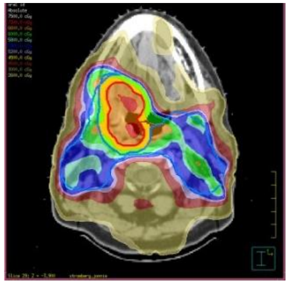
Adaptive radiotherapy: le variazioni degli organi a rischio e dell’anatomia del paziente

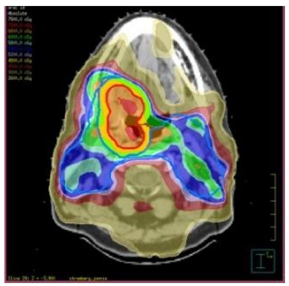
F. Ricchetti (Negrar, VR)

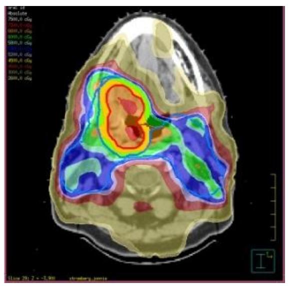
Adaptive RT for HN SCC



day 1

Adaptive RT for HN SCC





day 1

day 2


<polhamus^richard^^^>>
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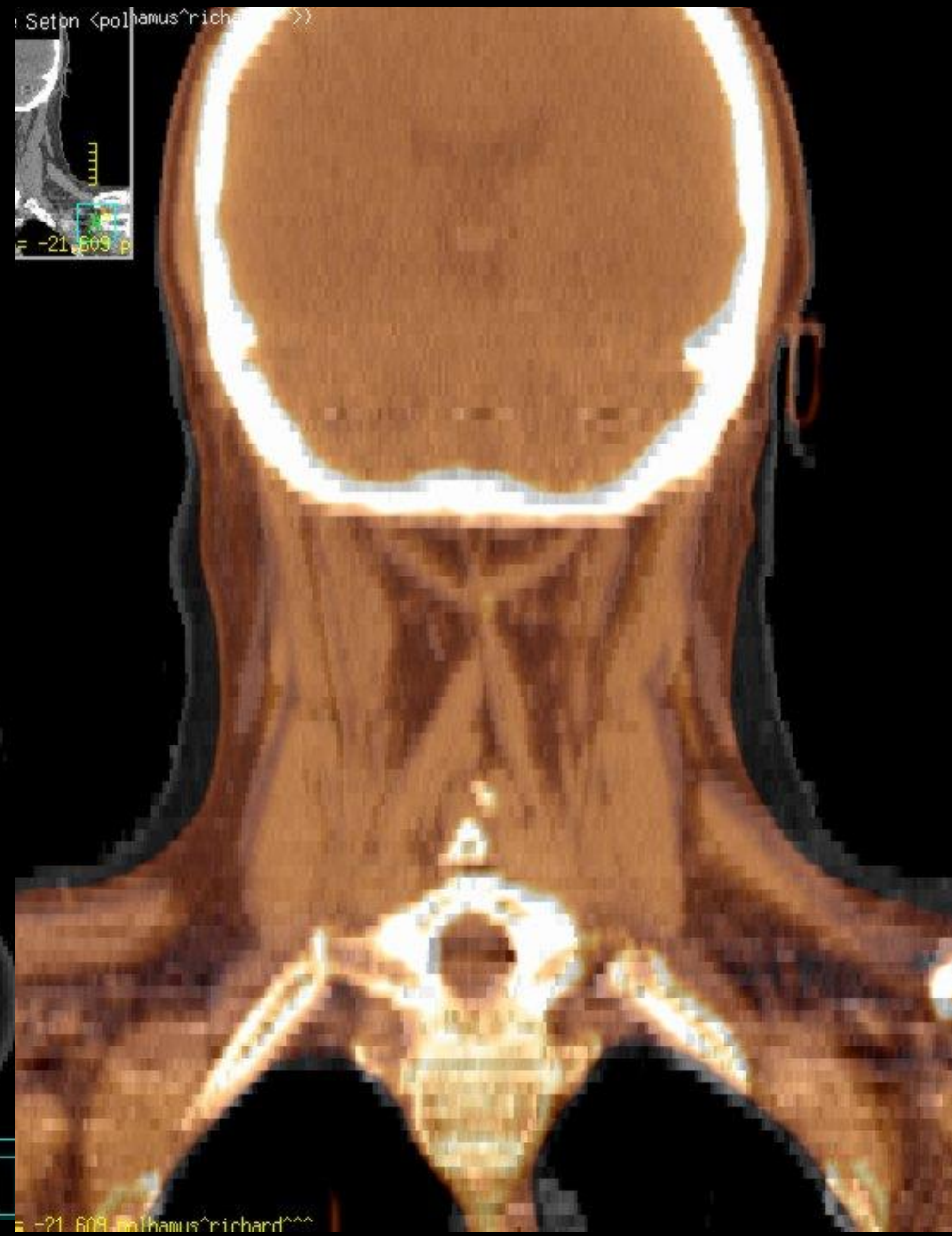
Seton <polhamus^rich
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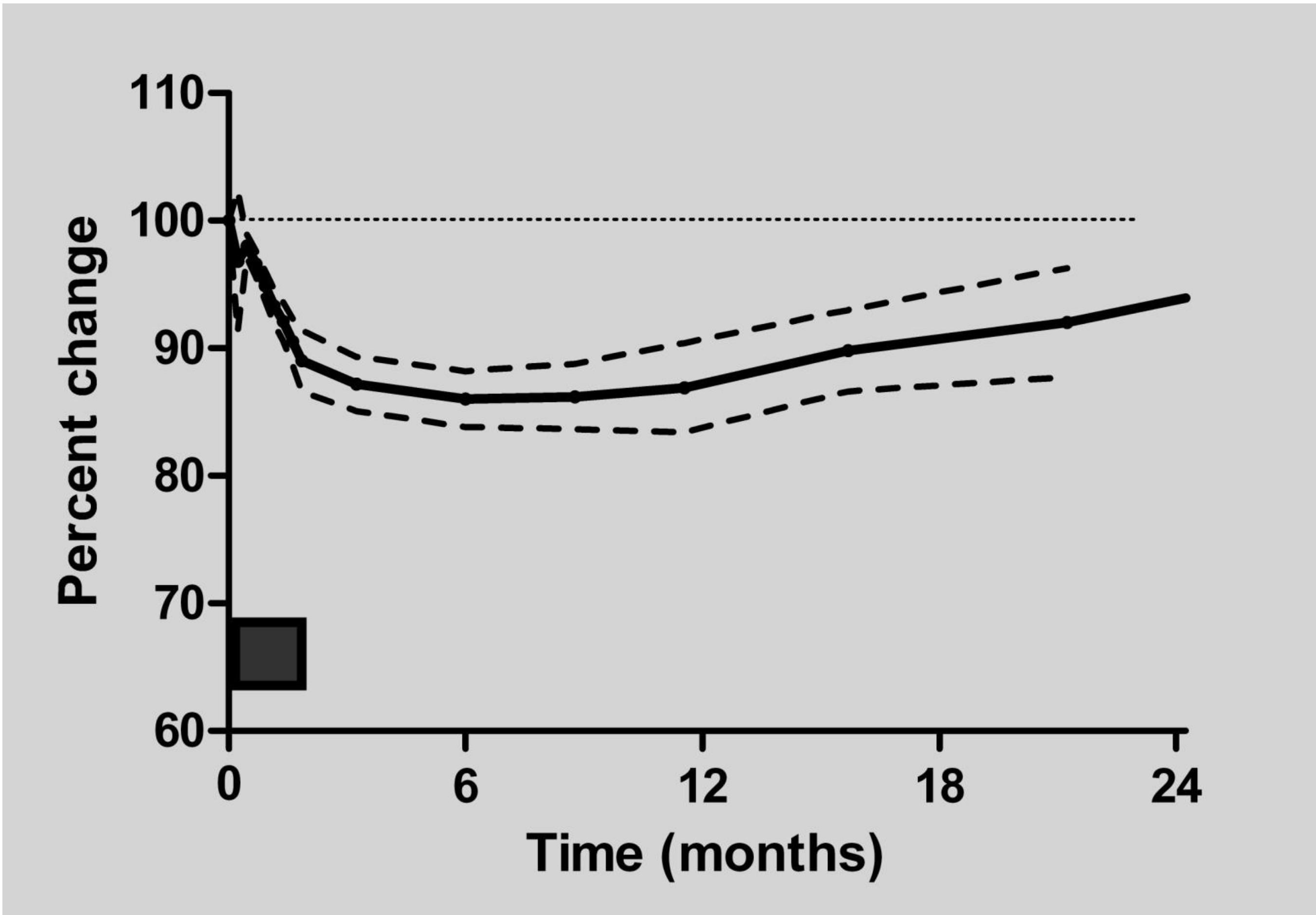
-21.609 polhamus^richard^^^

- Despite adequate nutritional status at baseline and nutritional supplement, during combined chemoradiotherapy for Stages III and IV H&N cancer, all patients started to lose weight within 1 week of treatment start and continued up to 1 month after treatment completion.

