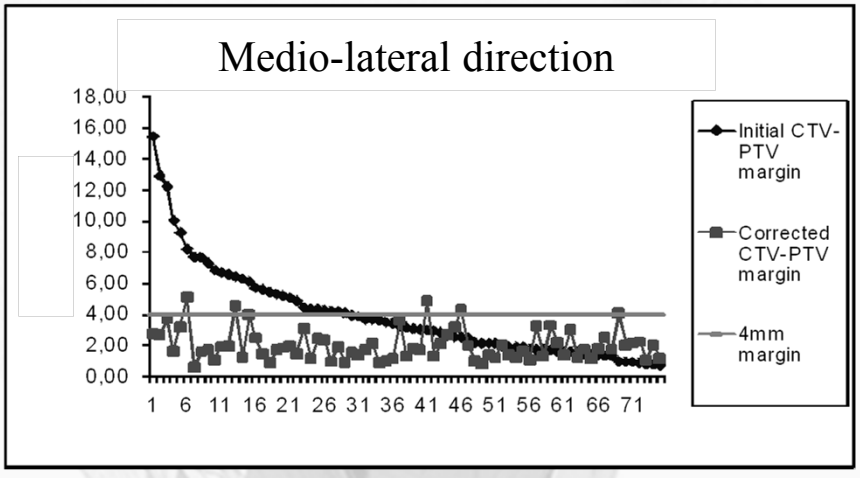
kVCT

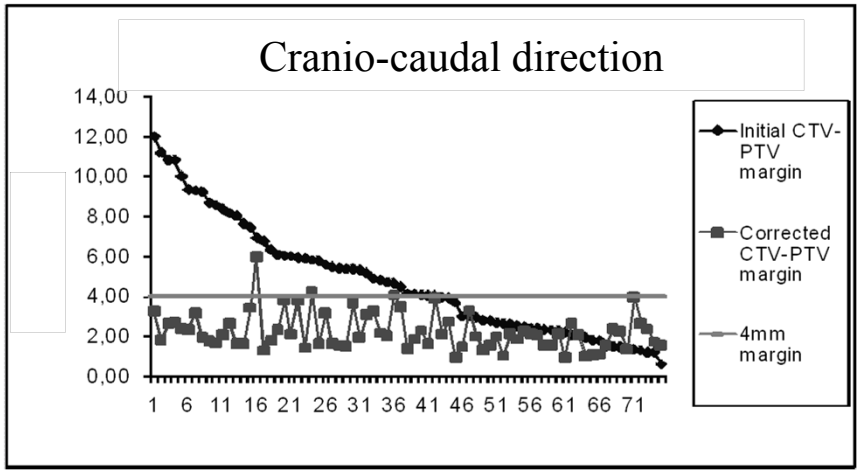


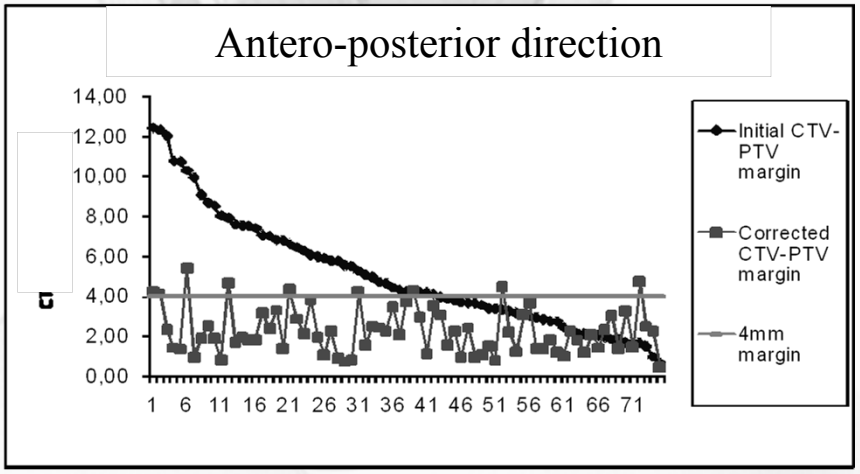
Geometric 4D-IMRT

Alternate week MVCTs: CTV-PTV margins

CTV to PTV margin







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

IMRT in Head and Neck Tumors

Where uncertainties could come from?

- selection and delineation of TVs and OARs
- choice of the optimal imaging modality
- patient positioning
- dose optimization
- treatment adaptation

IMRT in Head and Neck Tumors: conformal avoidance or anatomy-based IMRT

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0360-3016/$–see front matter

ELSEVIER

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PHYSICS CONTRIBUTION

EMPHASIZING CONFORMAL AVOIDANCE VERSUS TARGET DEFINITION FOR IMRT PLANNING IN HEAD-AND-NECK CANCER

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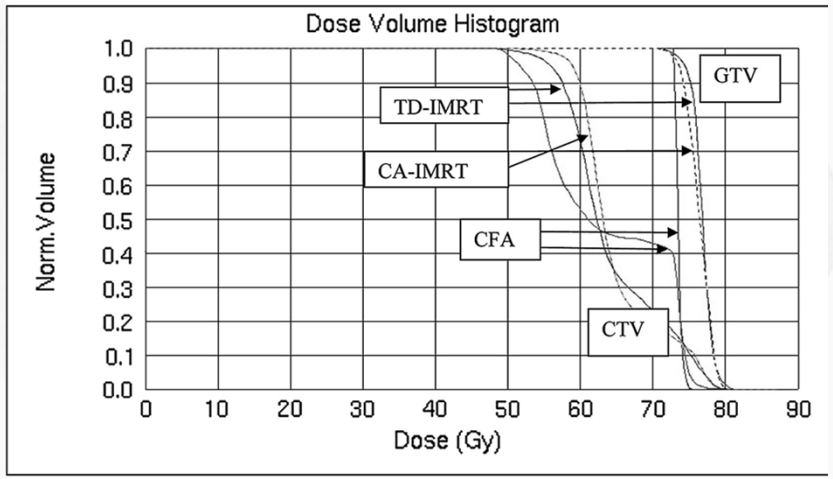
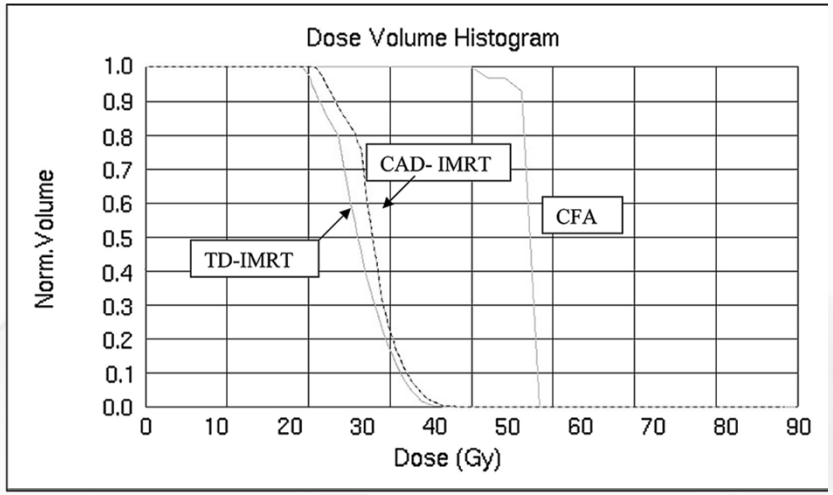
Harari et al., 2010

IMRT in Head and Neck Tumors: conformal avoidance or anatomy-based IMRT

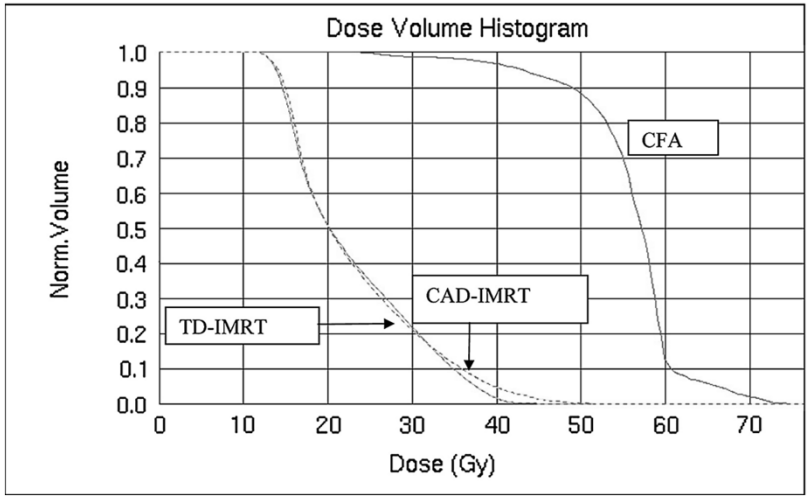
a) DVH comparison for GTV and CTV using TD-IMRT and CA-IMRT methods



b) DVH comparison for the Spinal Cord



c) DVH comparison for the spared parotid gland



Harari et al., 2010

IMRT in Head and Neck Tumors: D/V constraints

PTV / PRV	D_{95}[a]	D_{99}	D_5	D_2	Mean dose
Therapeutic PTV	≥ 95% of prescribed dose	≥ 90% of prescribed dose	≥ 107 of prescribed dose	-	-
Prophylactic PTV	≥ 95% of prescribed dose	≥ 90% of prescribed dose	?	-	-
PRV spinal cord	-	-	≥ 50 Gy	-	-
Spinal cord	-	-	-	≥ 48 Gy	-
Contralateral parotid	-	-	-	-	< 20 Gy
Ipsilateral parotid	-	-	-	-	< 25 Gy
Larynx[b]	-	-	≥ 45 Gy	-	-
Oral cavity	-	-	-	-	< 30 Gy
Phar constrictor m.			? < 45 Gy ?		
…					

[a]Dx: dose in x% of the volume
[b] for oropharyngeal primary only

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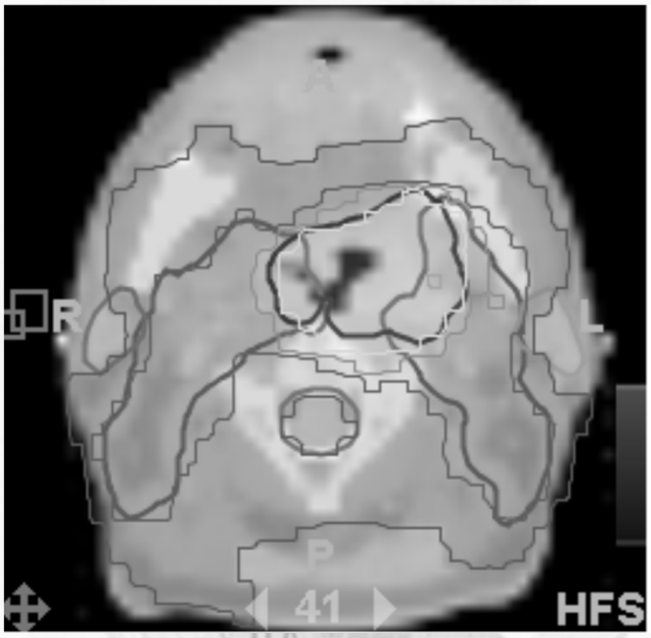
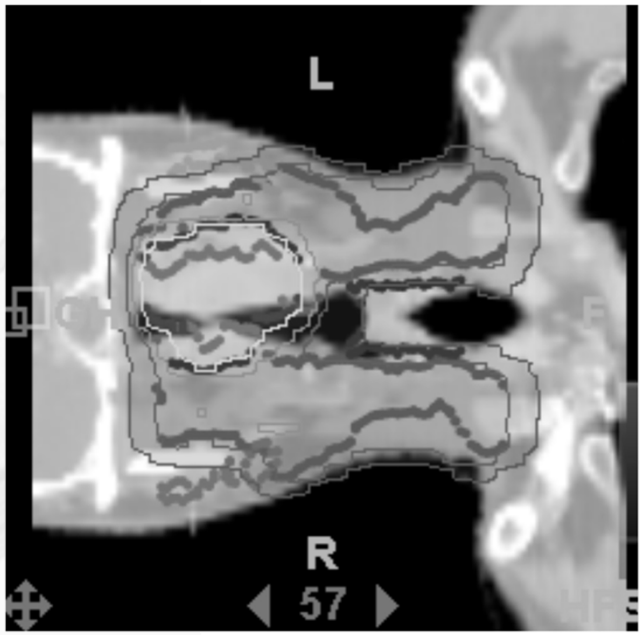
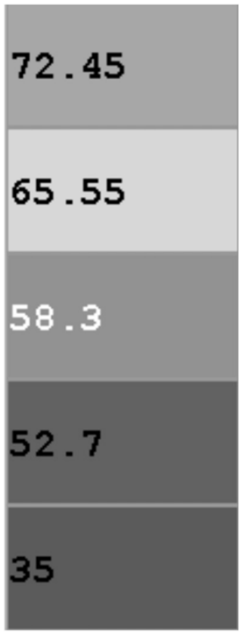
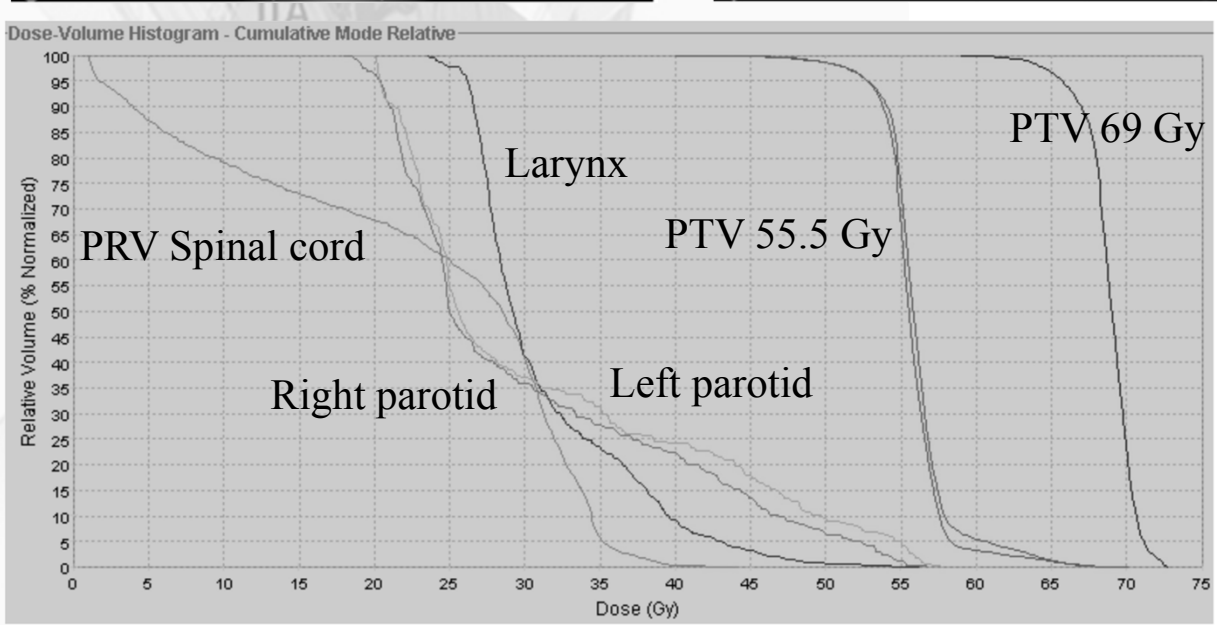
IMRT for Head and Neck Tumors









Oropharyngeal SCC

T2-N0-M0

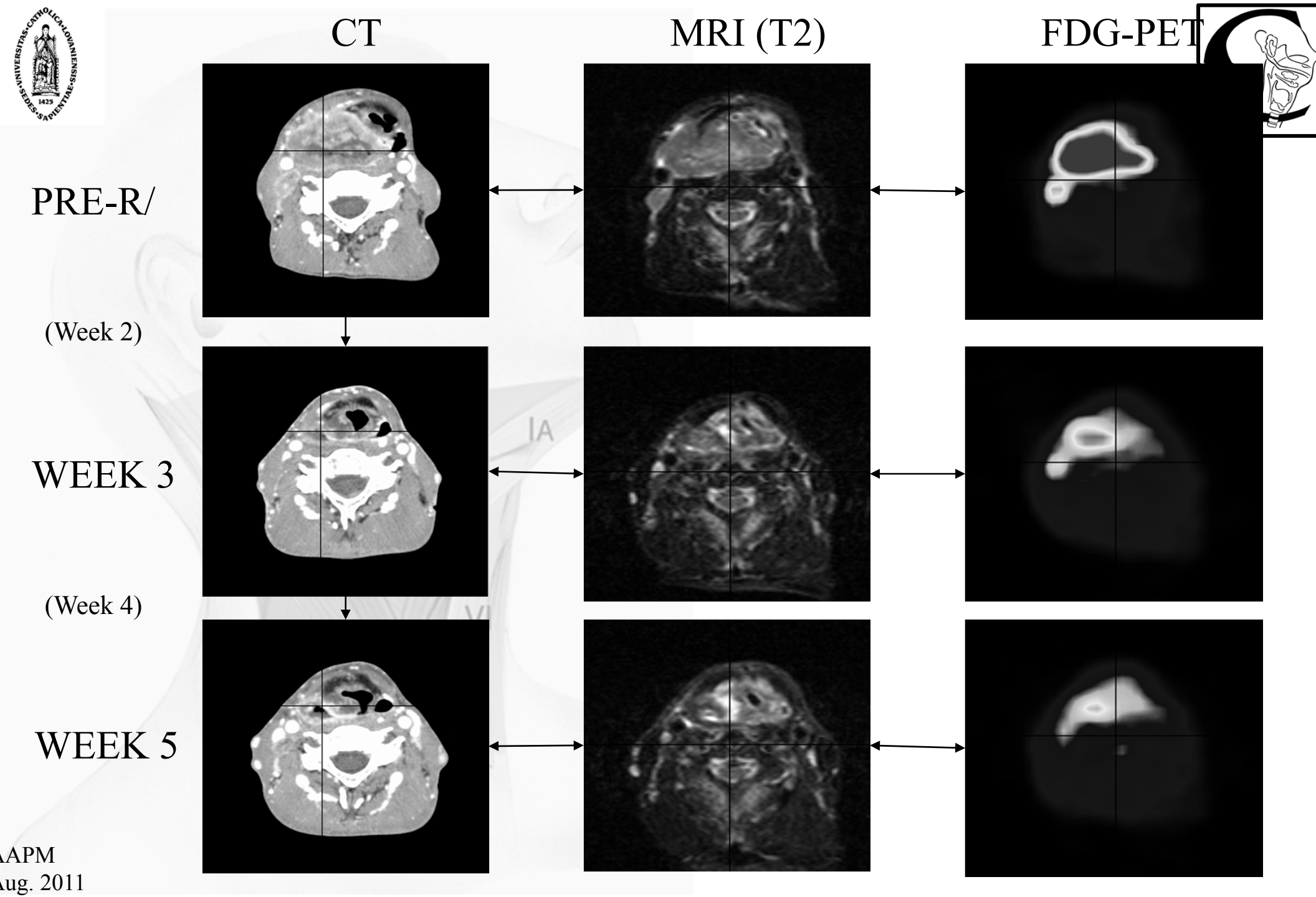
SIB-IMRT: 30x2.3 Gy

30x1.85 Gy

IMRT in Head and Neck Tumors

Where uncertainties could come from?

- selection and delineation of TVs and OARs
- choice of the optimal imaging modality
- patient positioning
- dose optimization
- treatment adaptation



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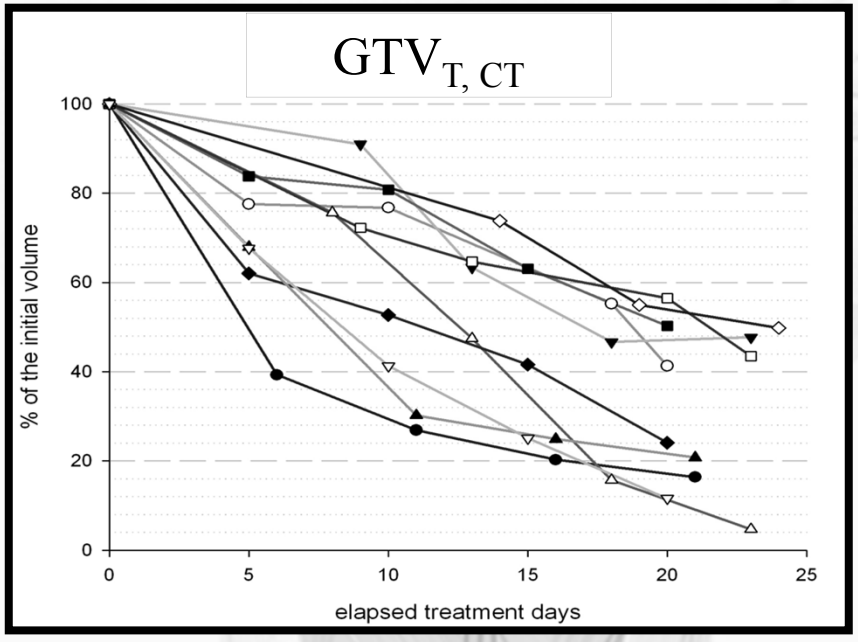
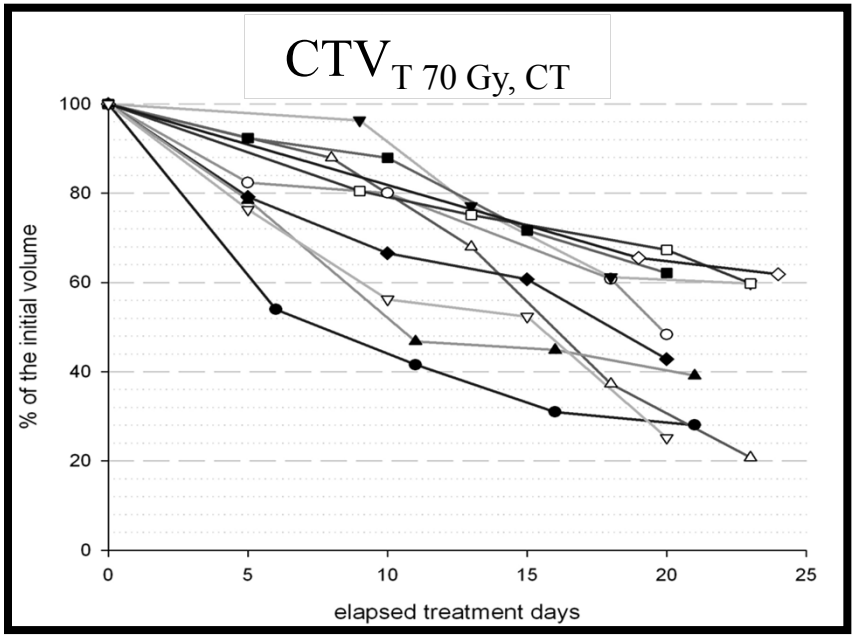
Variation in CT Target volumes during RT-CH (70 Gy – 3 courses chemo on w1, w4, w7)





Mean slope: -3.18% / treat day ($p<0.05$)

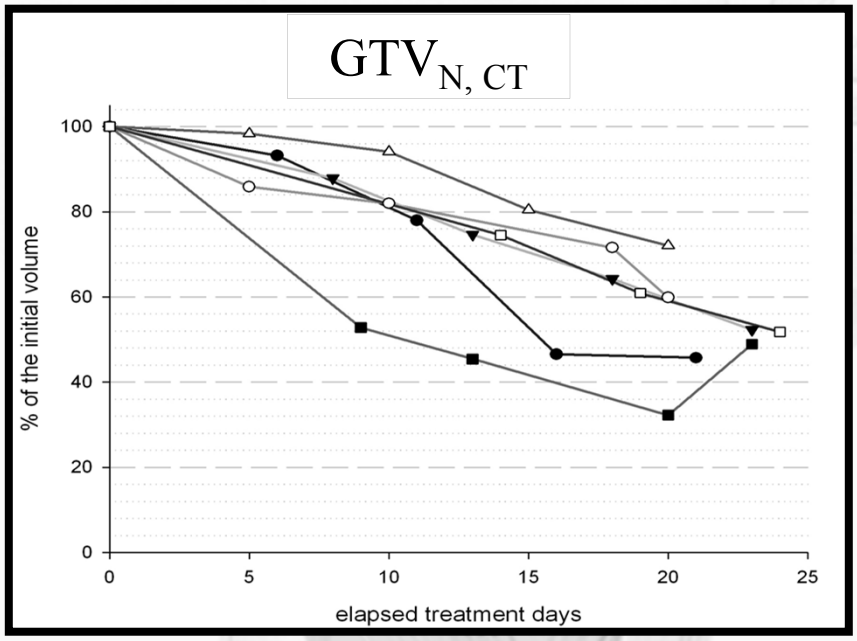
Lateral shift: 1.26mm after 25# ($p<0.05$)

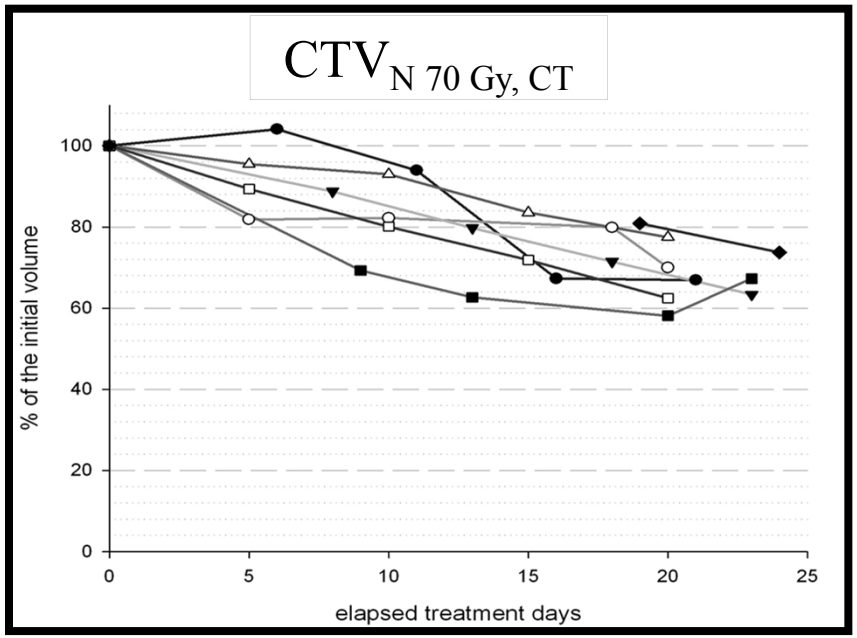
Mean slope: -2.55% / treat day ($p<0.05$)

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

Castadot & Lee, 2010

Variation in nodal Target Volumes during RT-CH (70 Gy – 3 courses chemo on w1, w4, w7)





Mean slope: -2.15% / treat day ($p<0.05$)

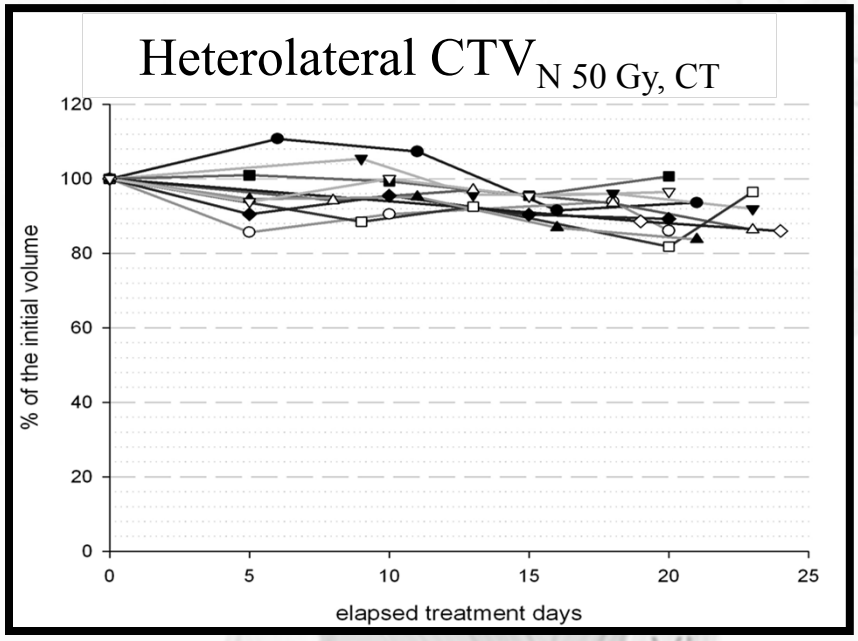
Medial shift: 0.95mm after 25# ($p<0.05$)

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

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

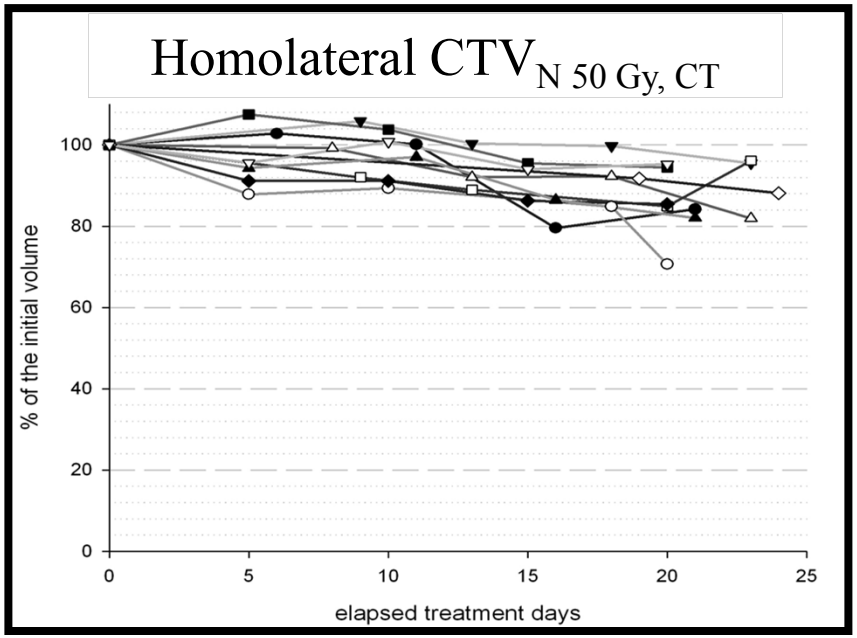
Castadot & Lee, 2010

Variation in prophylactic CTVs during RT-CH… (70 Gy – 3 courses chemo on w1, w4, w7)



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

No shift

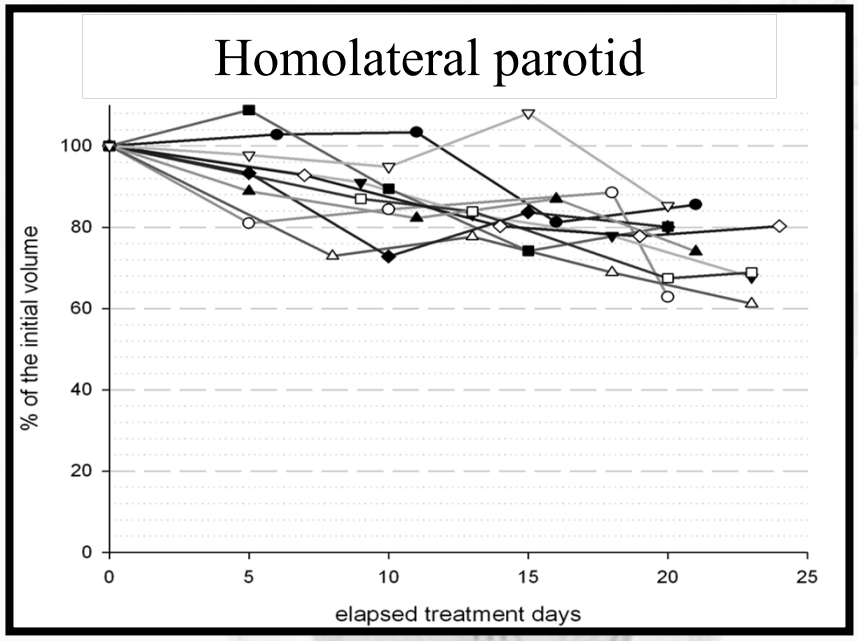


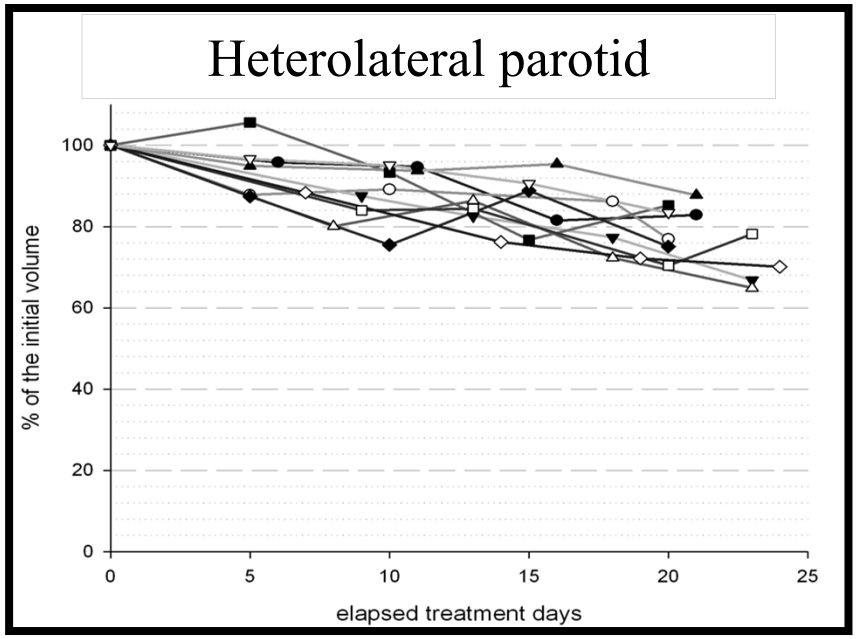
Mean slope: -0.41% / treat day ($p<0.05$)

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

Castadot & Lee, 2010

Variation in parotid volumes during RT-CH… (70 Gy – 3 courses chemo on w1, w4, w7)





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

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

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

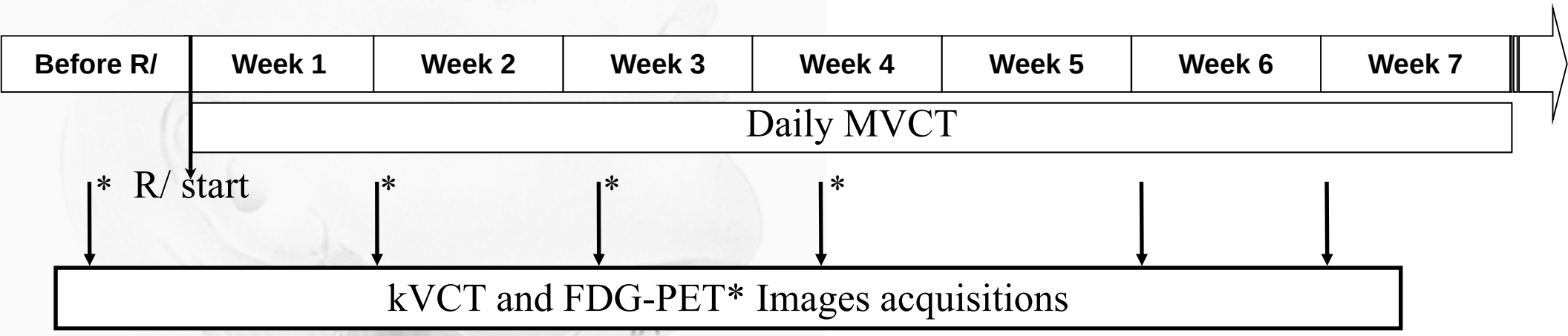
No shift

Castadot & Lee, 2010

Variation in parotid and TV during RT

Authors	Imaging	Parotid Gland		Target Volume	
		Δ COM	Δ Volume	Δ COM	Δ Volume
Barker, 2004	EXaCT	3.1 mm medial	0.6% / day	3.3 mm	1.8% / day
Hansen, 2006	kVCT	-	15.6% - 21.5% at 36 Gy	-	-
Robar, 2007	kVCT	0.8-0.9 mm / week	4.9% / week	-	-
Han, 2008	MVCT	-	1.1% / day	-	-
Vasquez-Osorio, 2008	kVCT	3 mm medial	17% loss at 46 Gy	-	-

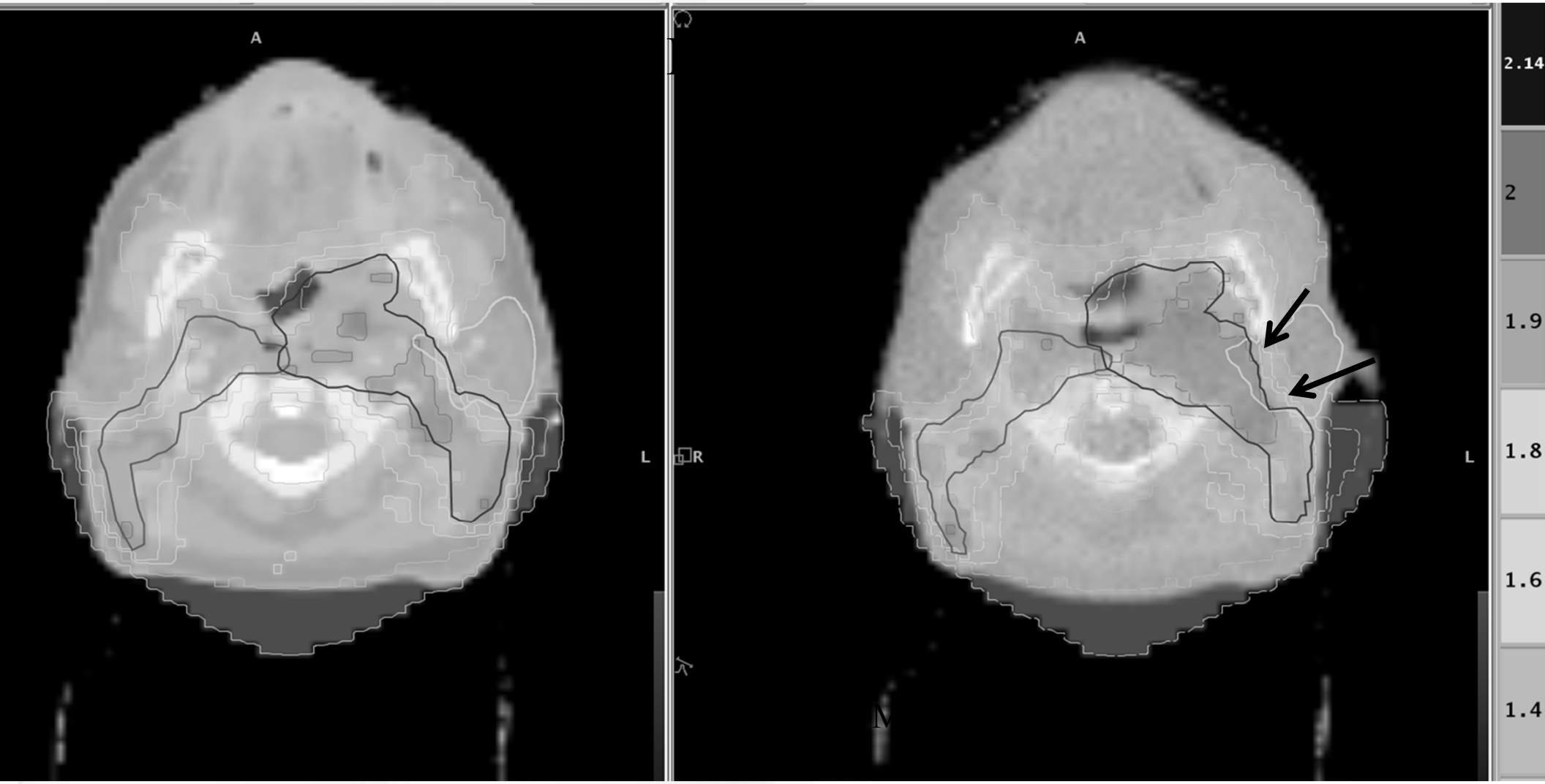
Adaptive Image-Guided IMRT in pharyngo-laryngeal squamous cell carcinoma