- Over this time, patients lost an average of 5.6 kg in lean mass, or 10% of lean mass at baseline

Silver et al. Head Neck 2007

Average (SD) weight loss in 162 pts with oropharyngeal SCC treated with IMRT + chemotherapy (UTMB-JHU)



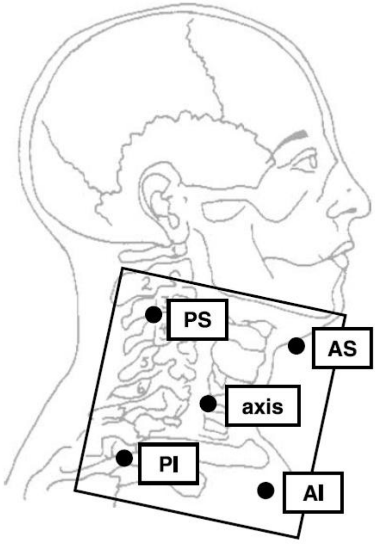
Sanguineti, unpublished data

Changes in lateral dimensions of irradiated volume and their impact on the accuracy of dose delivery during radiotherapy for head and neck cancer☆

Elżbieta Senkus-Konefka*, Edmund Naczk, Ilona Borowska, Andrzej Badzio, Jacek Jassem

Table 1
Degree of lateral dimension change between baseline and week 6 for various measurement points

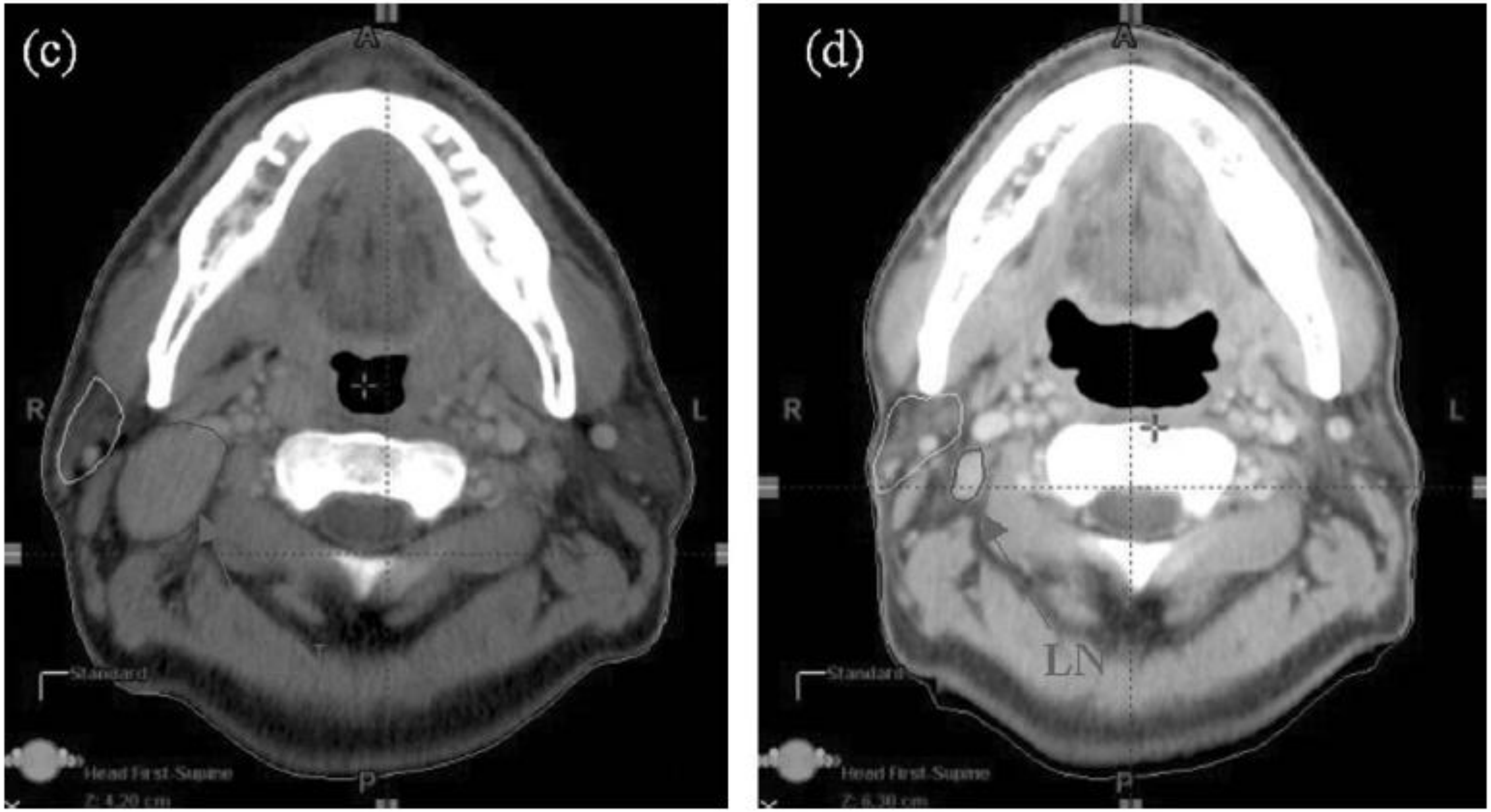
Measurement point	Lateral dimensions (mm)			
	Maximum decrease	Maximum increase	Mean change	Standard deviation
Beam axis	17.5	6.6	−5.8	5.7
Antero-superior	36.4	10.8	−3.9	8.8
Postero-superior	30.7	12.2	−6.2	9.2
Antero-inferior	25.0	13.5	−6.5	8.3
Postero-inferior	20.0	11.5	−3.7	6.7



Lateral dimension changes > 5 mm (range -37 to +16) in 32 patients (97%). Axis doses calculated for changed dimensions varied from those prescribed by -2.5 to +6% (median +2%). Differences larger than 5% were present in 4.8% of calculations.

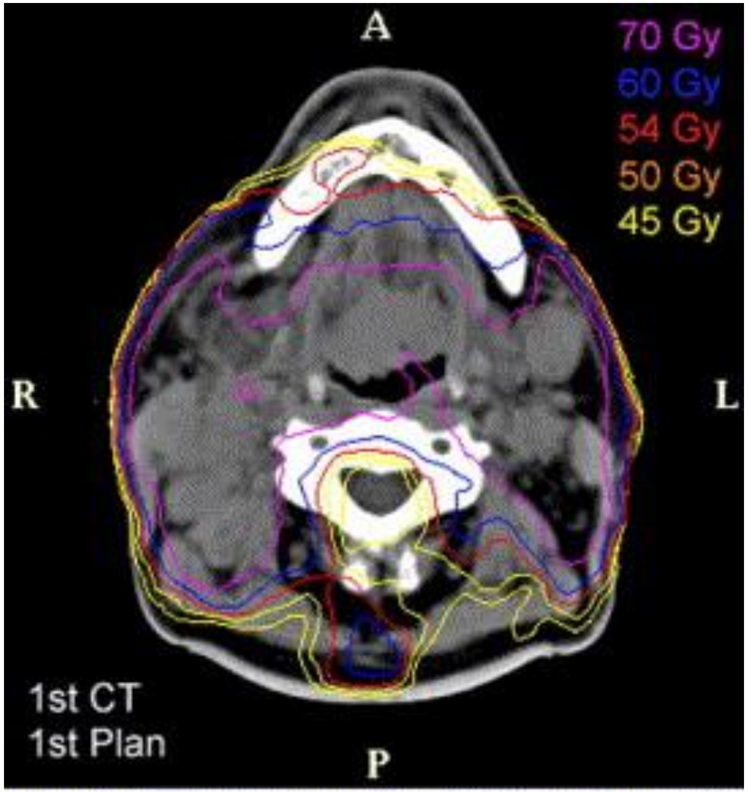
Radiotherapy and Oncology 79 (2006) 304-309

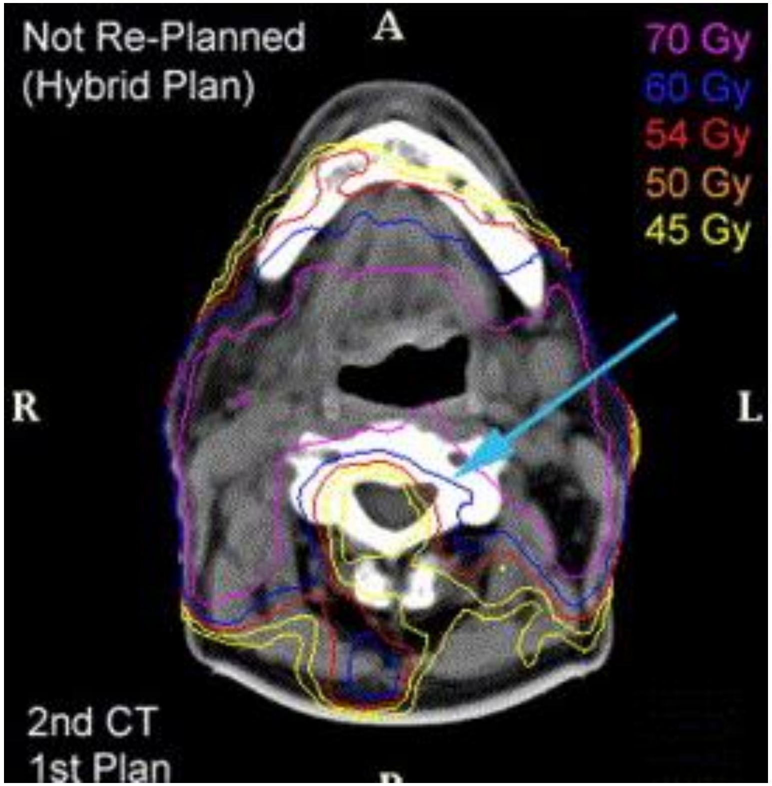
Parotid position vs nodal regression



Kuo et al, Am J Clin Oncol, 2006

Local loss of tissue can alter the dose to OAR (ie spinal cord)





Hansen, IJROBP 2006

Adaptive RT for HN SCC

♦ Multiple studies have shown that the dose distribution MAY change as well…

Adaptive Radiotherapy of Head and Neck Cancer

Pierre Castadot, MD, John A. Lee, Eng, PhD, Xavier Geets, MD, PhD, and Vincent Grégoire, MD, PhD, FRCR

Semin Radiat Oncol 20:84-93 © 2010

Adaptive RT in head and neck cancer

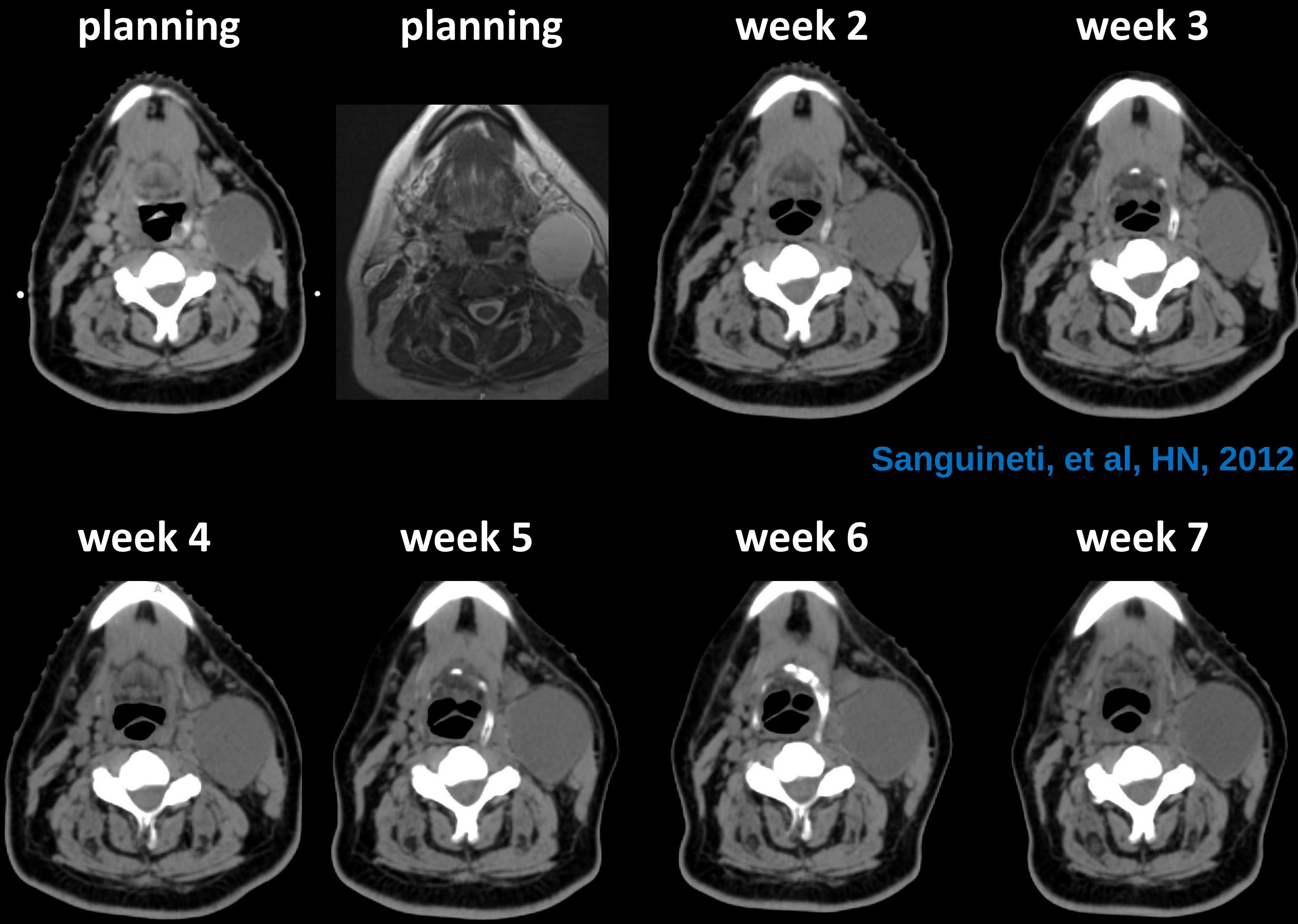
Adaptive functional image-guided IMRT in pharyngo-laryngeal squamous cell carcinoma: Is the gain in dose distribution worth the effort?

Pierre Castadot, Xavier Geets, John Aldo Lee, Vincent Grégoire *

Radiotherapy and Oncology 101 (2011) 343–350

From a TUMOR perspective

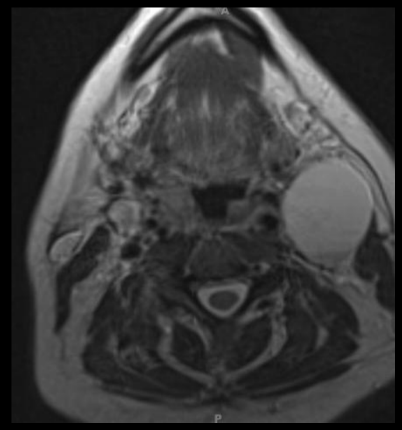
- ♦ Usually underdosage is minimal;
- ♦ Even potentially dangerous to modify original target contours:
  - ♦ poor visualization of the tumor
  - ♦ most of the times regression is NOT concentric
- ♦ Only exception is when anatomic barriers limit tumor diffusion