- 25 patients with stage III-IV pharyngo-laryngeal SCC treated by CT-RT
- MVCT images acquired daily
- kVCT and FDG-PET* images acquired before R/ and during RT after means doses of 10*, 24*, 34*, 50 and 60 Gy

Carruthers, 2010

Adaptive Image-Guided IMRT in pharyngo-laryngeal squamous cell carcinoma



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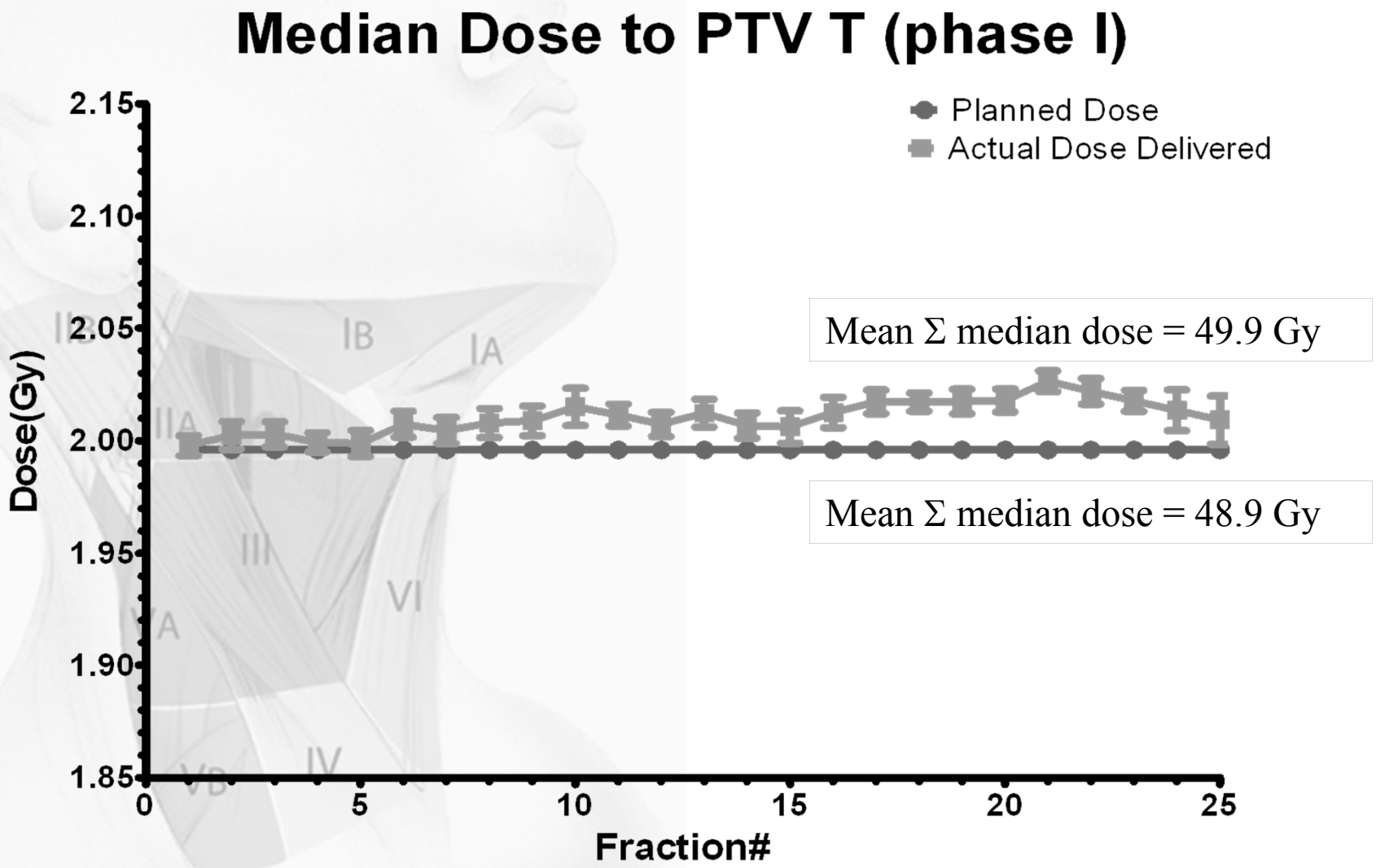
Carruthers, 2011

Adaptive Image-Guided IMRT in pharyngo-laryngeal squamous cell carcinoma



Carruthers, 2011

Adaptive Image-Guided IMRT in pharyngo-laryngeal squamous cell carcinoma

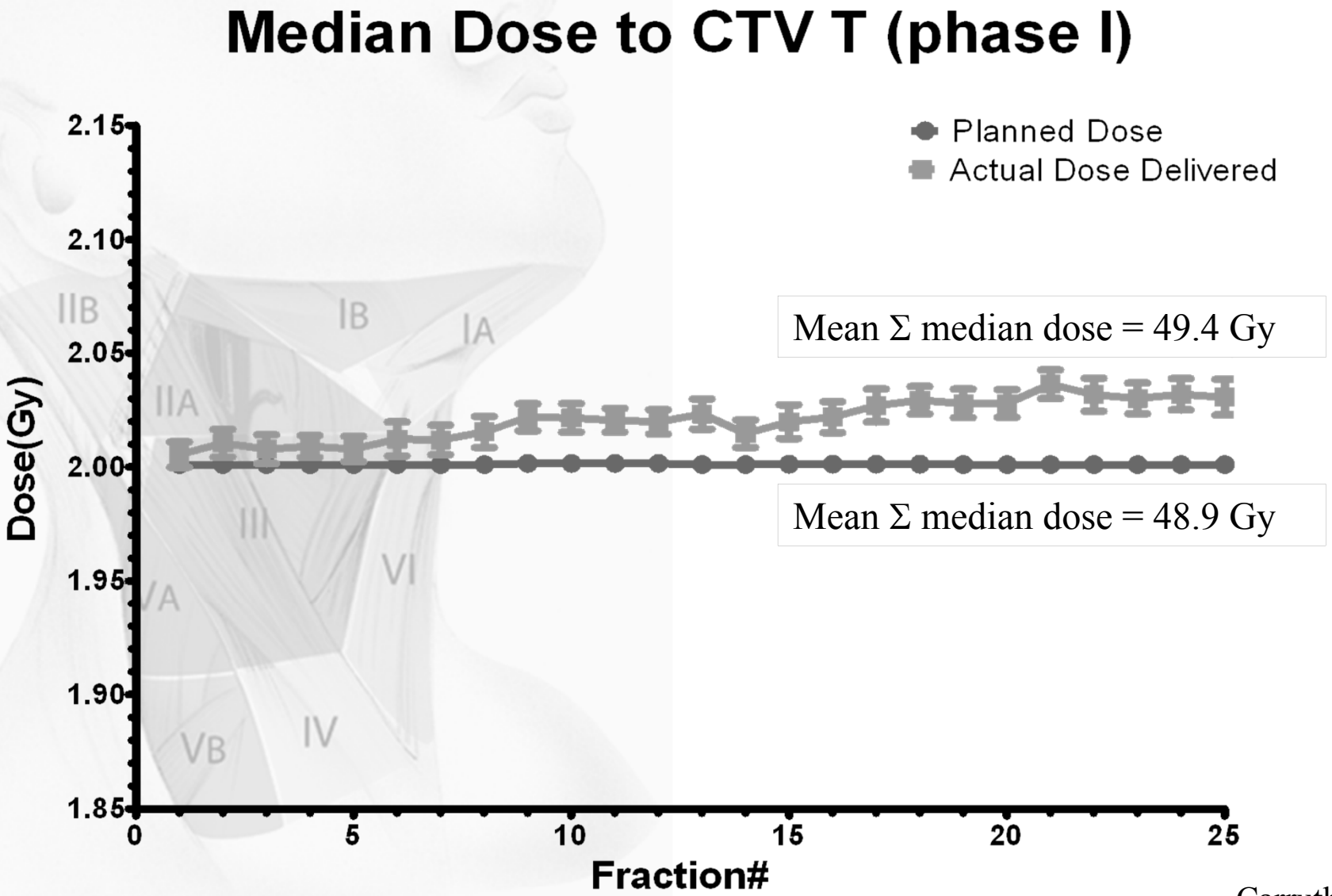
Mean Deviation (%) from PTV Planned dose (50 Gy)

Dose	PTV T	Ipsilateral Nodal PTV	Contralateral Nodal PTV
Near Max (2%)	1.25% (±0.28*)	1.78% (±0.36*)	0.79% (±0.32*)
Median (50%)	0.39% (±0.28*)	0.15% (±0.28*)	0.06% (±0.22*)
95%	-1.52% (±0.43*)	-2.45% (±0.54*)	-3.35% (±0.38*)
Near Min (98%)	-3.32% (±0.60*)	-4.38% (±0.62*)	-4.96% (±0.60*)
Mean	0.37% (±0.43*)	-0.20% (±0.25*)	0.70% (±0.39*)

*Standard Error of Mean

Carruthers, 2011

Adaptive Image-Guided IMRT in pharyngo-laryngeal squamous cell carcinoma



Carruthers, 2011

Adaptive Image-Guided IMRT in pharyngo-laryngeal squamous cell carcinoma

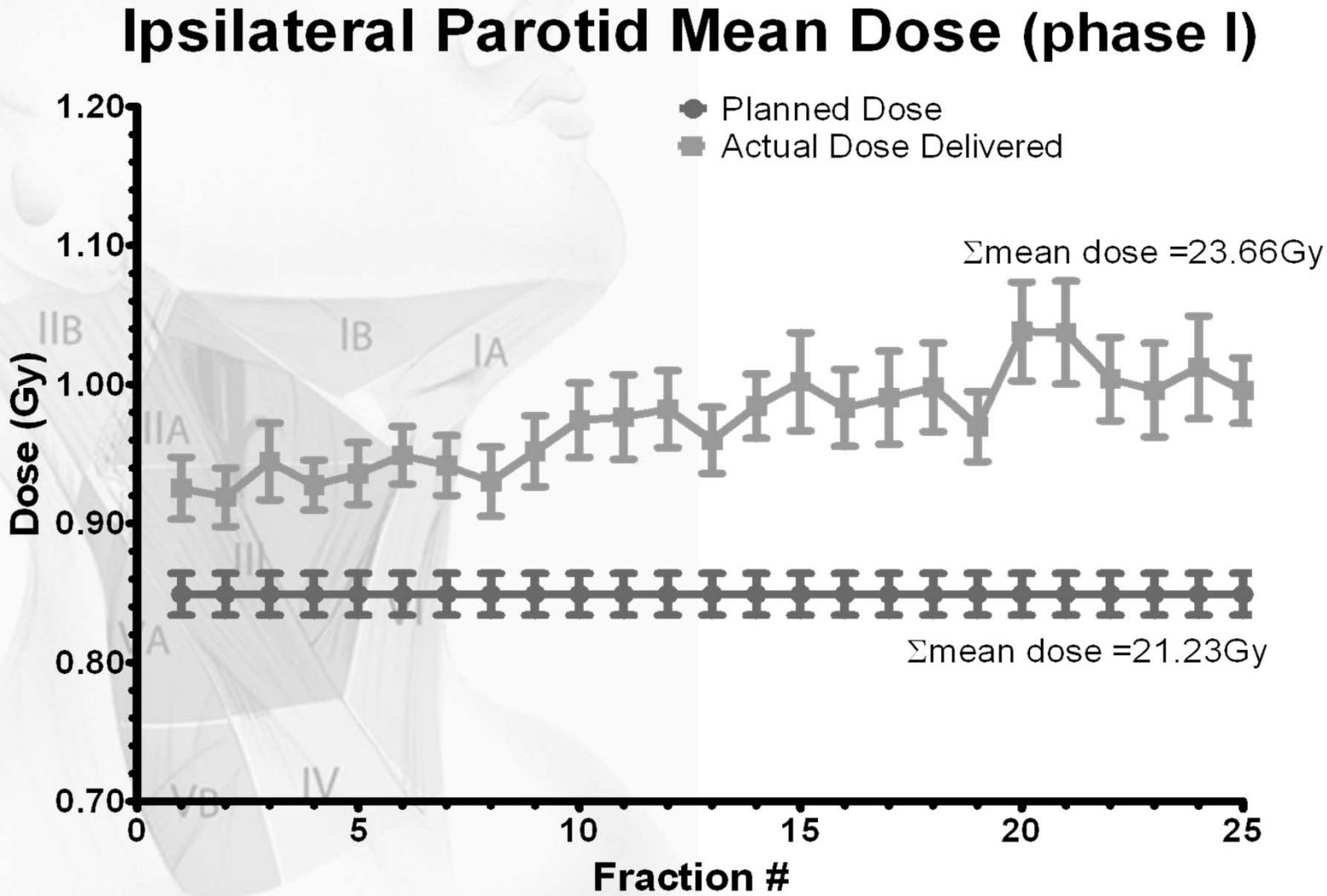
Mean Deviation (%) from CTV Planned dose (50 Gy)

Dose	CTV T	Ipsilateral Nodal CTV	Contralateral Nodal CTV
Near Max (2%)	1.26% (±0.31*)	1.18% (±0.25*)	0.96% (±0.34*)
Median (50%)	0.93% (±0.25*)	0.51% (±0.24*)	0.33% (±0.21*)
95%	-0.19% (±0.37*)	-1.00% (±0.54*)	-0.80% (±0.26*)
Near Min (98%)	-1.33% (±0.69*)	-1.12% (±0.26*)	-1.95% (±0.37*)
Mean	0.77% (±0.24*)	0.37% (±0.21*)	0.15% (±0.20*)

*Standard Error of Mean

Carruthers, 2011

Adaptive Image-Guided IMRT in pharyngo-laryngeal squamous cell carcinoma



Carruthers, 2011

Adaptive Image-Guided IMRT in pharyngo-laryngeal squamous cell carcinoma

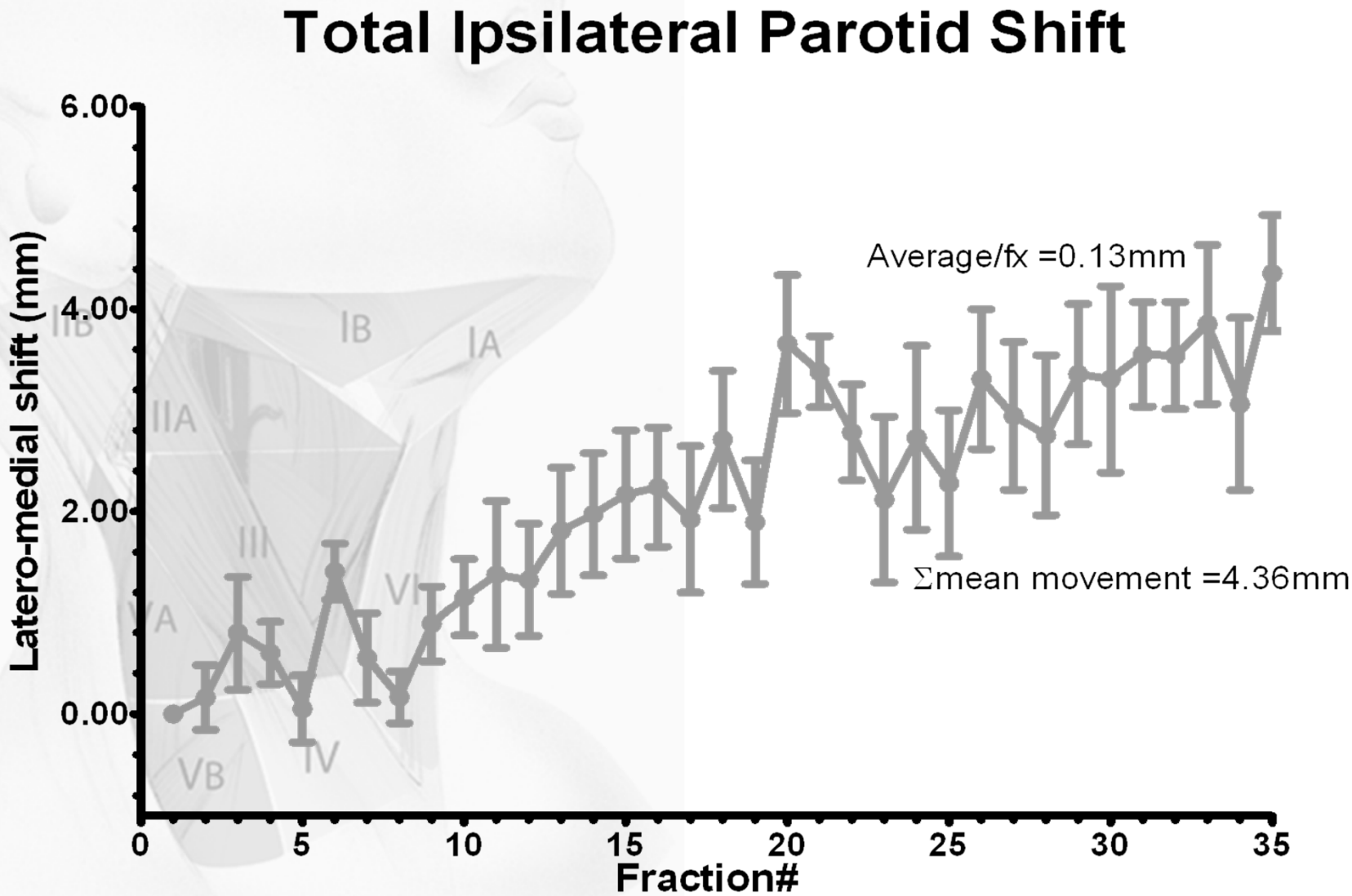
Mean Deviation(%) from OAR Planned dose (50 Gy)

Dose	Ipsilateral Parotid	Contralateral Parotid	Oral Cavity	PRV SC
Mean	16.09% (±1.79*)	10.55% (±2.46*)	4.38% (±1.15*)	-
Near Max (2%)	-	-	-	4.39% (±1.12*)