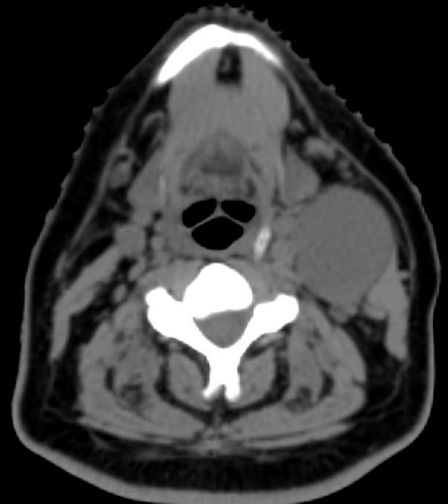
Sanguineti, et al, HN, 2012

planning

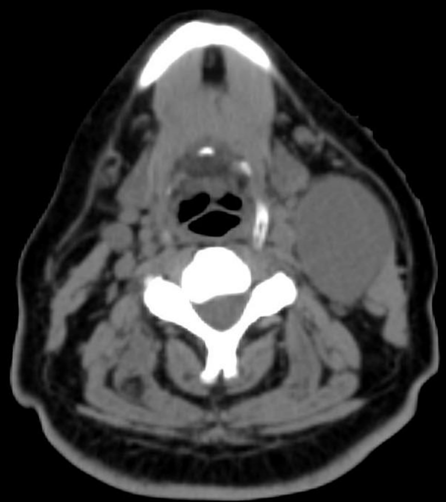
planning



week 2

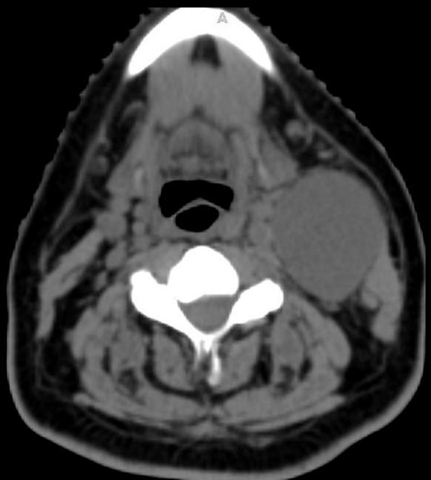


week 3



from ≈60 cc to ≈90cc, +50%

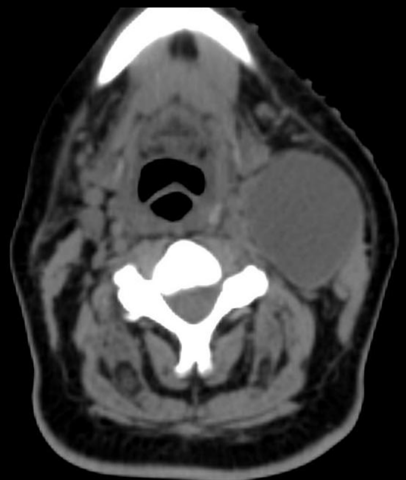
week 4



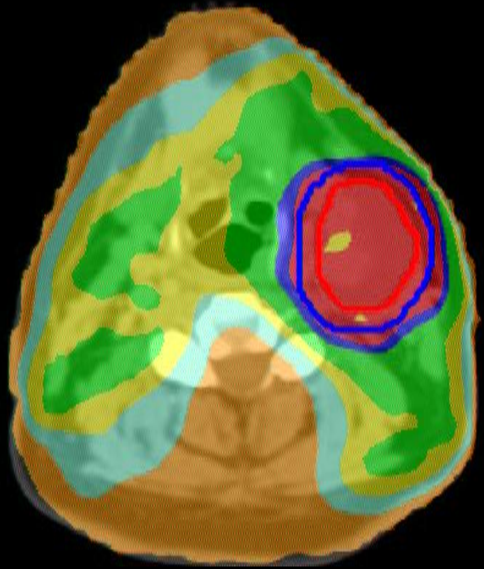
week 5

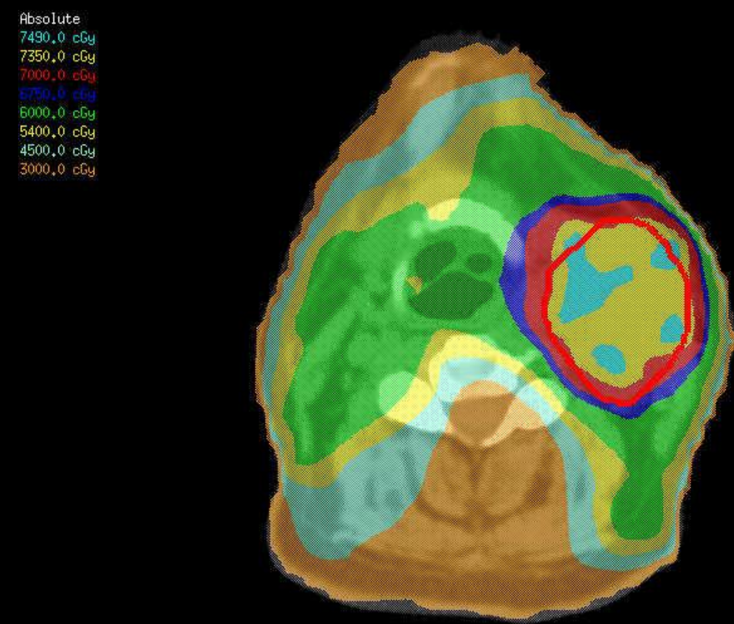
week 6

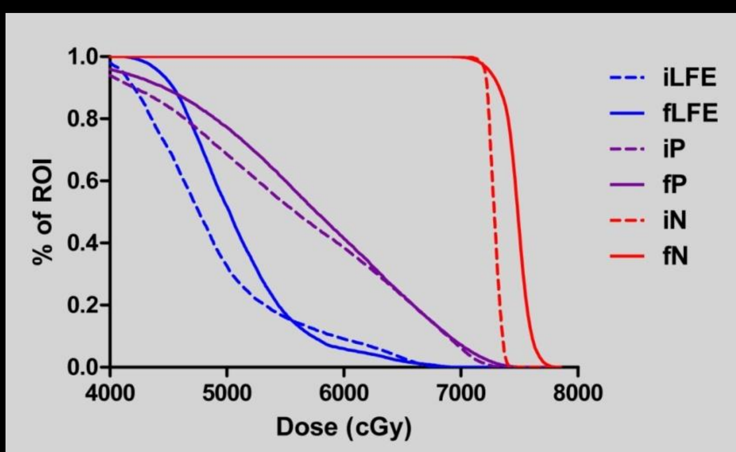
week 7

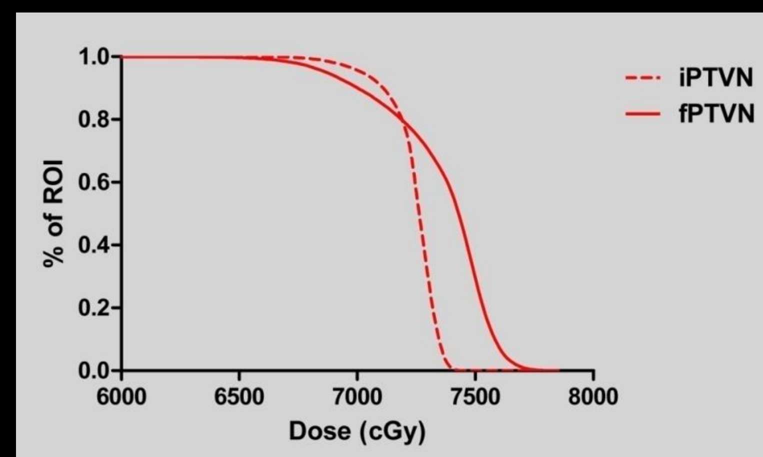


planning **week 5**







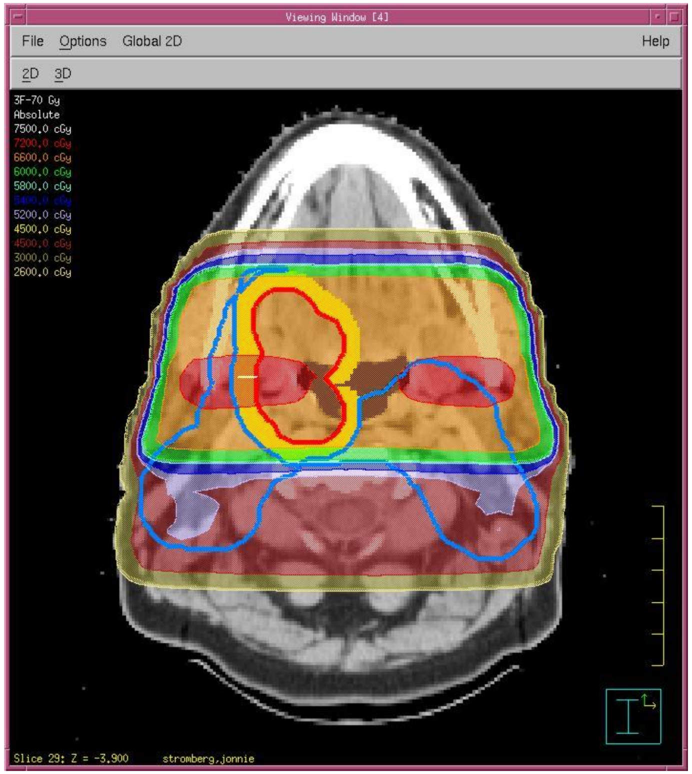


From a NORMAL STRUCTURE perspective

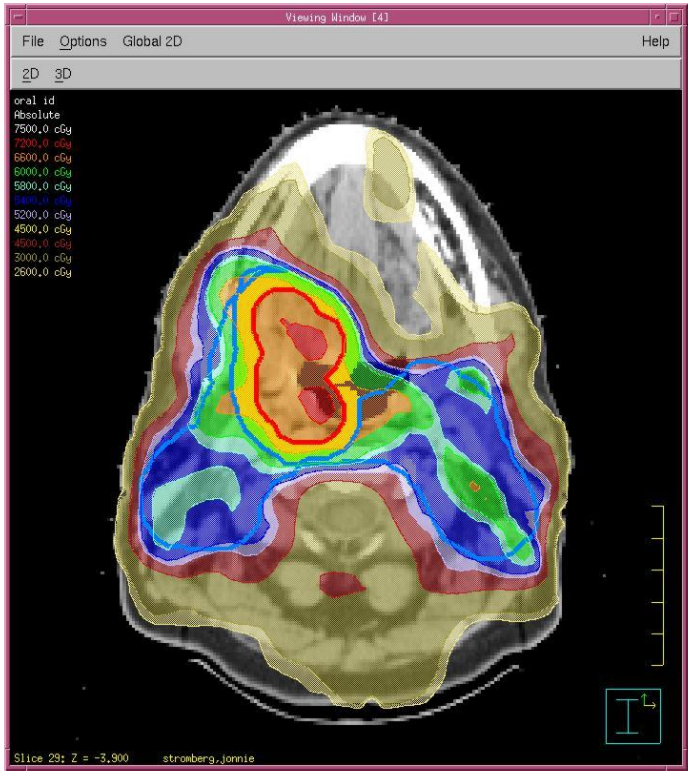
♦ Several studies show volumetric and spatial modifications of selected OAR that can predispose to a higher than planned delivered dose