*Standard Error of Mean

Carruthers, 2011

Adaptive Image-Guided IMRT in pharyngo-laryngeal squamous cell carcinoma



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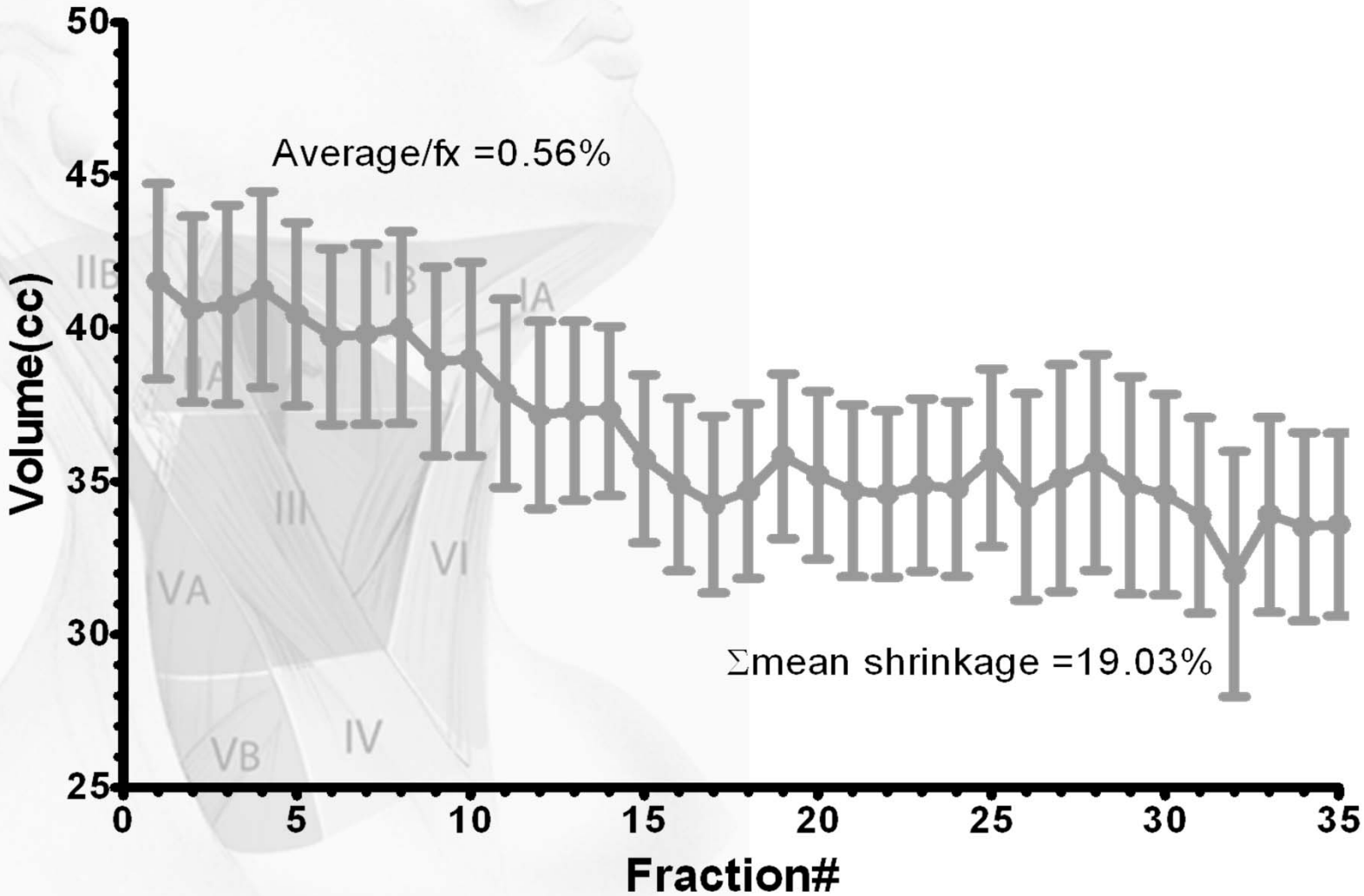
Adaptive Image-Guided IMRT in pharyngo-laryngeal squamous cell carcinoma

Total Ipsilateral Parotid Shrinkage



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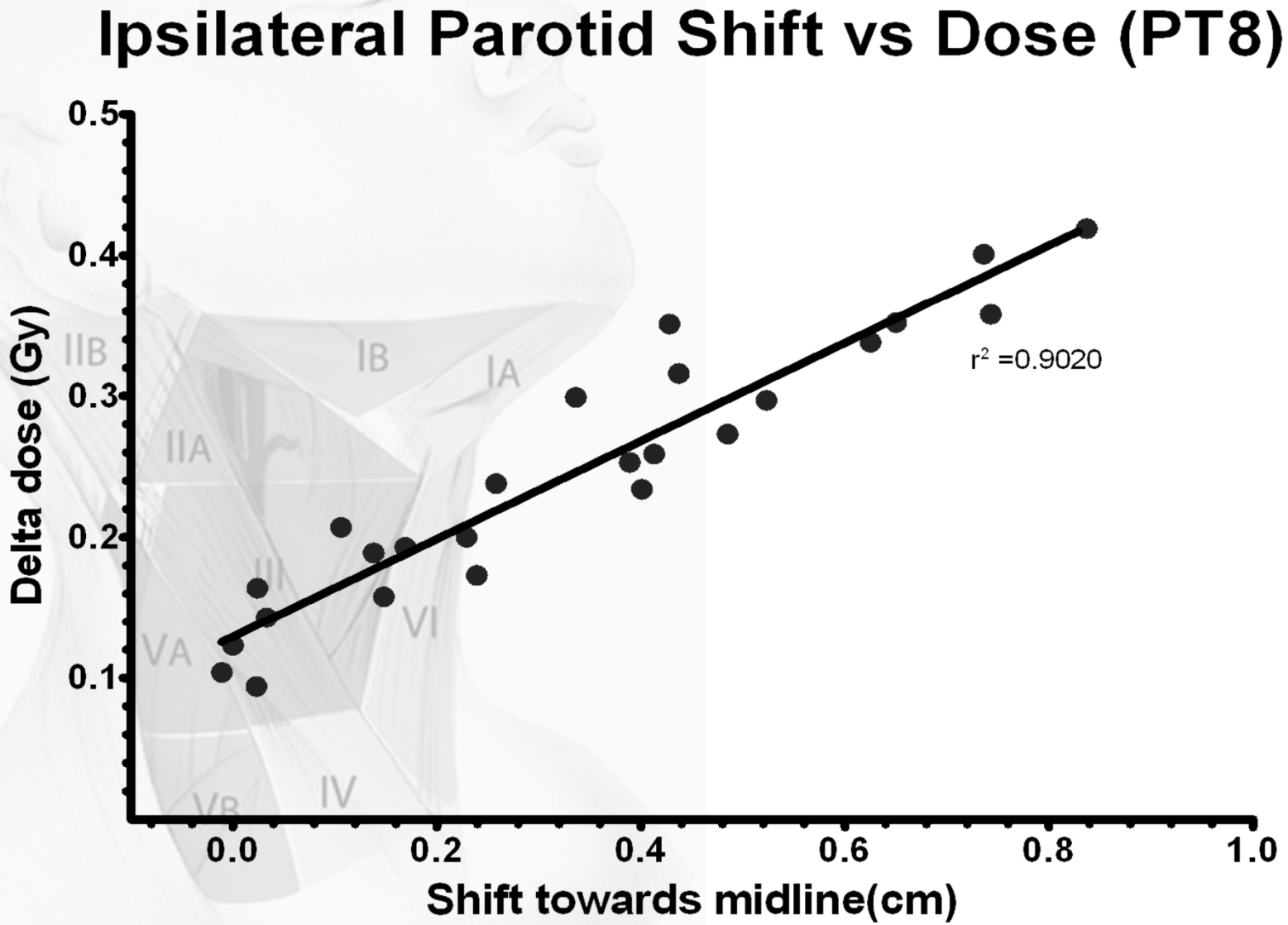
Carruthers, 2011

Adaptive Image-Guided IMRT in pharyngo-laryngeal squamous cell carcinoma



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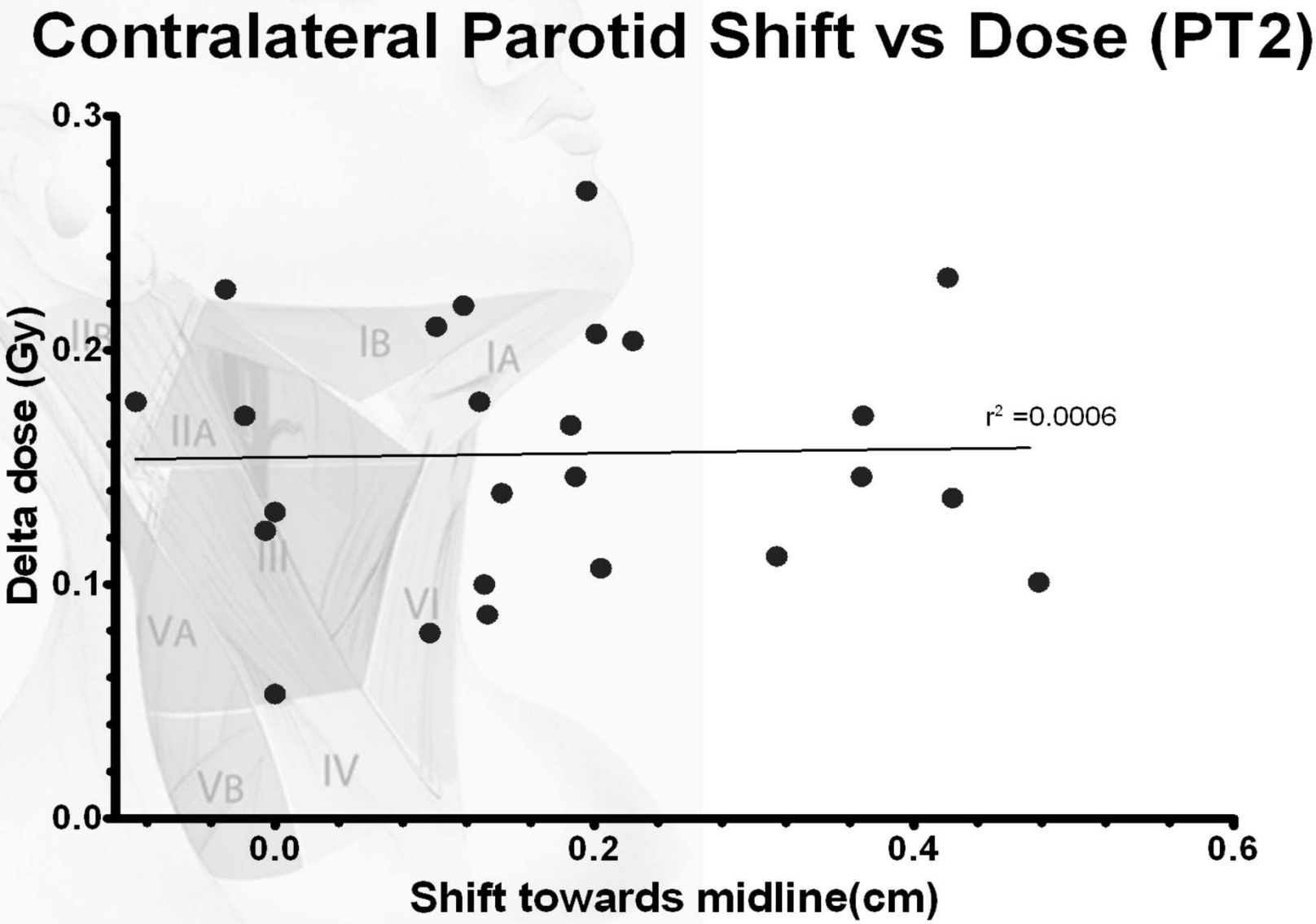
Carruthers, 2011

Adaptive Image-Guided IMRT in pharyngo-laryngeal squamous cell carcinoma



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Adaptive Image-Guided IMRT in pharyngo-laryngeal squamous cell carcinoma

Irradiated volume

	Planned dose distribution	95% CI	Delivered dose distribution	95% CI	Adaptive dose distribution	95% CI	*p*-value (ANOVA)
$V_{100\%}$ (cc)	140.4	[66.4 ; 214.4]	150.2	[69.3 ; 231.0]	112.1	[50.9 ; 173.3]	<0.01
$V_{95\%}$ (cc)	246.5	[137.6 ; 355.4]	261.4	[144.7 ; 378.1]	202.0	[111.5 ; 292.5]	<0.01
$V_{90\%}$ (cc)	274.7	[186.1 ; 363.3]	323.1	[189.5 ; 456.7]	262	[154.2 ; 369.7]	0.05
$V_{80\%}$ (cc)	681.3	[533.0 ; 829.7]	667.5	[499.1 ; 835.9]	678.4	[535.9 ; 820.8]	0.73
$V_{70\%}$ (cc)	1126.6	[921.4 ; 1331.9]	1142.3	[918.6 ; 1366.0]	1124.0	[901.4 ; 1346.7]	0.49
$V_{60\%}$ (cc)	1485.4	[1232.8 ; 1738.0]	1503.4	[1230.7 ; 1776.1]	1497.9	[1219.0 ; 1776.8]	0.55
$V_{50\%}$ (cc)	1822.5	[1540.5 ; 2104.4]	1845.2	[1539.1 ; 2151.2]	1848.3	[1525.1 ; 2171.5]	0.39

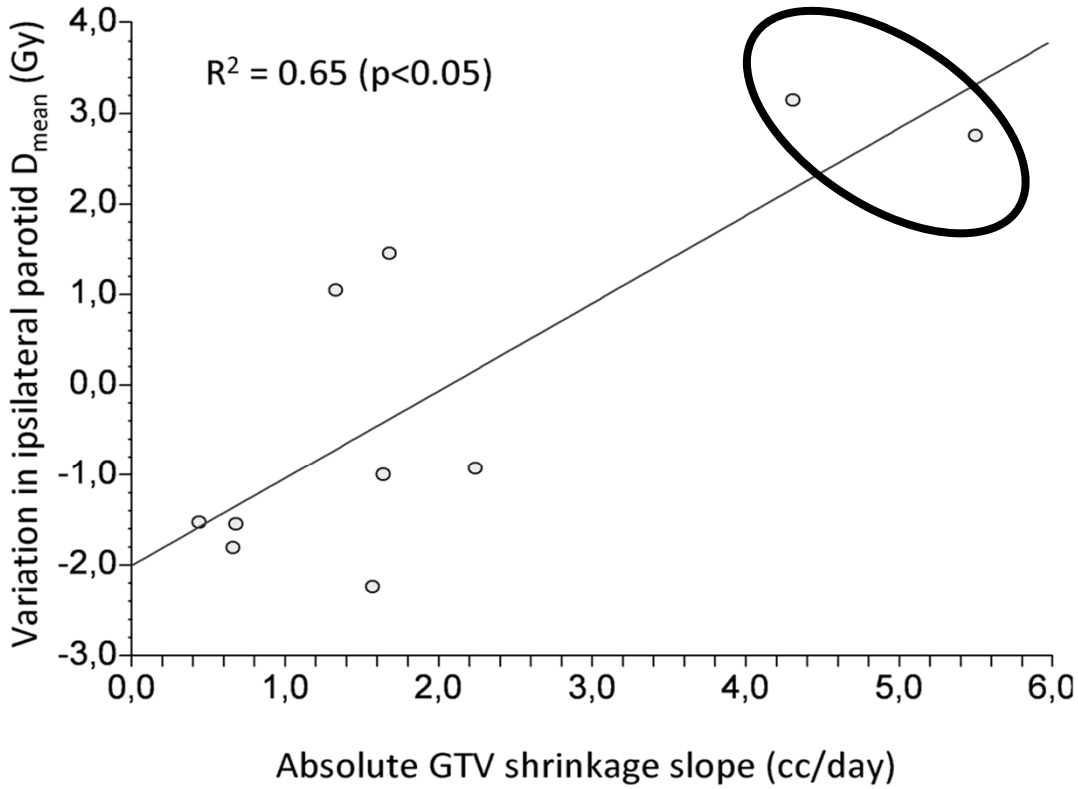
Adaptive Image-Guided IMRT in pharyngo-laryngeal squamous cell carcinoma

Organs at Risk

		Planned dose distribution	95% CI	Delivered dose distribution	95% CI	Adaptive dose distribution	95% CI	*p*-value (ANOVA)
Parotid glands	D_{mean} (Gy)	17.89	[16.13 ; 19.65]	18.68	[16.41 ; 20.95]	18.67	[16.71 ; 20.61]	0.07
Submandibular glands	D_{mean} (Gy)	51.90	[45.81 ; 57.99]	52.78	[46.92 ; 58.65]	51.73	[45.69 ; 57.77]	0.11
Oral Cavity	D_{mean} (Gy)	26.03	[13.81 ; 38.26]	26.74	[14.19 ; 39.29]	24.36	[11.96 ; 36.76]	<0.01
Spinal cord	$D_{2\%}$ (Gy)	40.12	[38.45 ; 41.79]	40.95	[38.77 ; 43.13]	39.42	[37.47 ; 41.36]	0.22
PRV spinal cord	$D_{2\%}$ (Gy)	42.31	[41.18 ; 43.44]	44.22	[41.59 ; 46.85]	41.23	[39.46 ; 43.00]	0.02
Larynx	$D_{5\%}$ (Gy)	67.94	[63.04 ; 72.83]	67.74	[62.50 ; 72.98]	67.65	[63.02 ; 72.29]	0.39
Mandible	$D_{2\%}$ (Gy)	56.87	[50.82 ; 62.93]	56.19	[50.24 ; 62.15]	54.74	[47.96 ; 61.53]	0.16
Mandible	V_{50Gy} (%)	9.73	[3.43 ; 16.04]	9.05	[3.05 ; 15.04]	10.21	[3.50 ; 16.91]	0.23

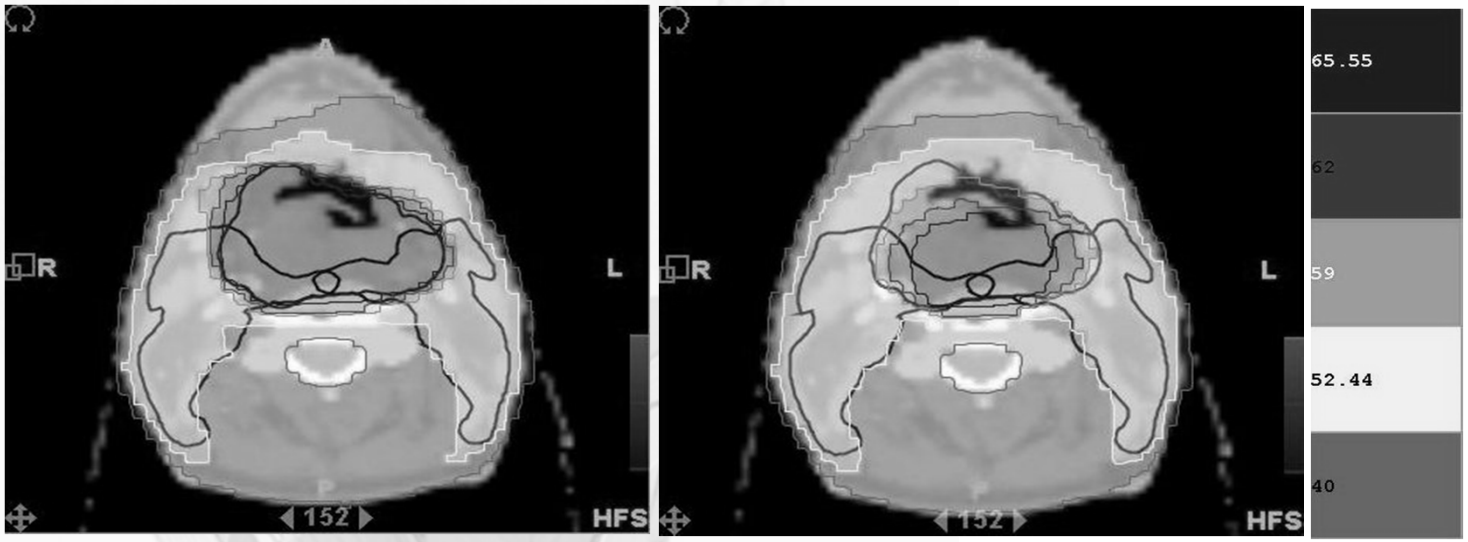
Adaptive Image-Guided IMRT in pharyngo-laryngeal squamous cell carcinoma

Adaptive approach and ipsilateral parotid irradiation



Impact on dose distribution

Classic CT-based planning Adaptive PET-based planning



SIB-IMRT

30x2.3 Gy

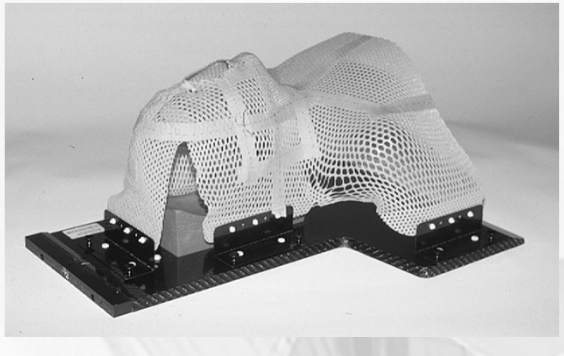
30x1.85 Gy

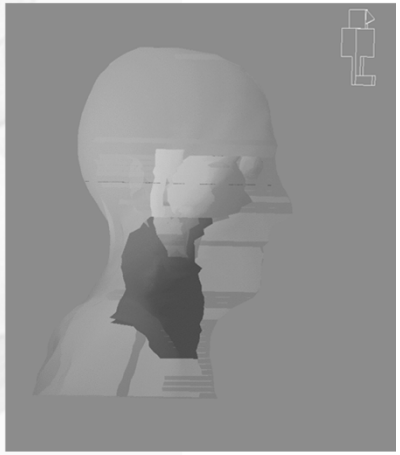
P<0.001

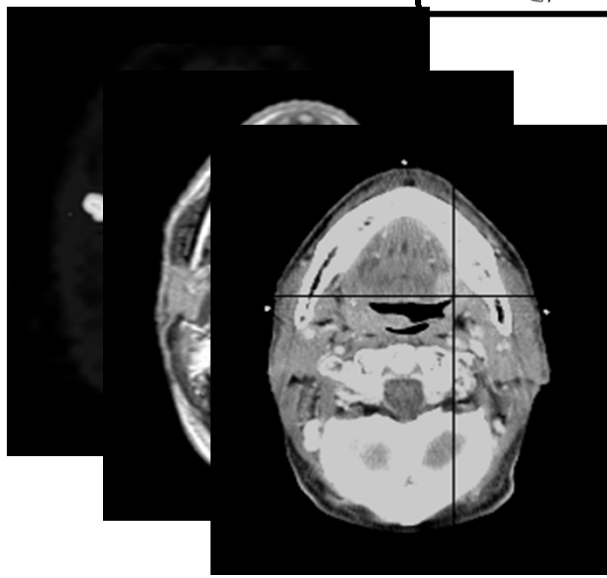
Planning	V_{10}	V_{50}	V_{80}	V_{90}	V_{95}	V_{100}
Classic CT-based	100%	100%	100%	100%	100%	100%
Adaptive CT-based	99%	100%	100%	85%	80%	66%
Classic PET-based	99%	99%	98%	83%	82%	81%
Adaptive PET-based	99%	100%	98%	73%	67%	58%

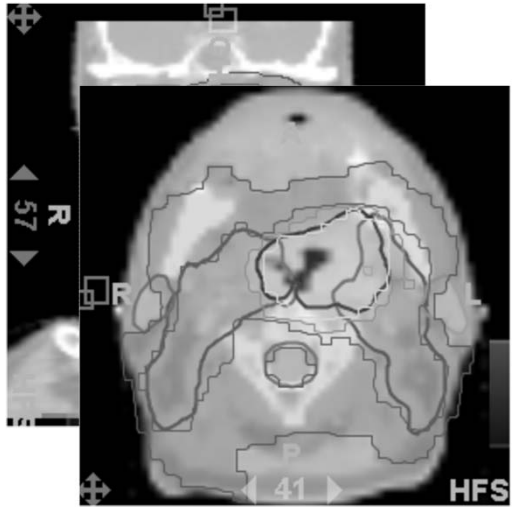
Geets, 2007

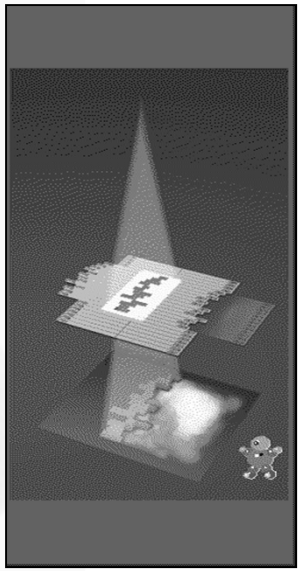
IMRT in Head and Neck Tumors
WYSINWYG… !!!





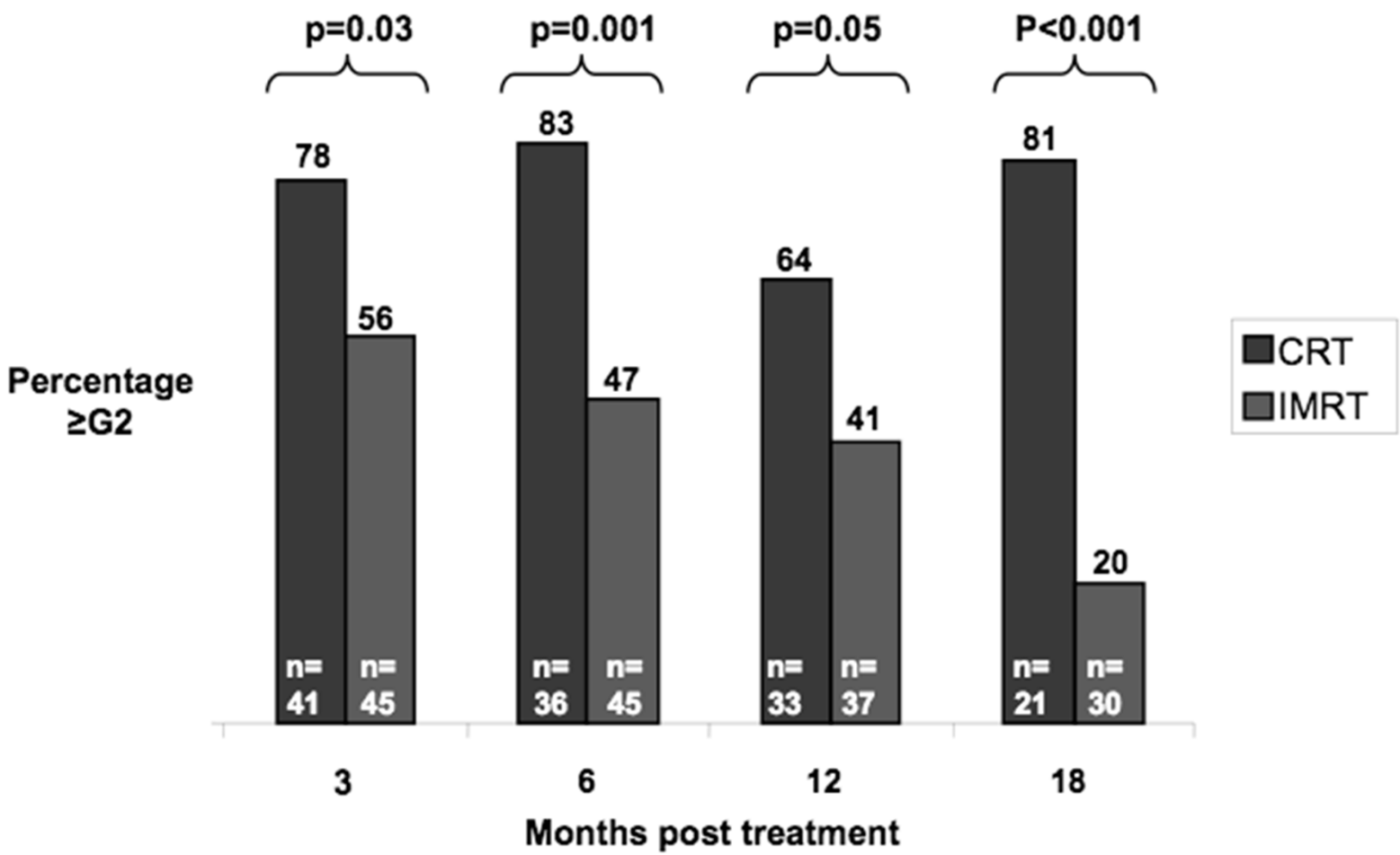






Parotid gland sparing in IMRT for HNSCC

RTOG Subjective Salivary Gland toxicity ≥G2*



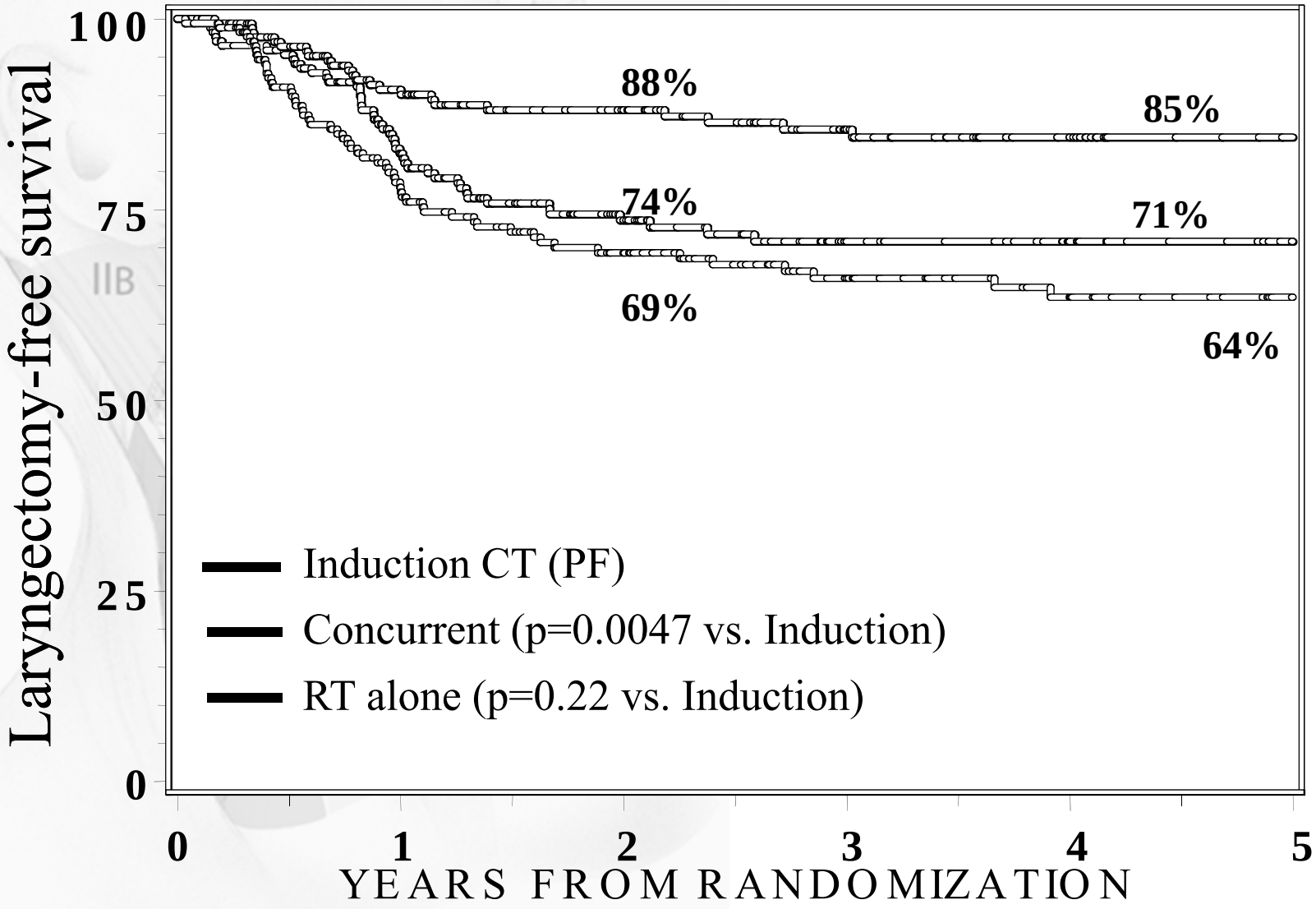
*Moderate or complete dryness of mouth poor or no response on stimulation

Nutting et al. JCO 2009:27 (18s);799s (LBA6006)

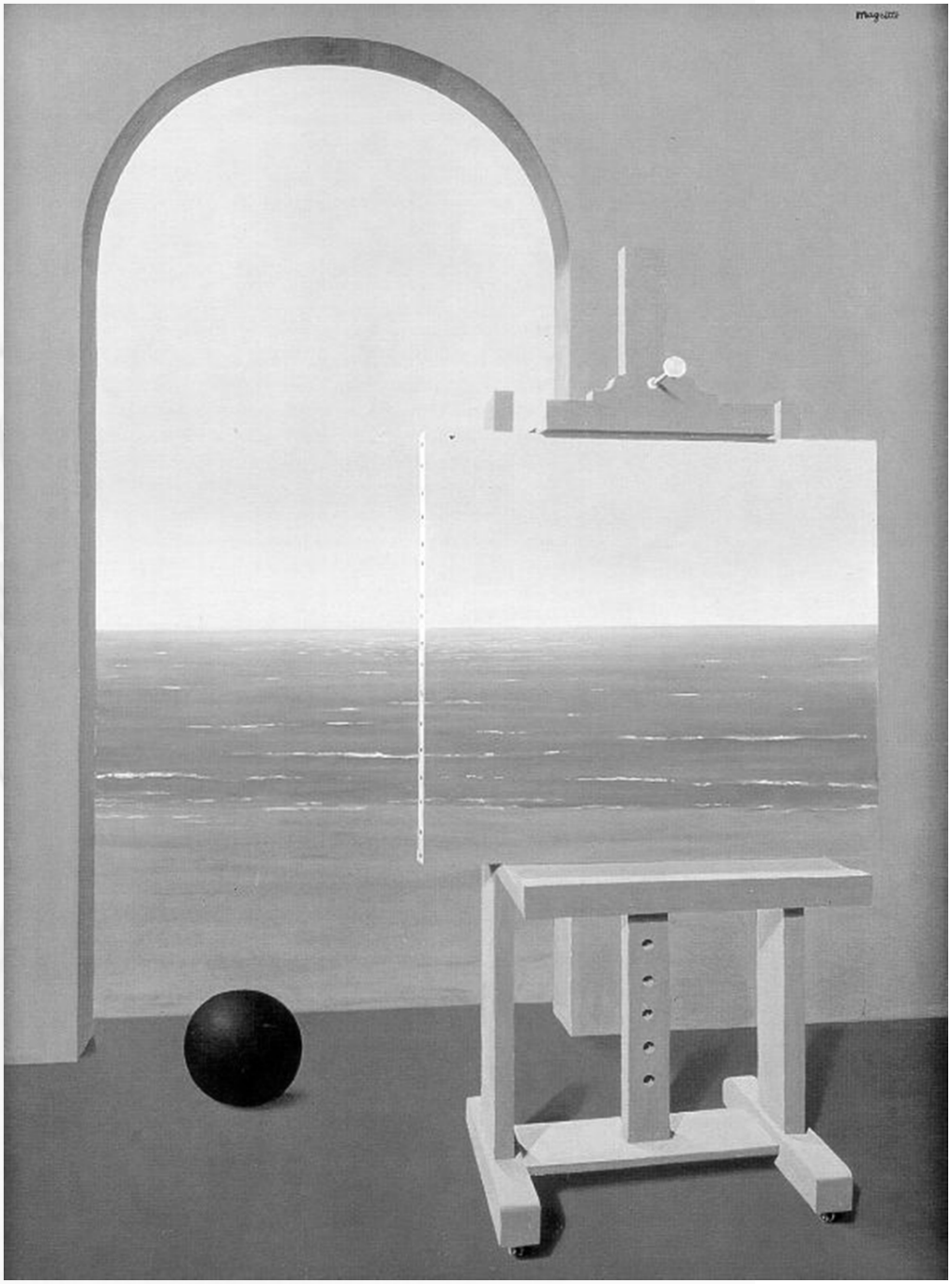
Nutting, 2009

Chemotherapy: Induction or Concomitant?

Intergroup trial R-91-11: laryngeal SCC



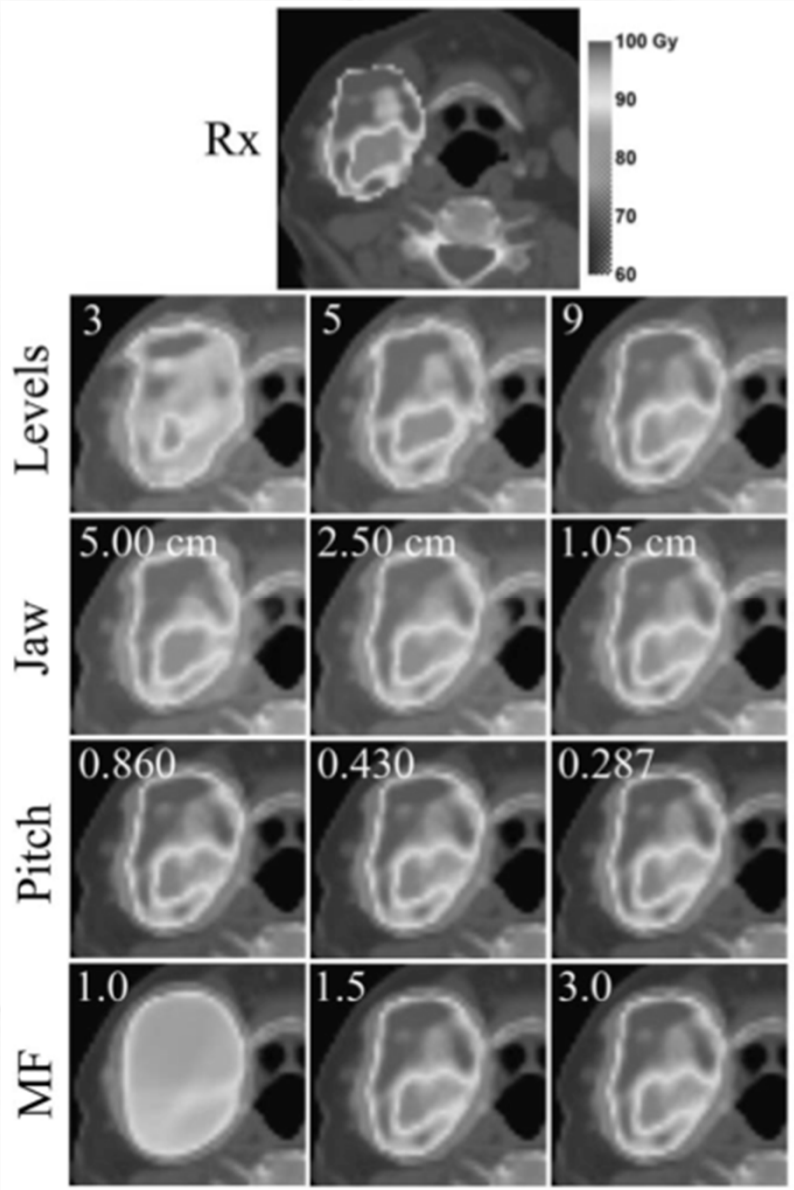
Forastiere, 2001



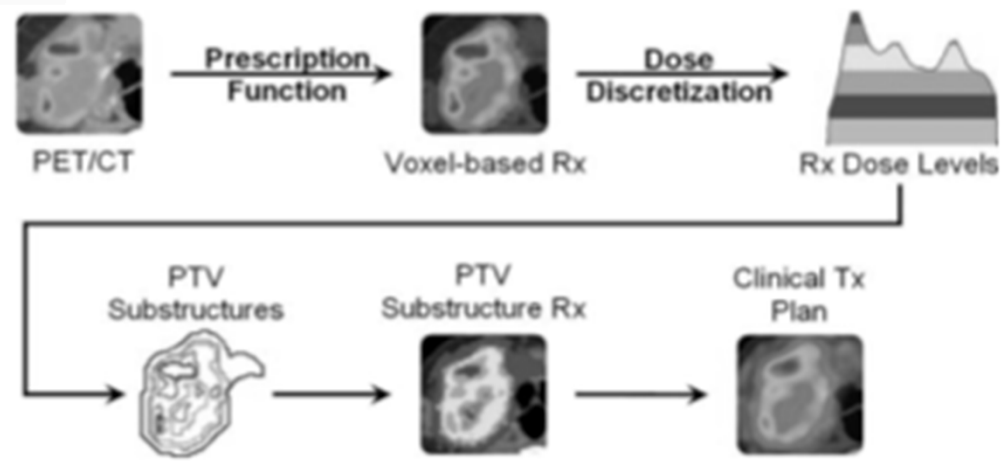
The Human Condition.