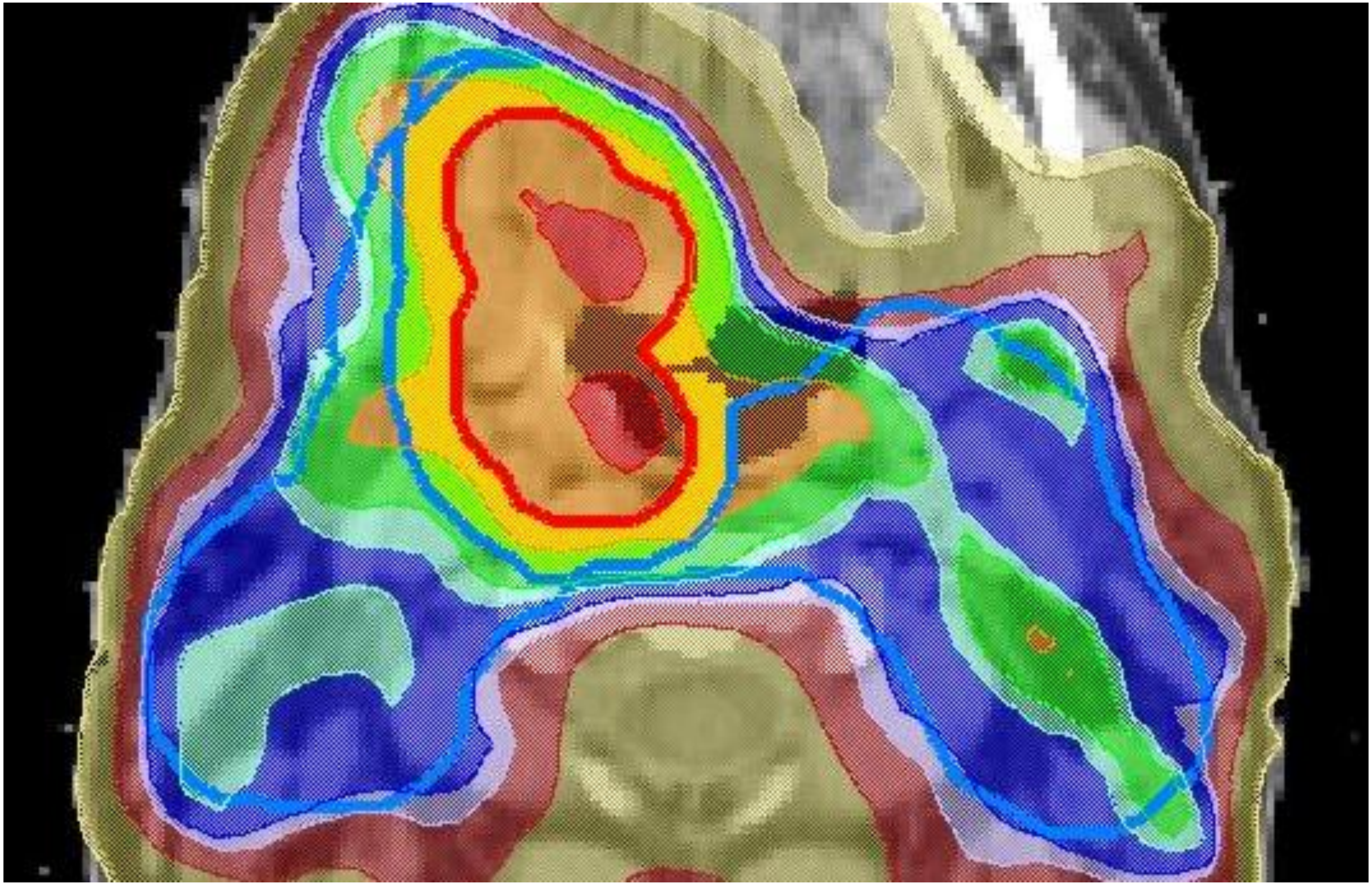
♦ Also tumor shrinkage can modify dose received by an OAR

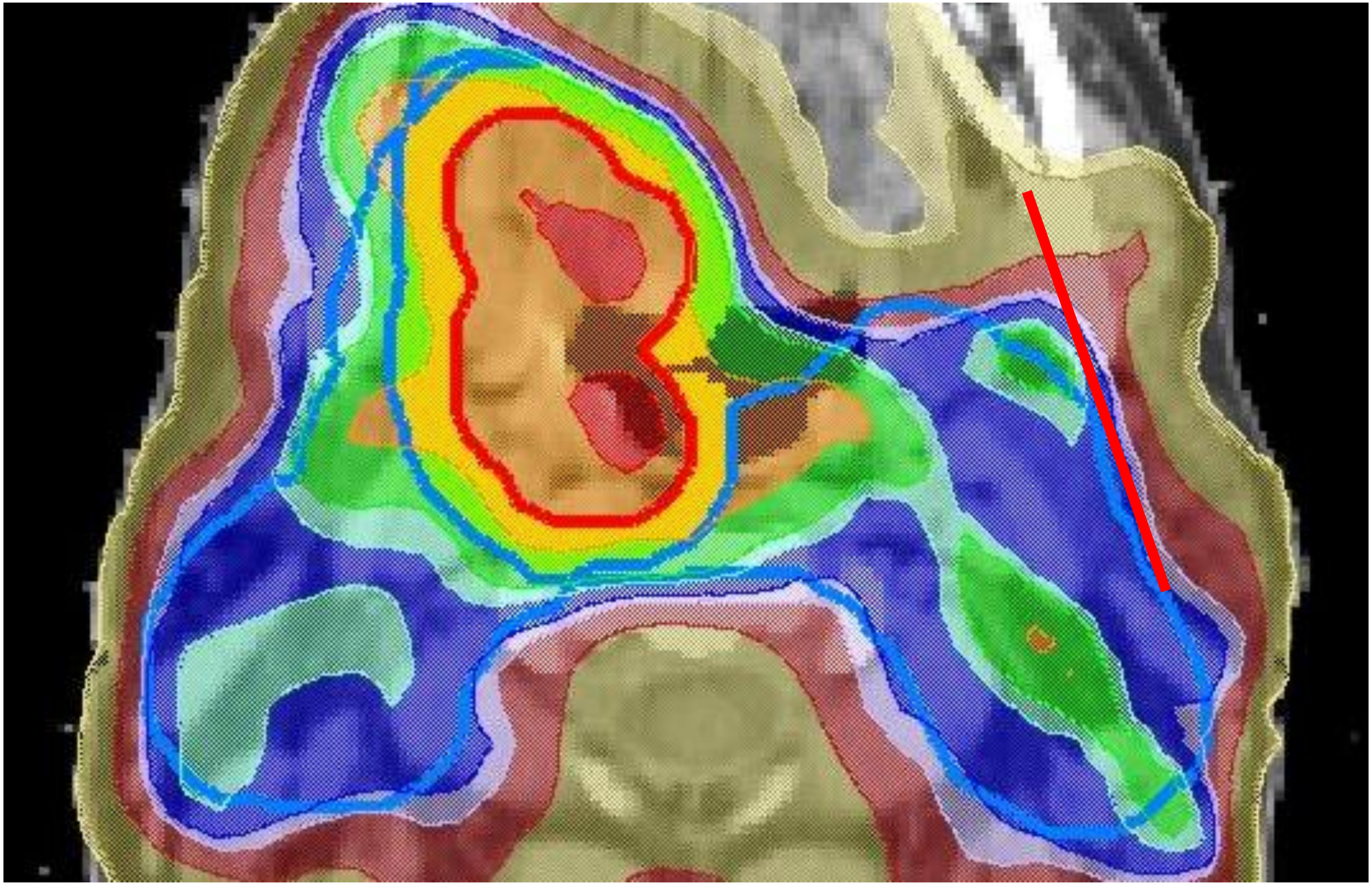
Parallel opposed



IMRT







…from a theoretical standpoint it seems reasonable to try to keep the dose gradient conformal to the target/OAR during the whole treatment

Adaptive RT for HN SCC

- ♦ <u>Which</u> organs at risk to follow during tmt?
- ♦ Is it possible to predict <u>which</u> patients?
- ♦ <u>When</u> to adapt during tmt?

Adaptive RT for HN SCC

- Which organs at risk to follow during tmt?
- Is it possible to predict which patients?
- When to adapt during tmt?