R. Magritte, 1935

Molecular imaging dose painting by number

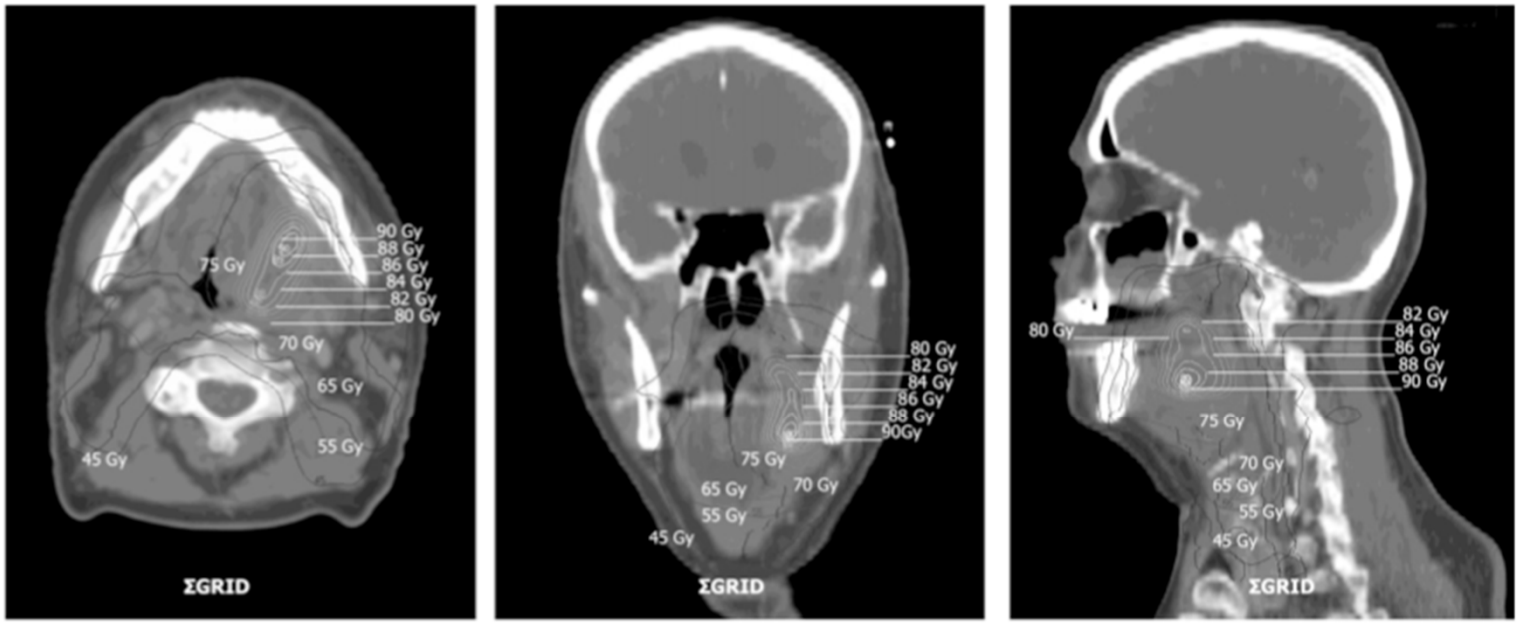


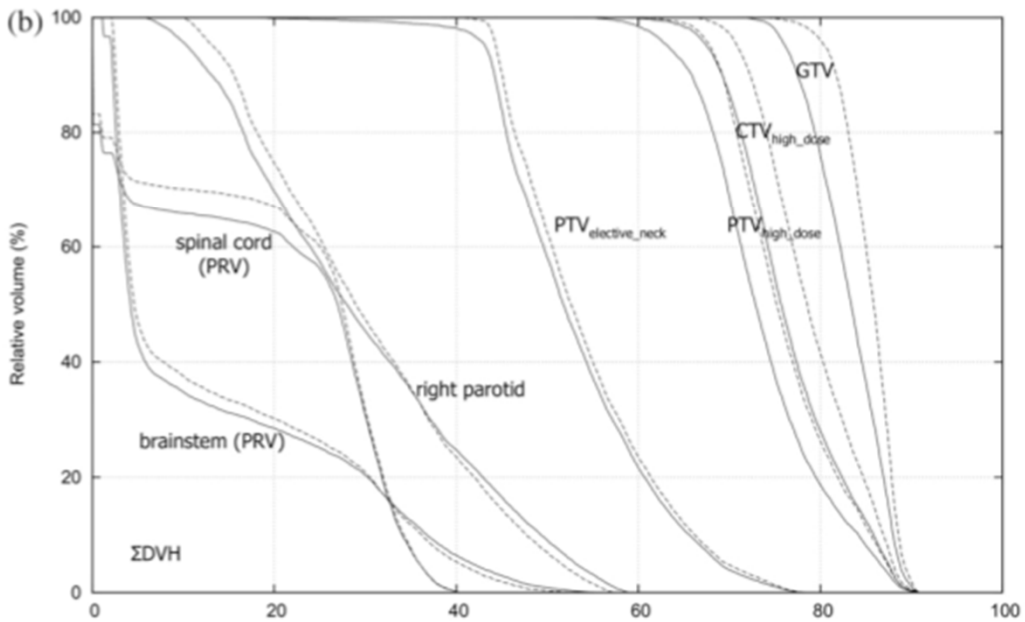
- Tomotherapy Hi-Art
- H&N SCC: T4N2bM0
- 60 Gy + SIB of 30 Gy
- Hypoxia (Cu-ATSM)



Deveau et al., 2010

Molecular imaging dose painting by number





- DPBN based on FDG-PET
- Median dose of 80.9 Gy (n=7) et 85.9 Gy (n=14)
- No grade 4 acute toxicity

Duprez et al., 2010

Radiobiological and clinical issues in IMRT for HNSCC

Comparison between SIB and 2-phase IMRT(50 Gy + 20 Gy)

Dose level (Gy)	Volume of non-target tissues (cc)		
	Two-phase IMRT	SIB IMRT	% difference
10	2,183	2,169	0.6
20	1,975	1,941	1.8
30	1,557	1,459	6.7
40	1,096	1,016	7.9
50	732	604	21.2
60	388	238	63.0
70	83	62	34.0

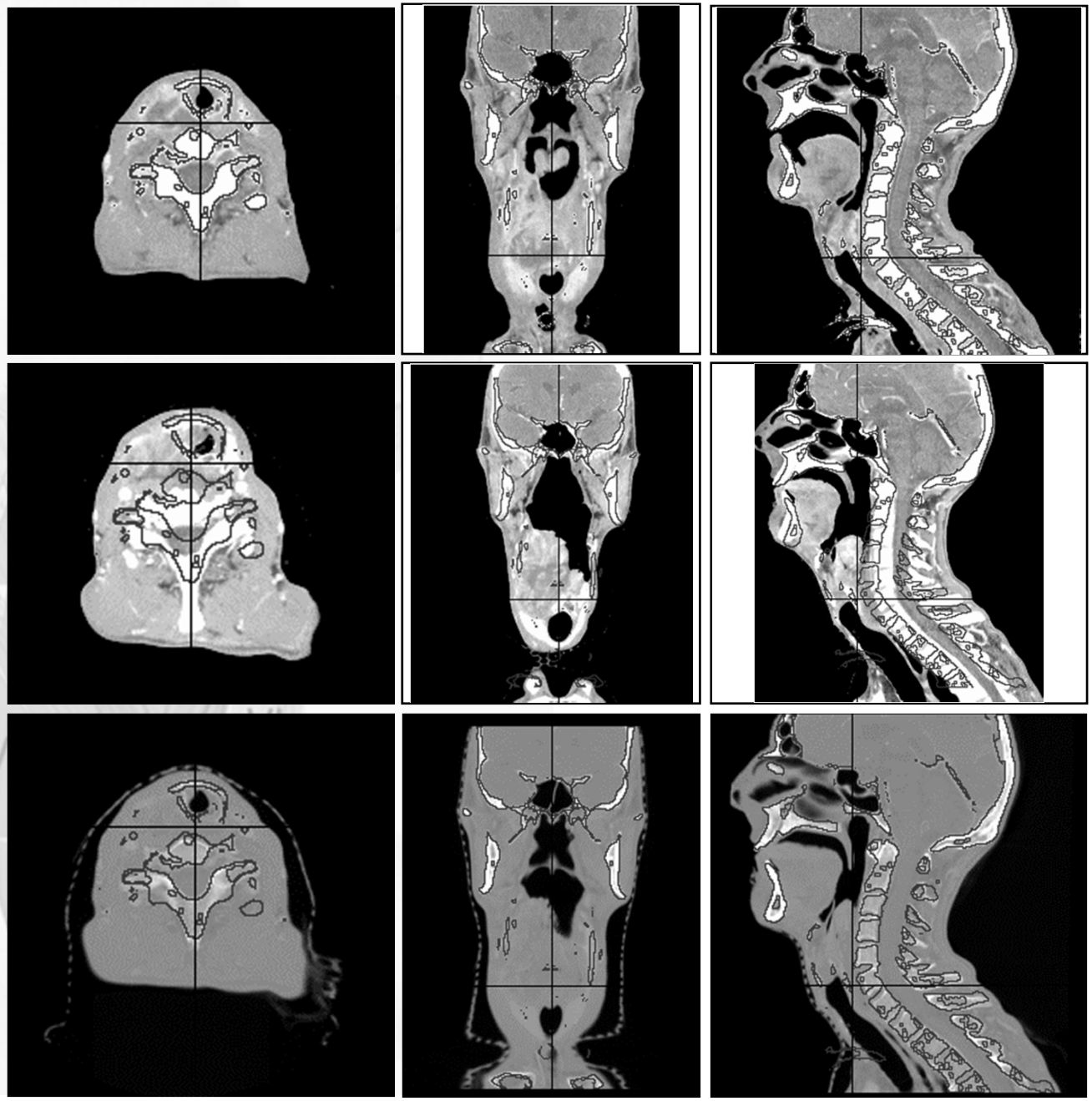
Mohan et al., 2000

Work in progress

Reference image

Rigid registration

Non-rigid registration



Loeckx & Maes
ESAT, 2004

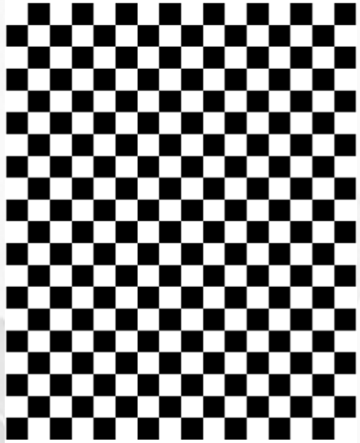
Work in progress

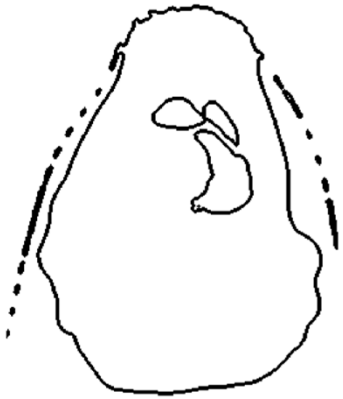
Checkerboard

Body contour

Dose distribution at T_1

T_1



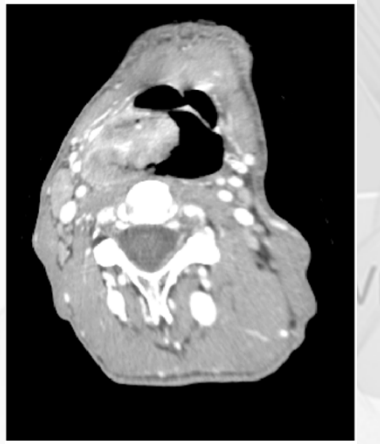


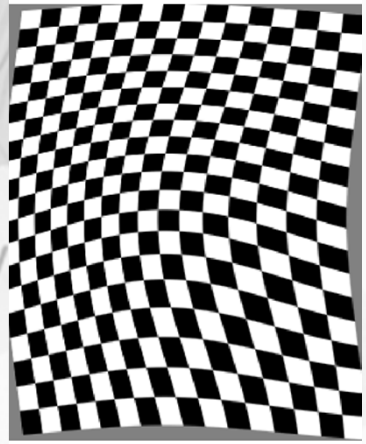
Non-rigid checker-board transformation

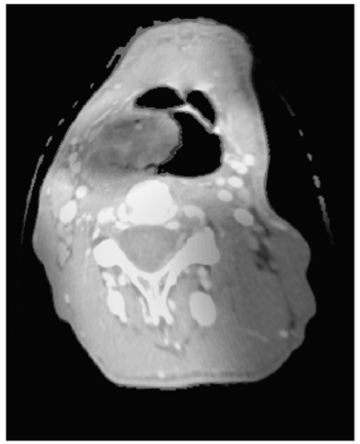
Deformed body contour

Deformed dose distributionon CT at T_2

T_2

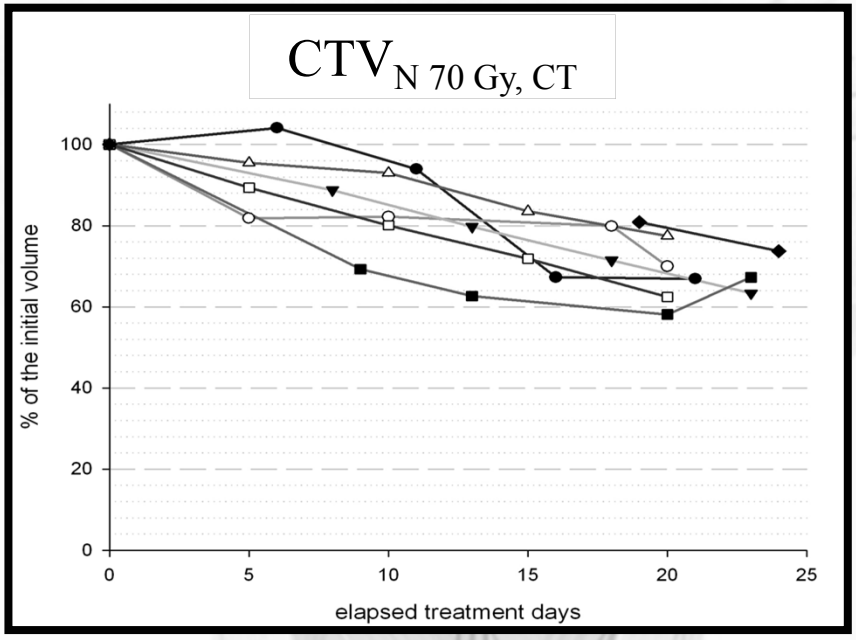


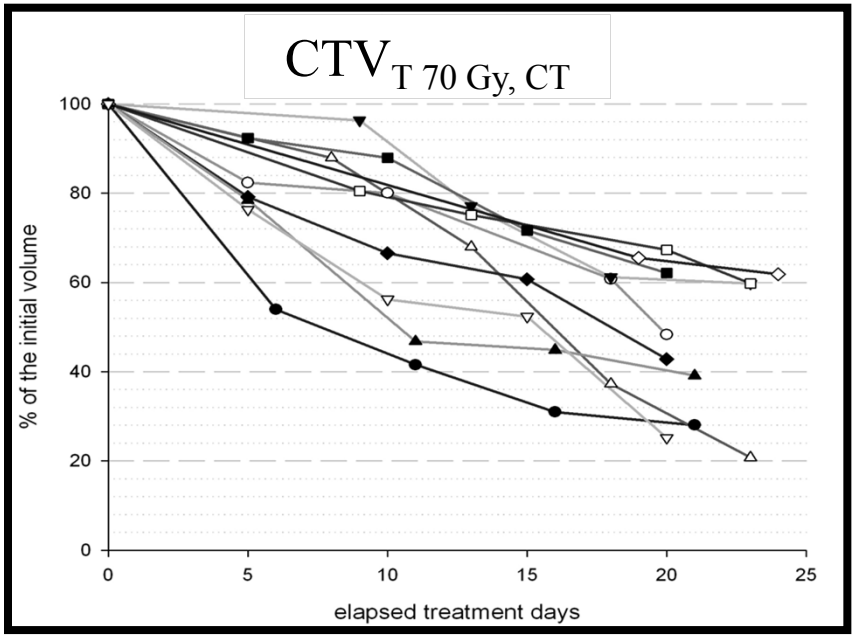




J. Lee, 2005

Variation in therapeutic CTVs during RT-CH… (70 Gy – 3 courses chemo on w1, w4, w7)





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# ($p<0.05$)

Castadot & Lee, 2010

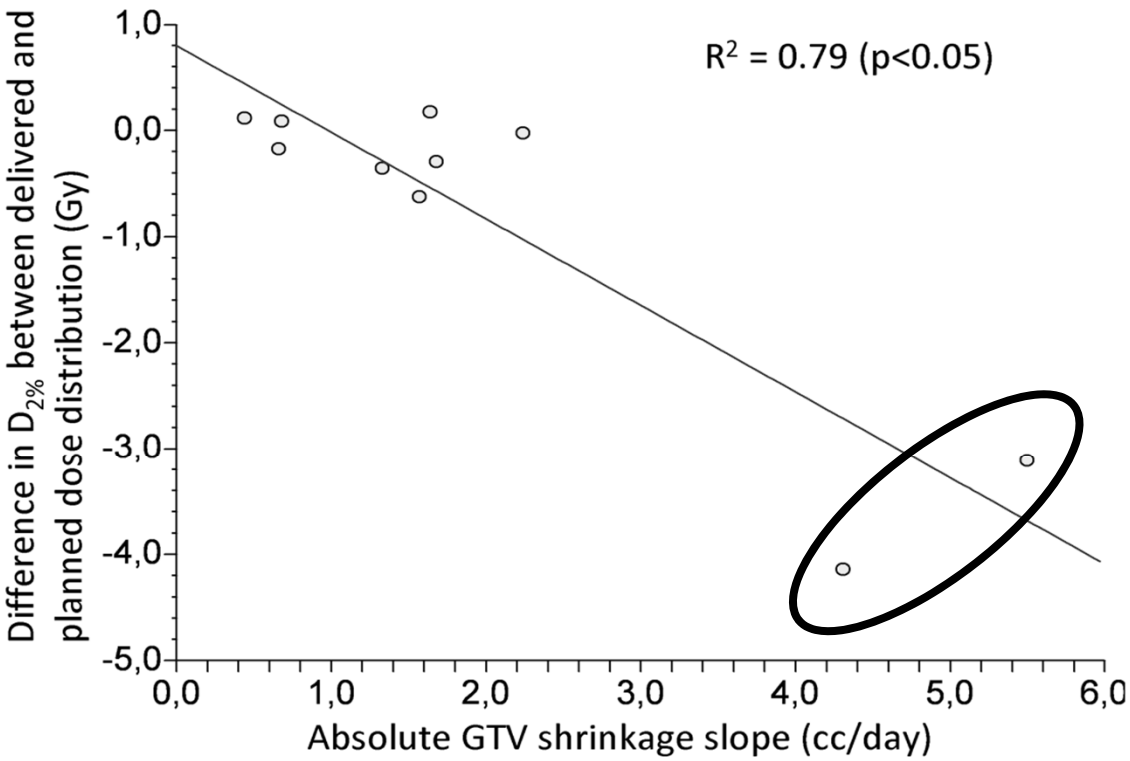
Adaptive Image-Guided IMRT in pharyngo-laryngeal squamous cell carcinoma

Target volumes

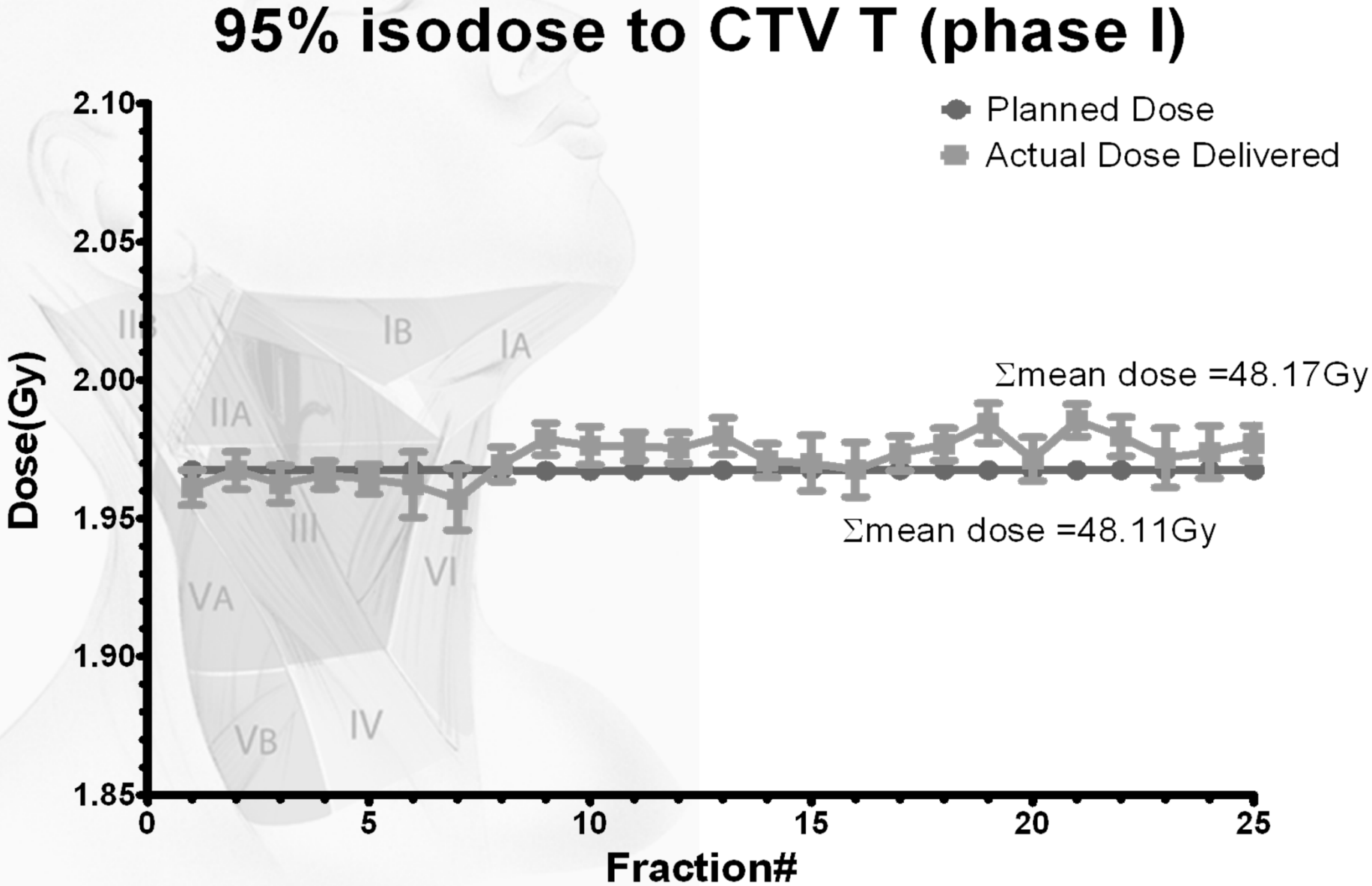
		Planned dose distribution	95% CI	Delivered dose distribution	95% CI	Adaptive dose distribution	95% CI	*p*-value (ANOVA)
CTV_{ther}	$D_{2\%}$	71.02	[70.57 ; 71.48]	70.63	[70.36 ; 70.89]	70.52	[69.87 ; 71.17]	0.07
	$D_{50\%}$	69.35	[69.25 ; 69.45]	69.39	[69.28 ; 69.51]	69.13	[69.00 ; 69.26]	<0.01
	$D_{95\%}$	68.38	[68.15 ; 68.61]	68.42	[68.21 ; 68.63]	65.34	[64.00 ; 66.68]	0.02
CTV_{proph}	$D_{2\%}$	70.55	[70.25 ; 70.84]	70.36	[70.14 ; 70.56]	70.11	[69.61 ; 70.60]	0.02
	$D_{50\%}$	63.48	[59.74 ; 67.22]	63.62	[59.86 ; 67.38]	62.71	[59.07 ; 66.35]	<0.01
	$D_{95\%}$	54.88	[54.66 ; 55.10]	54.85	[54.55 ; 55.16]	55.19	[54.96 ; 55.41]	<0.01
PTV_{ther}	$D_{2\%}$	71.33	[70.95 ; 72.52]	70.87	[70.32 ; 71.43]	71.02	[70.22 ; 71.81]	0.01
	$D_{50\%}$	69.15	[69.05 ; 69.25]	69.21	[69.06 ; 69.36]	68.78	[68.18 ; 69.39]	0.08
	$D_{95\%}$	68.57	[66.10 ; 67.04]	66.59	[65.94 ; 67.23]	62.02	[60.54 ; 63.50]	<0.01
PTV_{proph}	$D_{2\%}$	70.57	[70.12 ; 71.01]	70.26	[70.00 ; 70.51]	70.06	[69.55 ; 70.57]	0.01
	$D_{50\%}$	60.19	[57.38 ; 63.01]	60.64	[57.31 ; 63.98]	58.70	[56.97 ; 60.42]	0.03
	$D_{95\%}$	54.11	[53.94 ; 54.27]	53.96	[53.70 ; 54.22]	54.31	[54.06 ; 54.56]	0.01

Adaptive Image-Guided IMRT in pharyngo-laryngeal squamous cell carcinoma

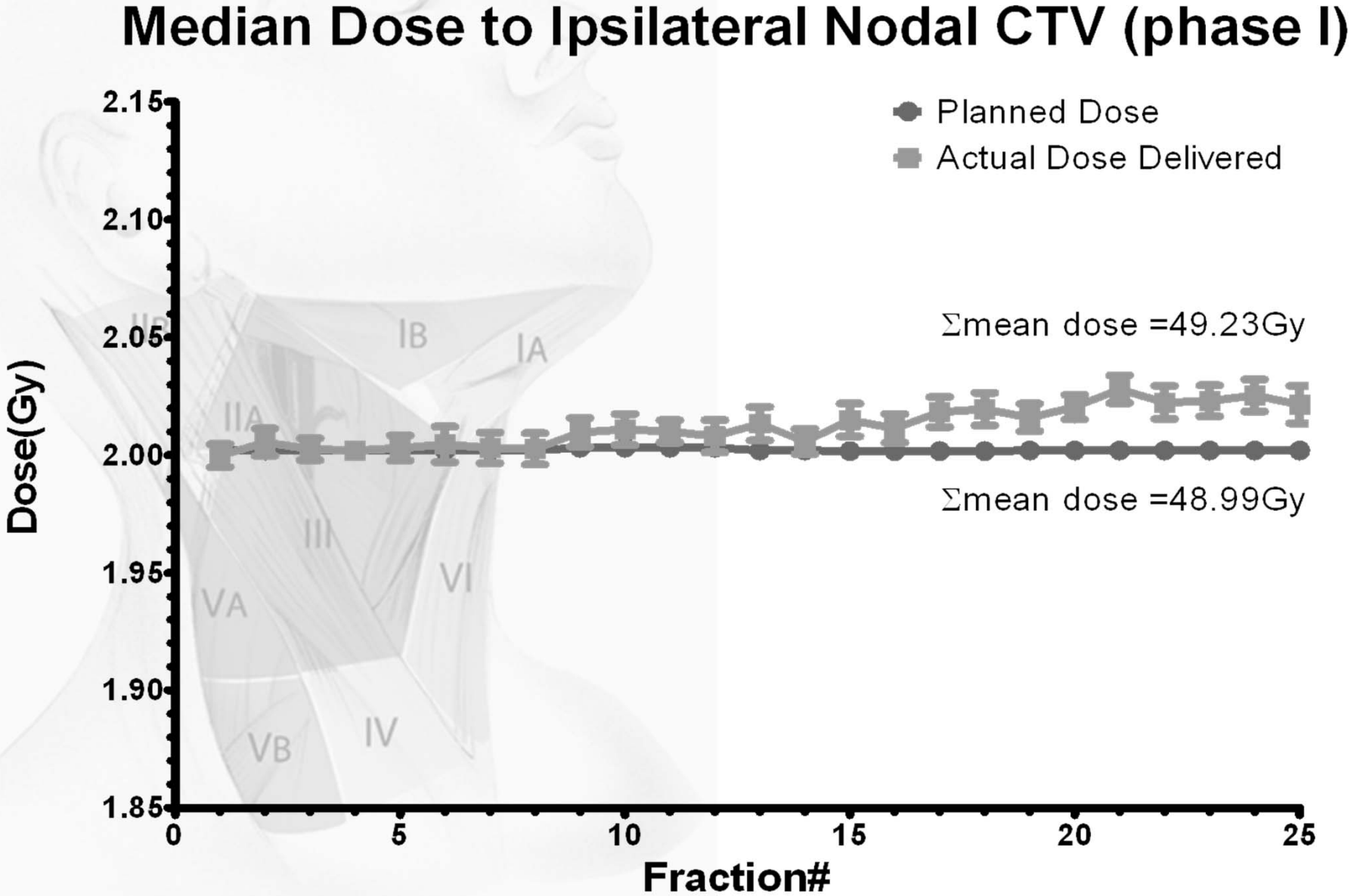
Non-adaptive approach and spinal cord irradiation



RESULTS

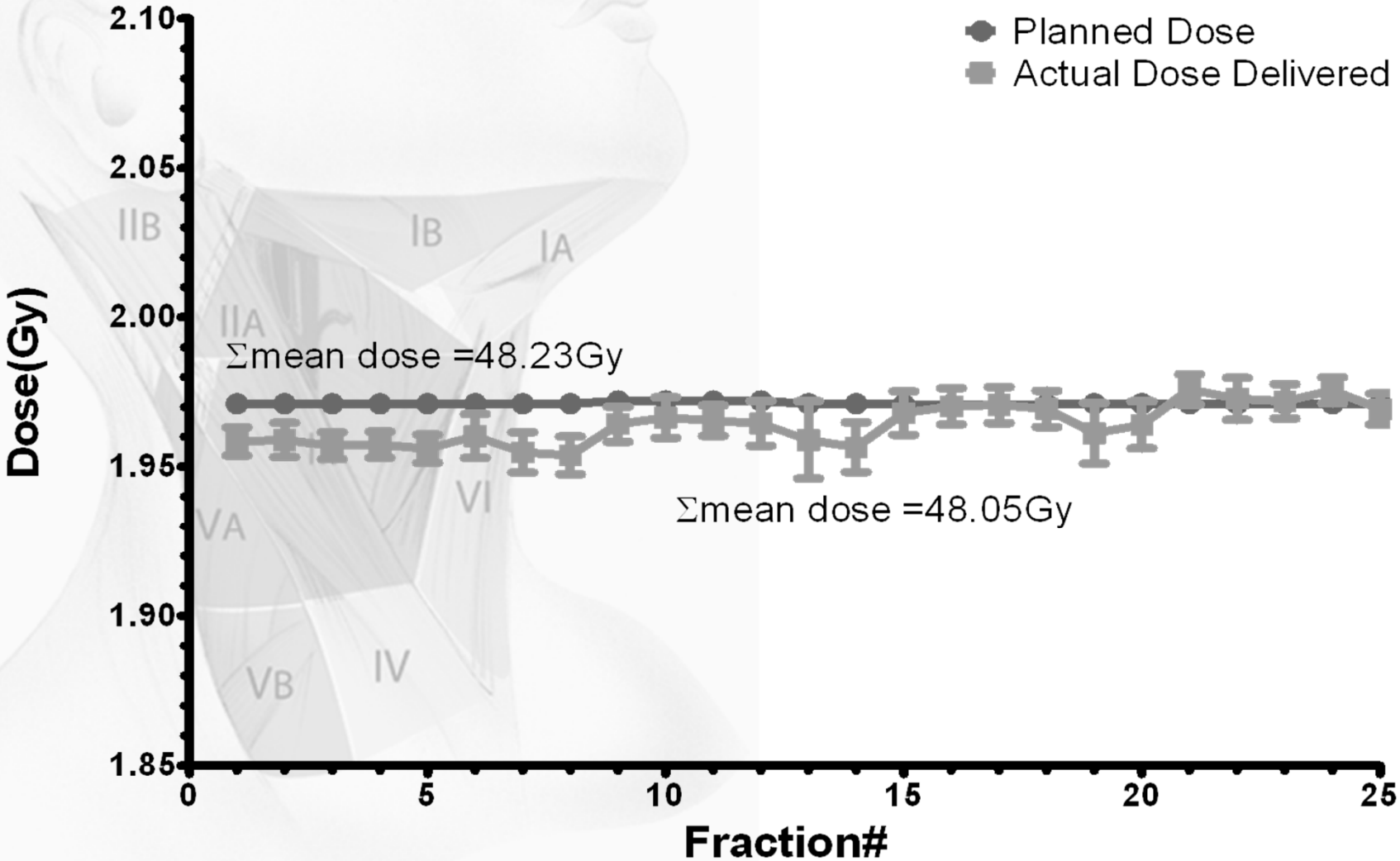

95% isodose to CTV T (phase I)
Planned Dose
Actual Dose Delivered
Σmean dose =48.17Gy
Σmean dose =48.11Gy
Dose(Gy)
2.10
2.05
2.00
1.95
1.90
1.85
0
5
10
15
20
25
Fraction#
IB
IA
IIA
III
VI
VA
VB
IV

RESULTS


Median Dose to Ipsilateral Nodal CTV (phase I)
Planned Dose
Actual Dose Delivered
Σmean dose =49.23Gy
Σmean dose =48.99Gy
Dose(Gy)
2.15
2.10
2.05
2.00
1.95
1.90
1.85
0
5
10
15
20
25
Fraction#
IB
IA
IIA
III
VI
VA
VB
IV

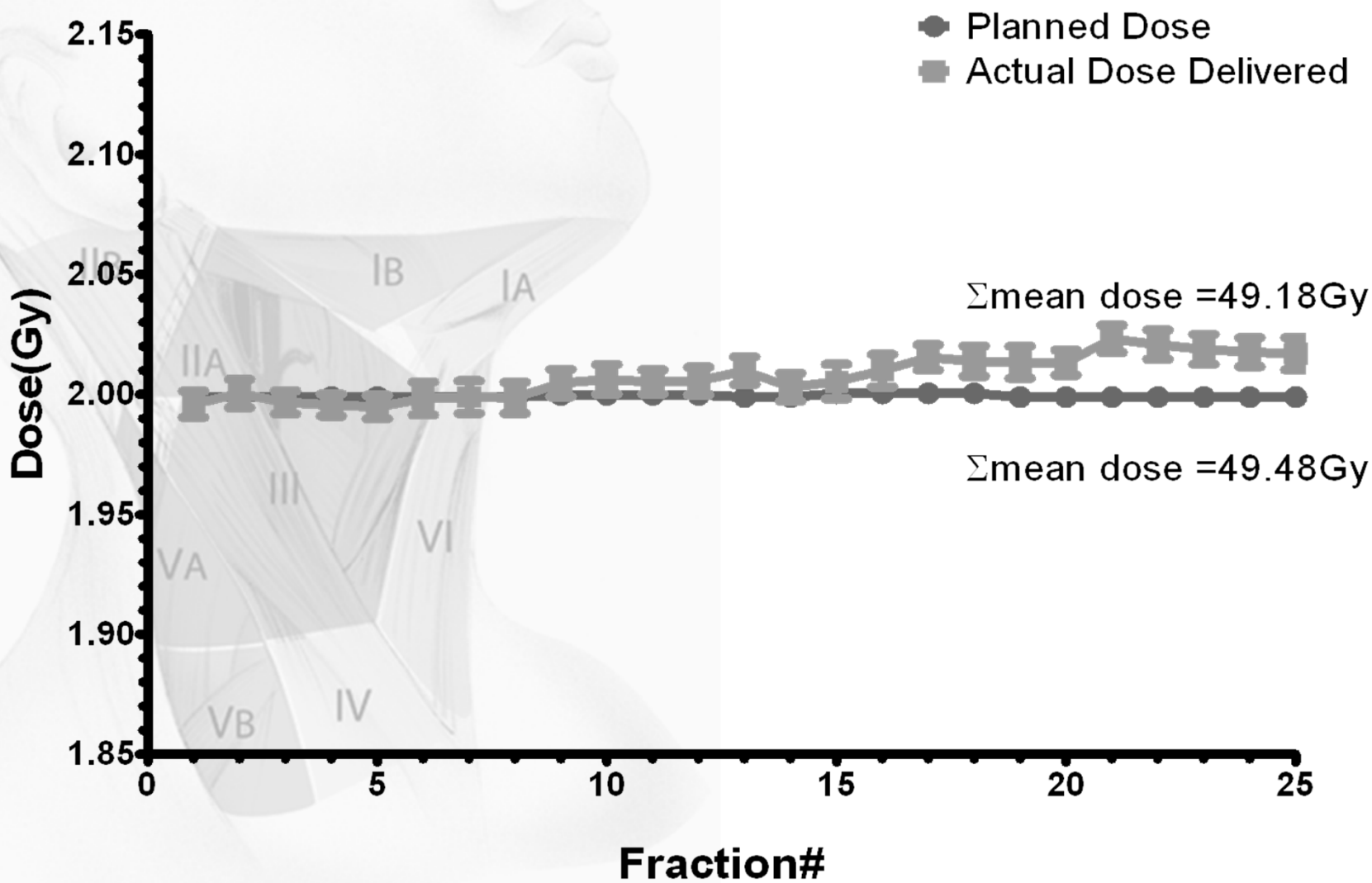
RESULTS

95% isodose to Ipsilateral Nodal CTV (phase I)



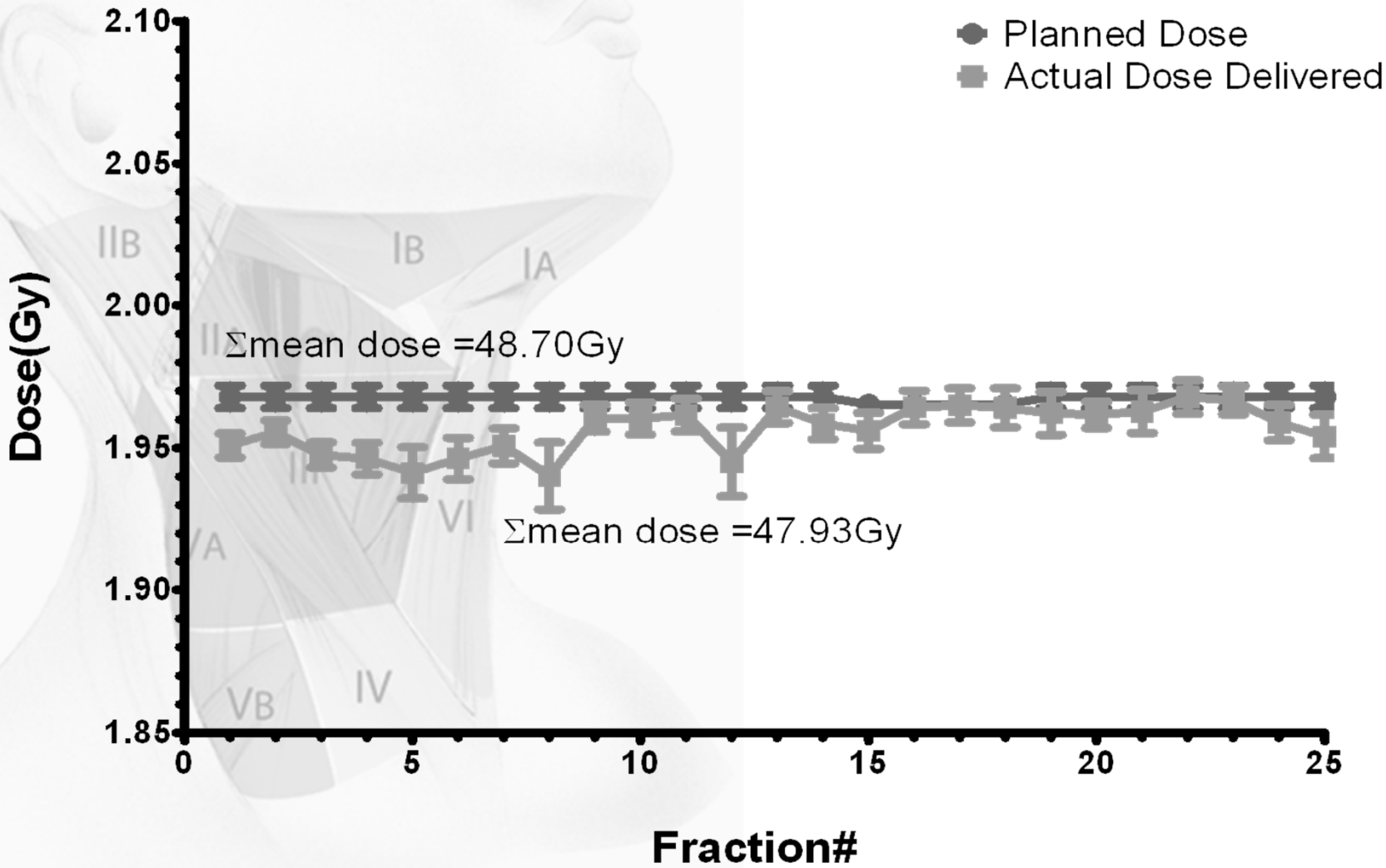
RESULTS

Median Dose to Contralateral Nodal CTV (phase I)