VOLUMETRIC CHANGE OF SELECTED ORGANS AT RISK DURING IMRT FOR OROPHARYNGEAL CANCER

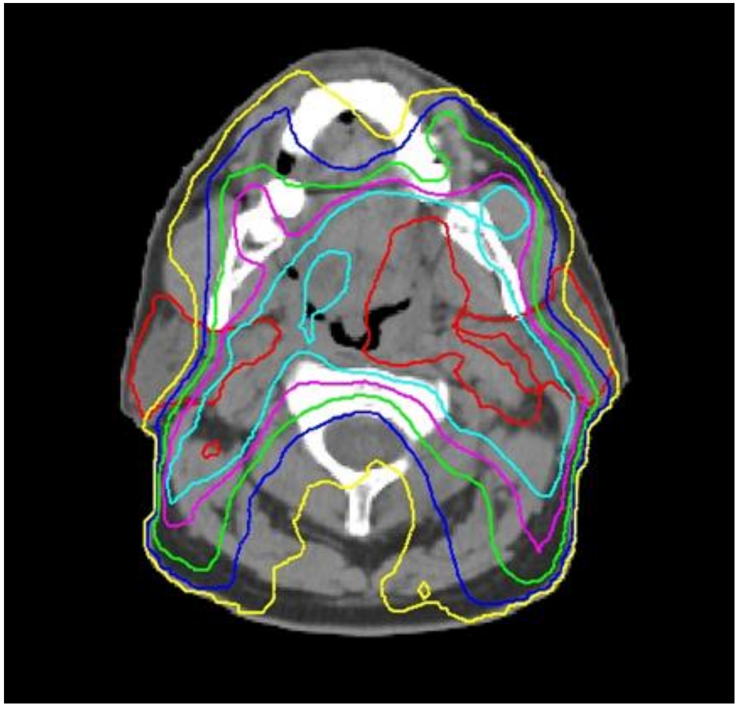
FRANCESCO RICCHETTI, M.D.,* BINBIN WU, PH.D.,* TODD MCNUTT, PH.D.,* JOHN WONG, PH.D.,* ARLENE FORASTIERE, M.D.,† SHANTHI MARUR, M.D.,† HEATHER STARMER, M.A., CCC-SLP,‡ AND GIUSEPPE SANGUINETI, M.D.*

- ♣ 26 pts w orophar SCC, definitive IMRT±chemo
- ♣ weekly KVCT
- ♣ single observer, contour propagation tool
- ♣ **Volumetric changes** w respect to baseline (plCT)
- ♣ Non parametric comparison and adjustment for multiple testing

- Contoured structures had to be clinically grossly uninvolved by the tumor and clearly identifiable on the initial planning CT

- Selected OAR were not available if they had been surgically removed or infiltrated by the tumor to the point that the structure was no longer clearly identifiable as a separate structure on the pl-CT

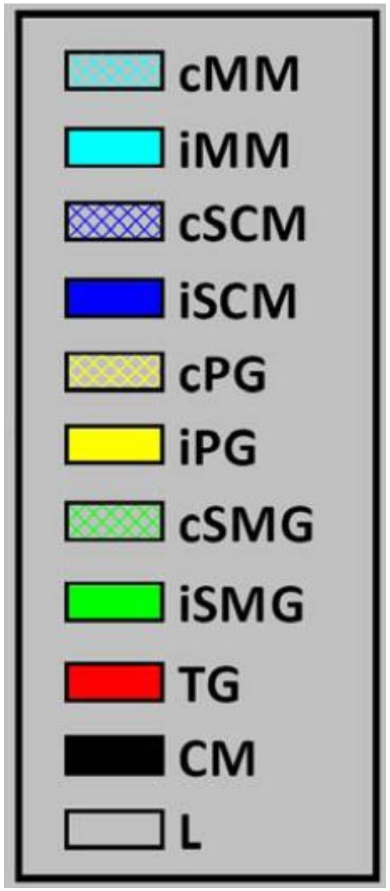
- Three-level dose painting IMRT: 70 Gy to macroscopic disease; 63 Gy to microscopic high-risk disease; 58.1 Gy to microscopic low-risk disease (35 fractions, 7 weeks.)



- CTV-PTV expansion: 5 mm

- Intra-observer variability was assessed for its impact on observed differences over time. The same observer recontoured the repeated structures at least 2 months after the first pass using the same procedure and was blinded to the previous result.

- The measurement error (ME) was computed as the difference between the two measured volumes of the same OAR at the two readings.

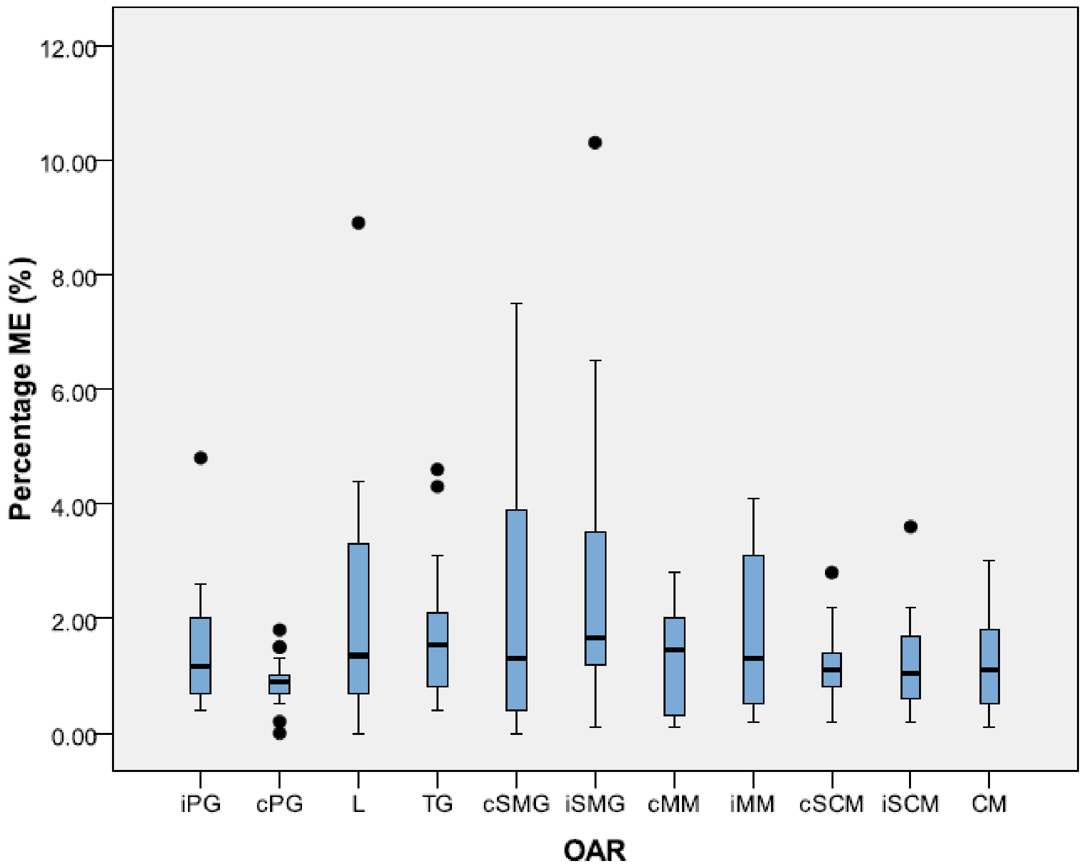


cMM: contralateral masticatory muscles
iMM: ipsilateral masticatory muscles
cSCM: contralateral sternocleidomastoid m
iSCM: ipsilateral sternocleidomastoid m
cPG: contralateral parotid gland
iPG: ipsilateral parotid gland
cSMG: contralateral submandibular gland
iSMG: ipsilateral submandibular gland
TG: thyroid gland
CM: constrictor muscles
L: larynx (for edema)