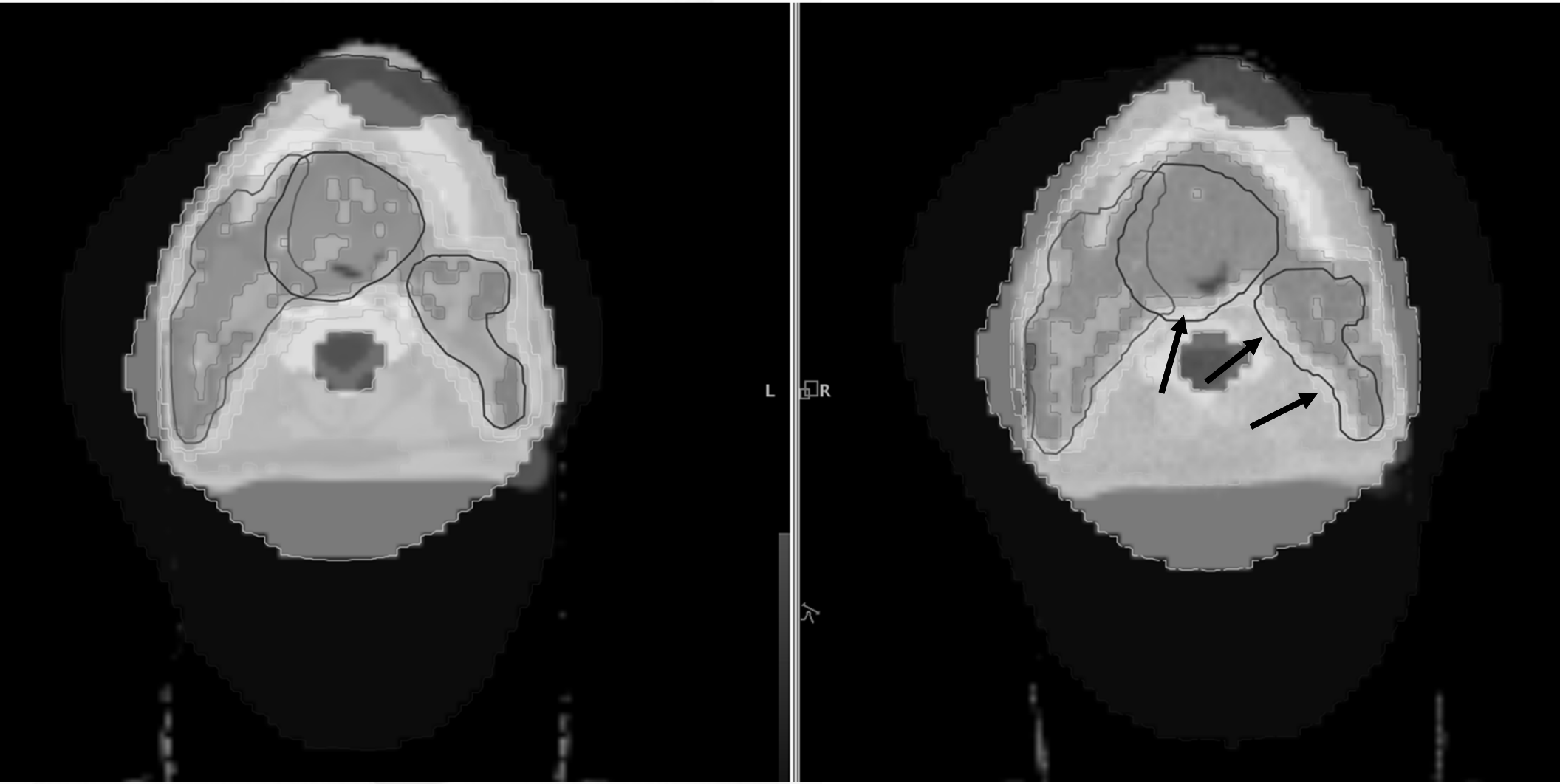


RESULTS

95% isodose to Contralateral Nodal CTV (phase I)



Adaptive Image-Guided IMRT in pharyngo-laryngeal squamous cell carcinoma

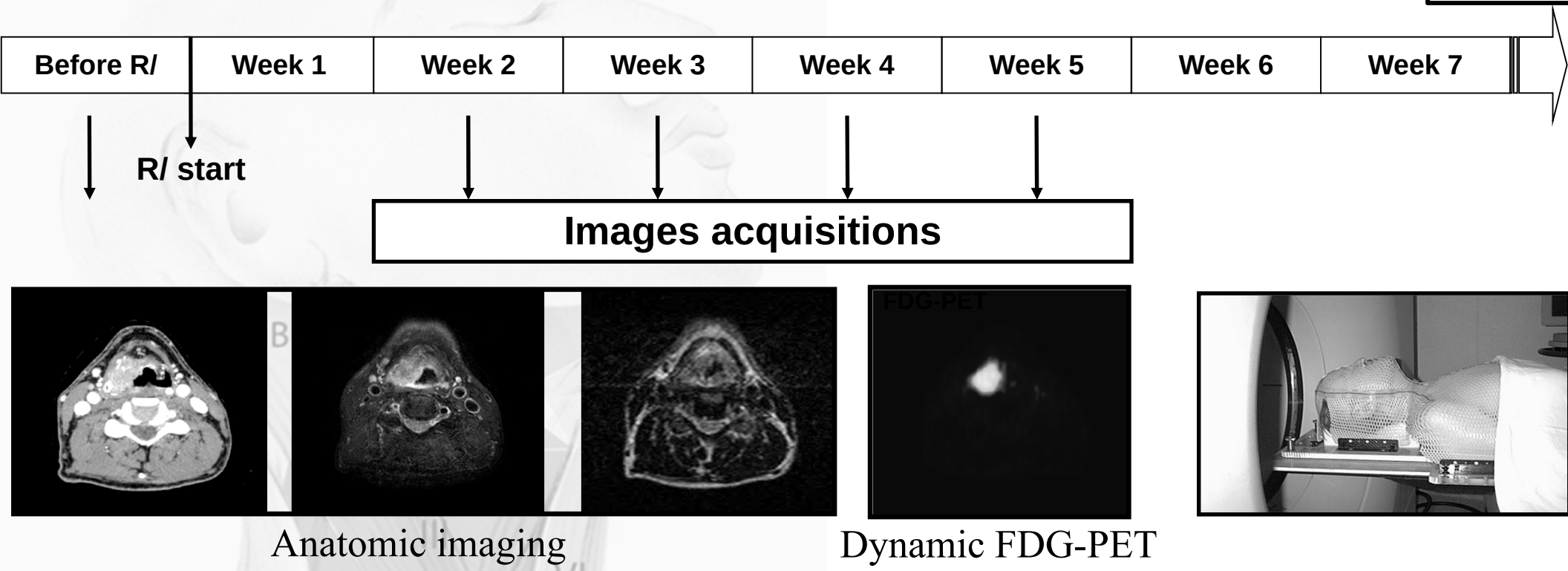


Carruthers, 2011

Factors analysed for adverse impact on TCP after secondary review: Investigator factors

Country	Number of patients	Number with major adverse impact	Percent
W Europe C	39	0	0.0%
Oceania A	154	8	5.2%
N America A	101	6	5.9%
E Europe A	48	5	10.4%
S America A	54	6	11.1%
W Europe B	67	8	11.9%
W Europe E	25	3	12.0%
Oceania B	16	2	12.5%
W Europe A	127	17	13.4%
S America B	42	6	14.3%
E Europe B	28	4	14.3%
N America B	63	10	15.9%
W Europe D	30	5	16.7%
W Europe F	6	2	33.3%
W Europe G	4	2	50.0%
E Europe C	14	13	92.9%

Biological adaptive IMRT



Anatomic imaging

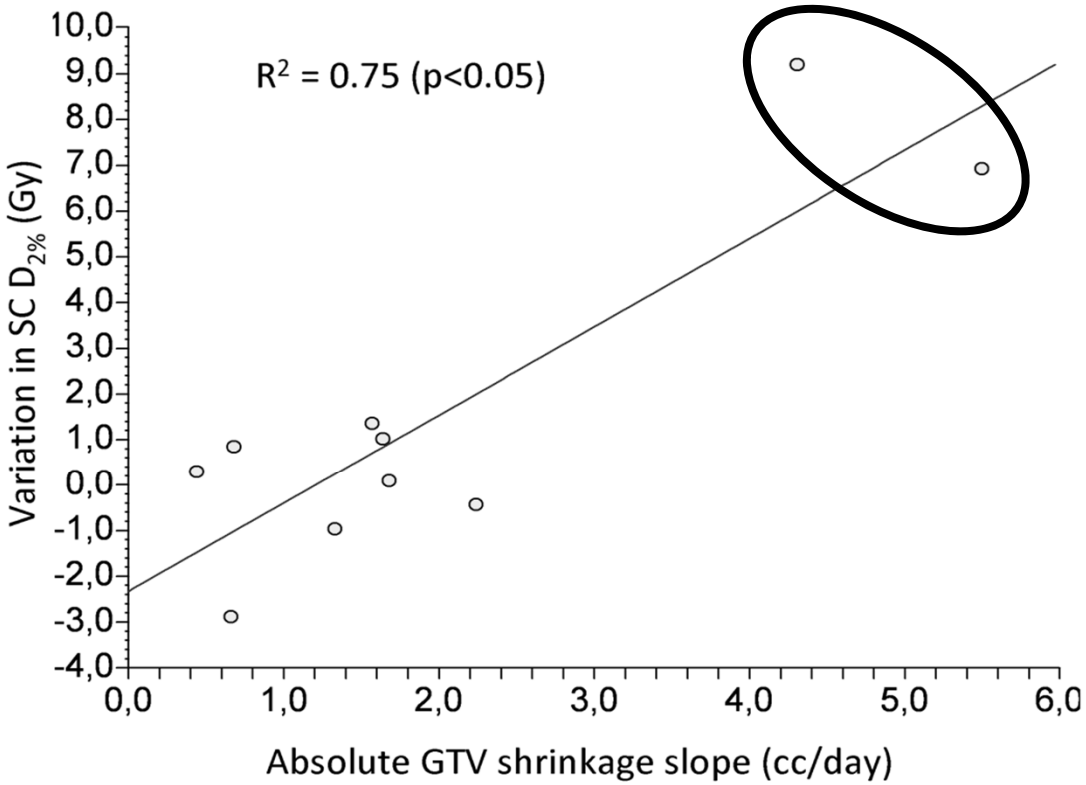
Dynamic FDG-PET

- 10 patients with stage III-IV pharyngo-laryngeal SCC treated by CT-RT
- Images acquired before R/ and during RT after means doses of 14, 25, 35 and 45 Gy

Geets, 2006

Adaptive Image-Guided IMRT in pharyngo-laryngeal squamous cell carcinoma

Adaptive approach and spinal cord irradiation



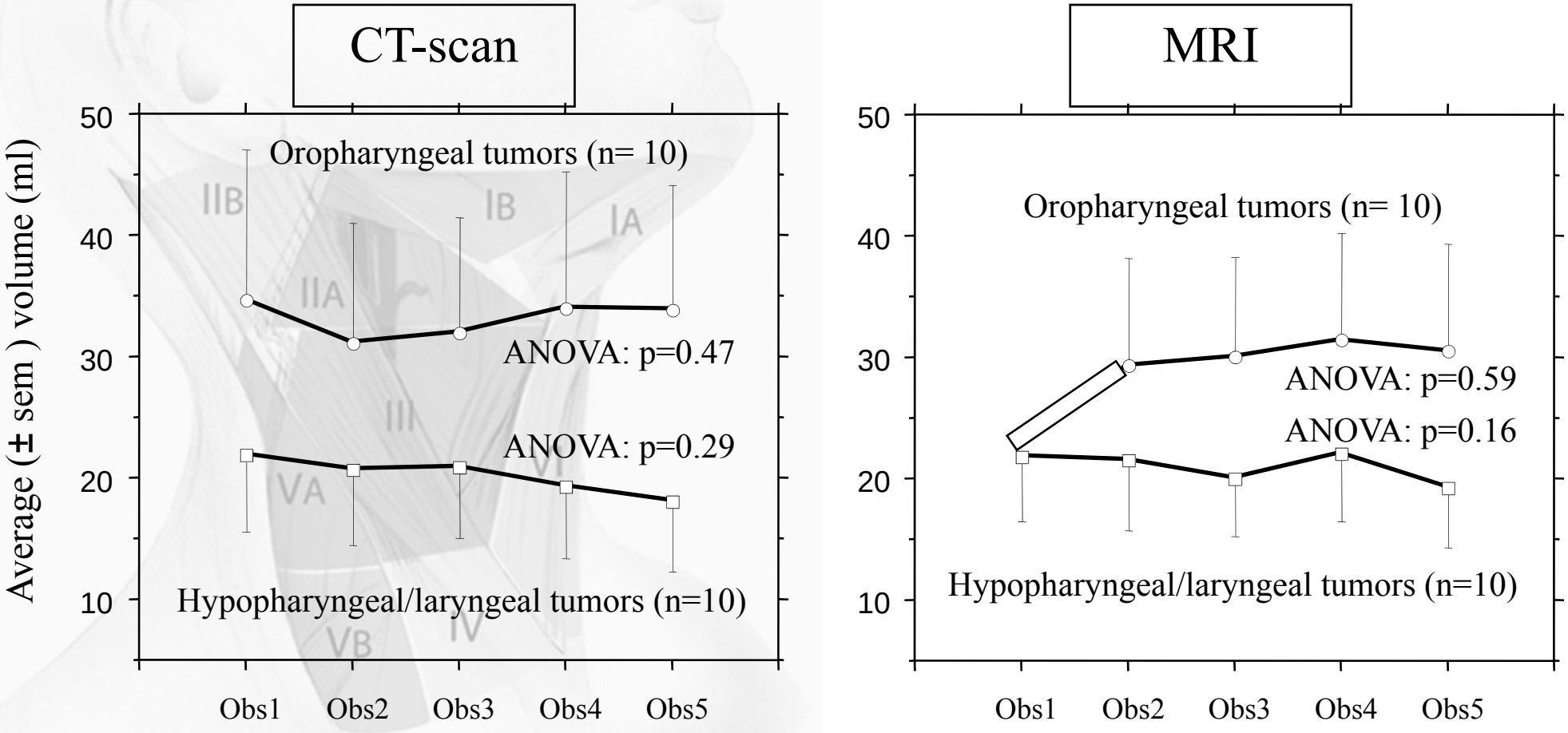
Adaptive Image-Guided IMRT in pharyngo-laryngeal squamous cell carcinoma

Conclusions 1

- Planned dose distribution ≠ delivered dose distribution
- Adaptive approach useful for selected patients
- GTV shrinkage as a good surrogate for plan adaptation

Inter-observer variability on target volume delineation with CT-scan and MRI

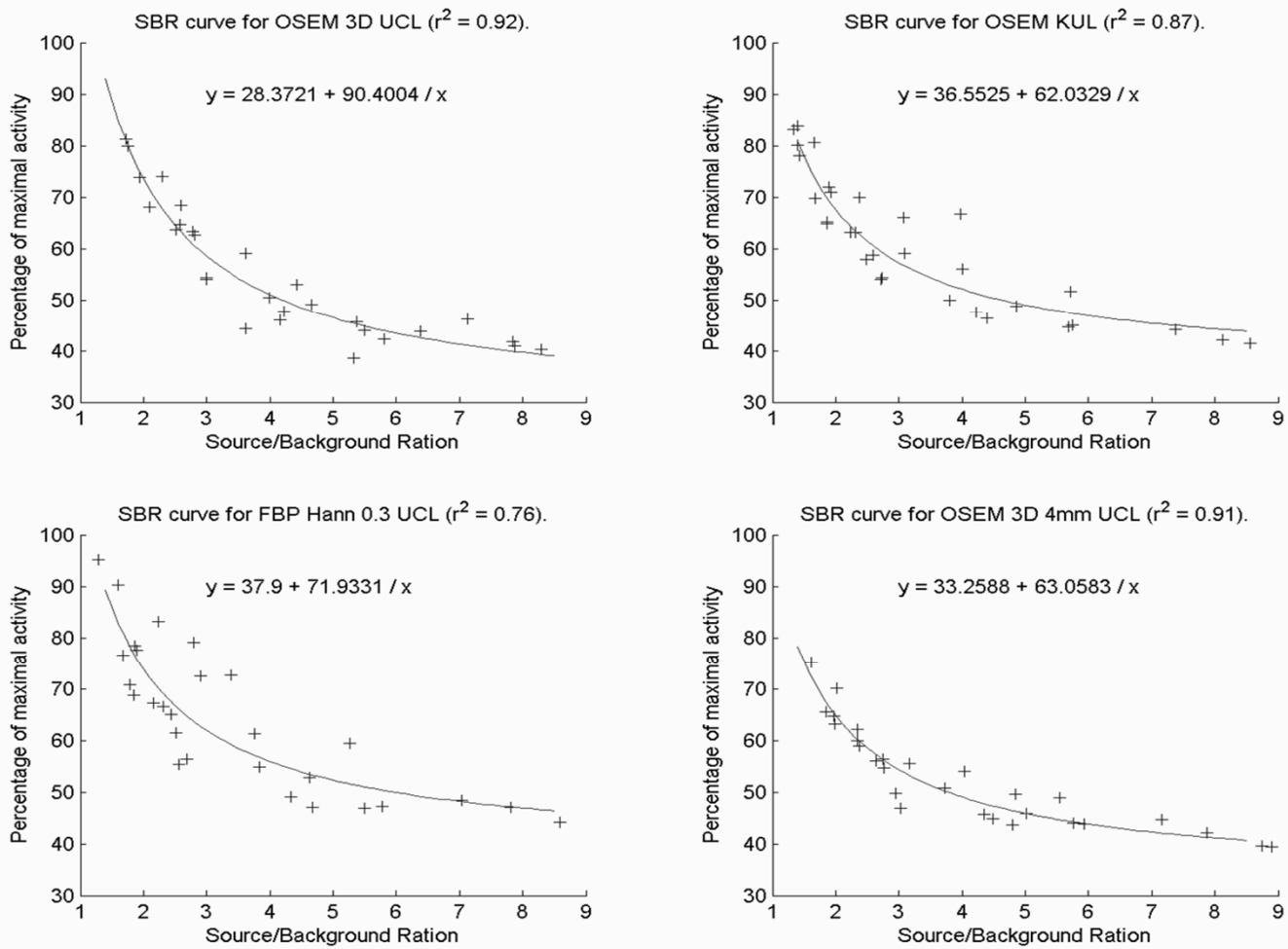
Gross Tumor volume (GTV)



Geets *et al*, 2005

Functional imaging and automatic segmentation

Volume delineation based on automatic thresholding with ^{18}F-FDG



Daisne *et al*, 200
Geets *et al*, 2004