Ricchetti et al, IJROBP, 2011

Intraobserver variation

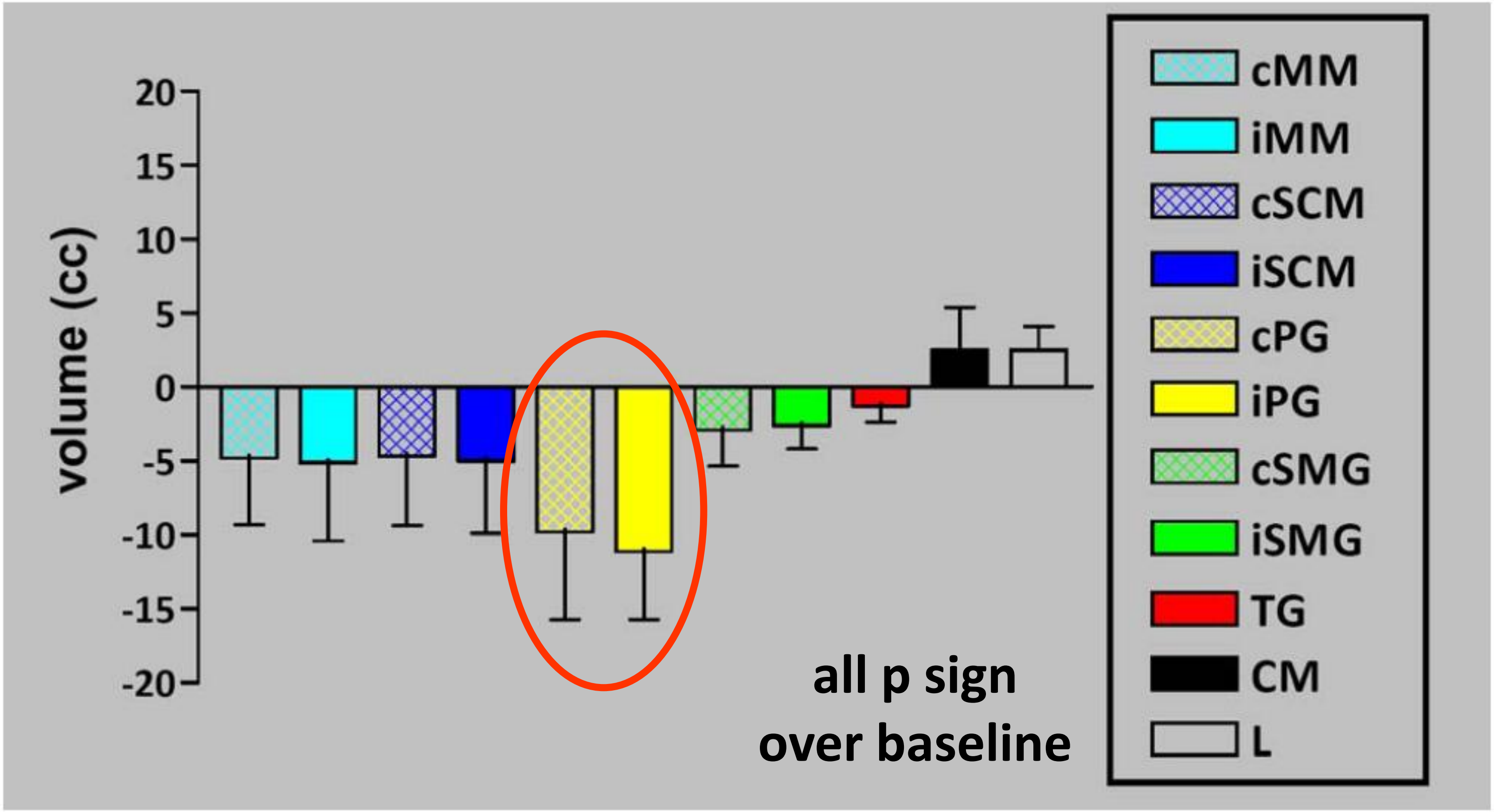
Contours were drawn by a single observer with the help of a propagation tool between subsequent high-quality KVCT



	%ME				
OAR	Mean	SD	Median	Minimum	Maximum
cMM	1.3%	0.9%	1.4%	0.1%	2.8%
iMM	1.8%	1.3%	1.3%	0.2%	4.1%
cSCM	1.1%	0.7%	1.1%	0.2%	2.8%
iSCM	1.2%	0.8%	1.0%	0.2%	3.6%
cPG	0.9%	0.4%	0.9%	0.0%	1.8%
iPG	1.5%	1.1%	1.1%	0.4%	4.8%
cSMG	2.2%	2.3%	1.3%	0.0%	7.5%
iSMG	2.8%	2.8%	1.6%	0.1%	10.3%
TG	1.8%	1.2%	1.5%	0.4%	4.6%
CM	1.4%	1.0%	1.2%	0.1%	3.4%
L	2.1%	2.2%	1.4%	0.0%	8.9%

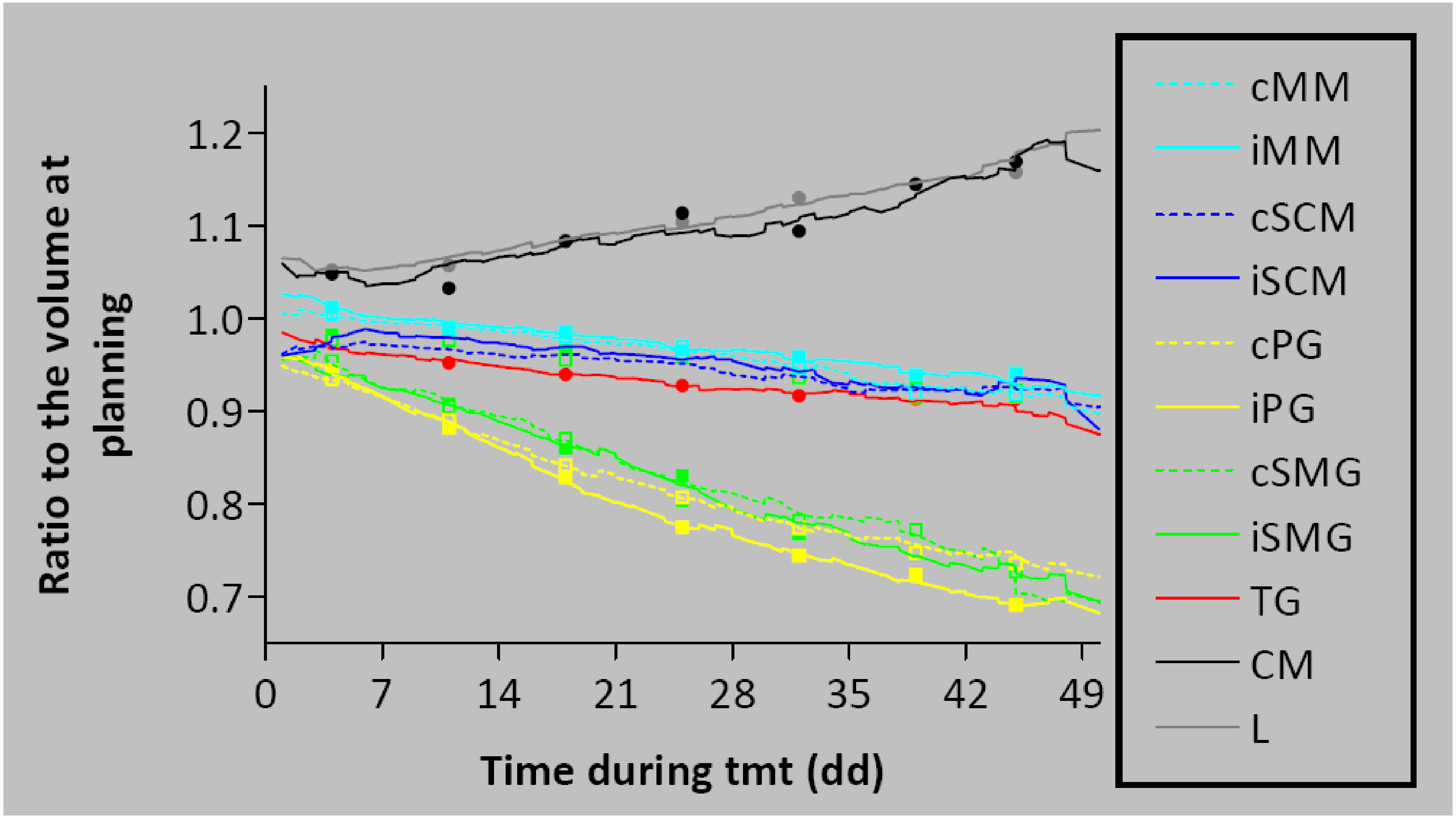
Ricchetti et al, IJROBP, 2011

Average abs volume change at week 7



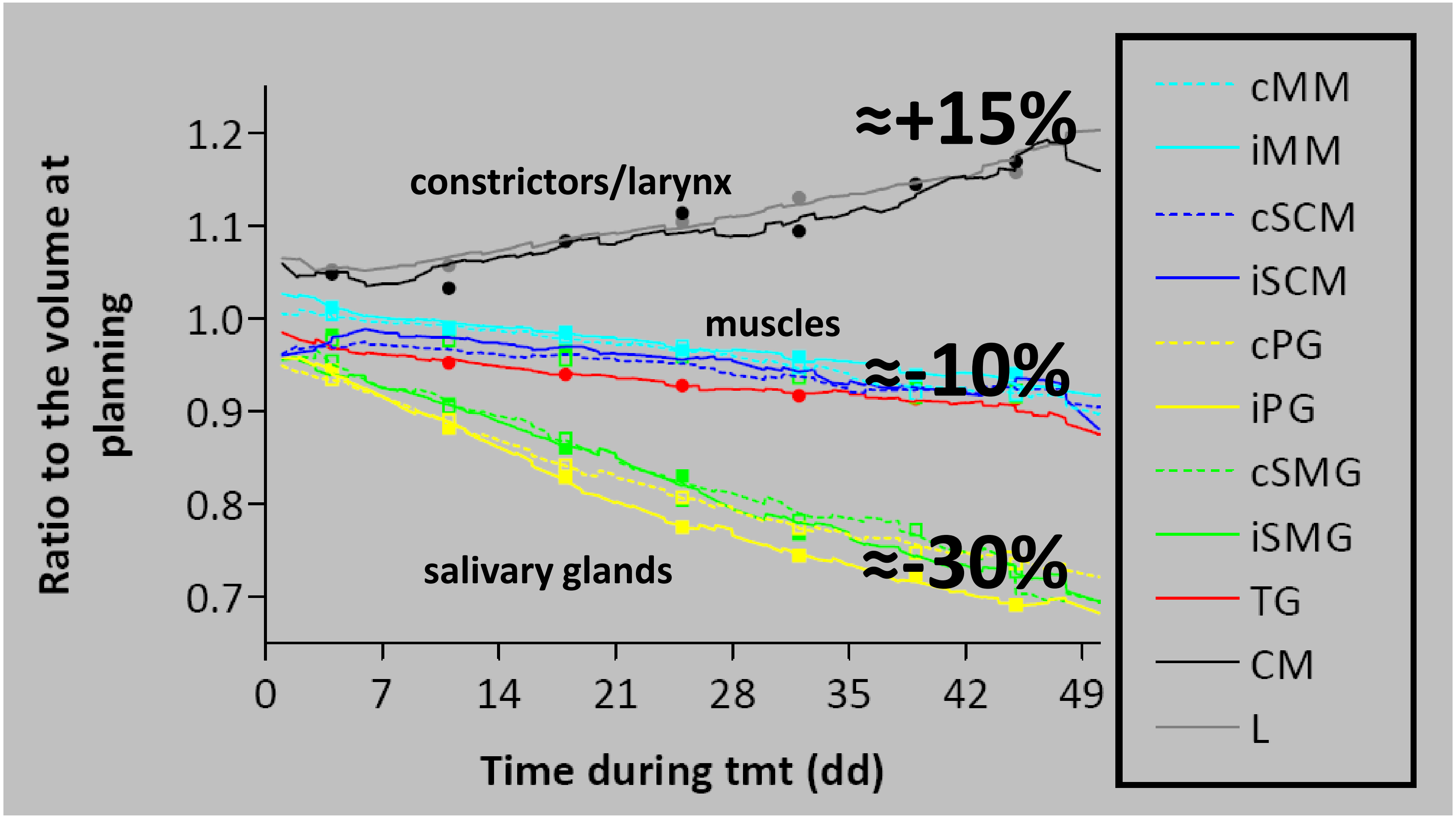
Ricchetti et al, IJROBP, 2011

Temporal average relative volume change



Ricchetti et al, IJROBP, 2011

Temporal average relative volume change



Ricchetti et al, IJROBP, 2011

OAR volume change

OAR can be pooled into three groups:

- Large (30%) reduction toward the end of treatment (PG and SMG)
- Smaller (5–10%) shrinkage (TG, MM, and SCM)
- Average 15–20% increase during treatment (L and CM)

Ricchetti et al, IJROBP, 2011

OAR volume change

- All structures showed statistically significant volumetric changes over baseline from the fifth week on.
- For the larynx, thyroid gland, both parotid glands, and the iSMG, a statistically significant difference was already apparent from the first week of treatment

Table 4. Mean (SD) absolute and relative change of each structure over baseline at weeks 1 and 7

	Week 1				Week 7			
		Mean (SD) volume change				Mean (SD) volume change		
OAR	No. patients	mL	%	a-p	No. patients	mL	%	a-p
cMM	16	0.2 (1.8)	0.5 (3.5)	0.776	22	–4.8 (4.5)	–8.2 (7.3)	<0.001
iMM	16	0.5 (1.3)	1.1 (2.9)	0.727	22	–3.6 (4.4)	–5.9 (7.3)	0.009
cSCM	16	–1.3 (2.0)	–2.3 (3.3)	0.054	22	–4.7 (4.7)	–7.8 (8.9)	0.004
iSCM	10	–1.3 (1.8)	–1.8 (4.5)	0.418	12	–5.0 (4.9)	–8.4 (10.3)	0.023
cPG	16	–2.2 (2.1)	–6.6 (5.3)	0.009	22	–9.8 (5.9)	–26.4 (11.9)	<0.001
iPG	14	–1.9 (1.6)	–5.6 (4.4)	0.019	19	–11.1 (4.6)	–31.9 (8.2)	<0.001
cSMG	16	–0.5 (0.6)	–4.6 (6.5)	0.107	22	–2.9 (2.4)	–27.3 (19.7)	<0.001
iSMG	15	–0.5 (0.5)	–4.6 (5.0)	0.026	20	–2.6 (1.6)	–26.9 (13.7)	<0.001
TG	16	–0.4 (0.4)	–3.3 (3.1)	0.036	22	–1.3 (1.1)	–8.7 (6.9)	<0.001
CM	15	0.7 (0.9)	4.8 (6.3)	0.066	21	2.5 (2.9)	16.9 (18.9)	<0.001
L	13	0.9 (0.8)	5.2 (5.2)	0.033	19	2.5 (1.6)	15.7 (9.8)	<0.001

Ricchetti et al, IJROBP, 2011

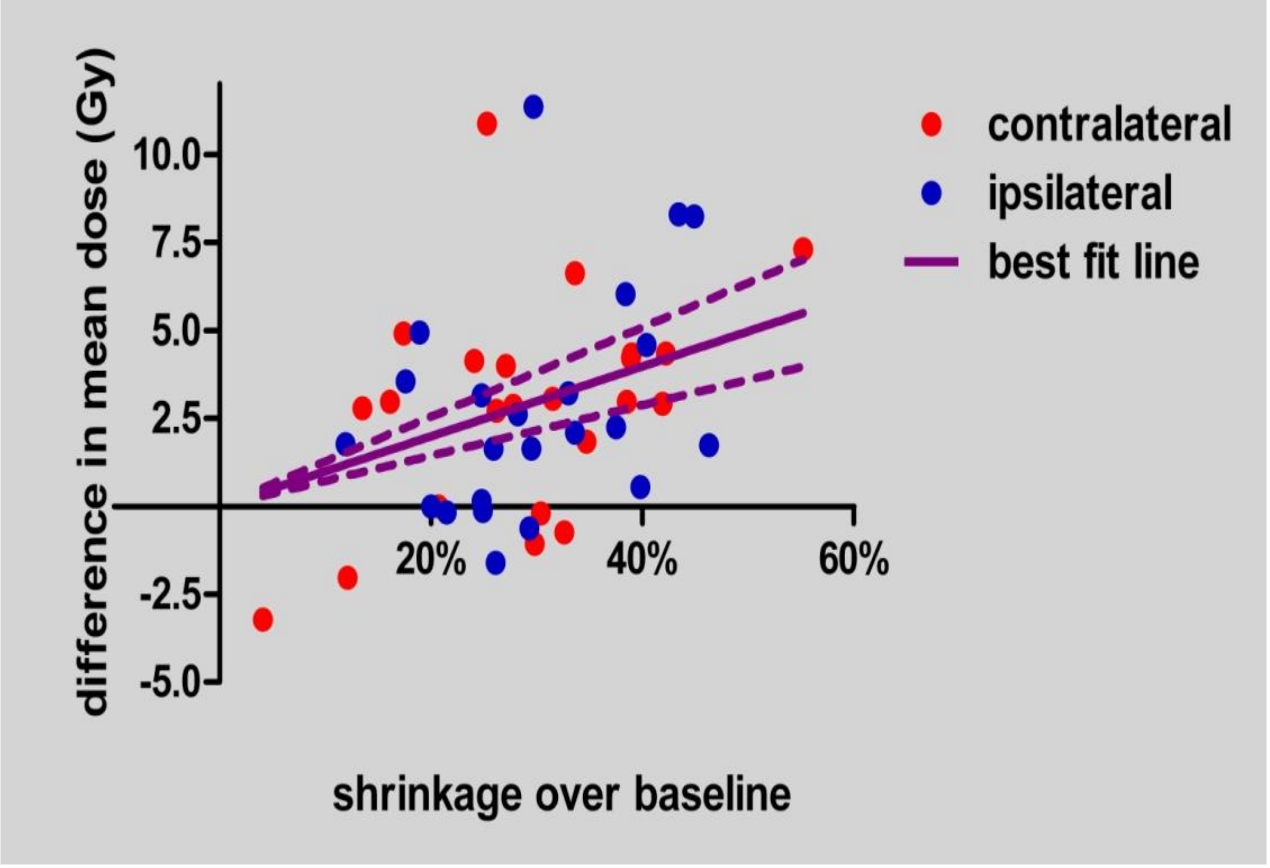
OAR volume change

- All observed changes in volume were progressive and irreversible.

- Once a statistically significant change over baseline was recorded for a given OAR, it was maintained or strengthened in the subsequent weeks.

Ricchetti et al, IJROBP, 2011

Average Change in Mean Dose by Percent Shrinkage of Parotids (JHU pts)



23 pairs of parotids, mean D at planning vs last week of tmt

The parotids undergo the largest absolute and relative shrinkage during IMRT (30%)

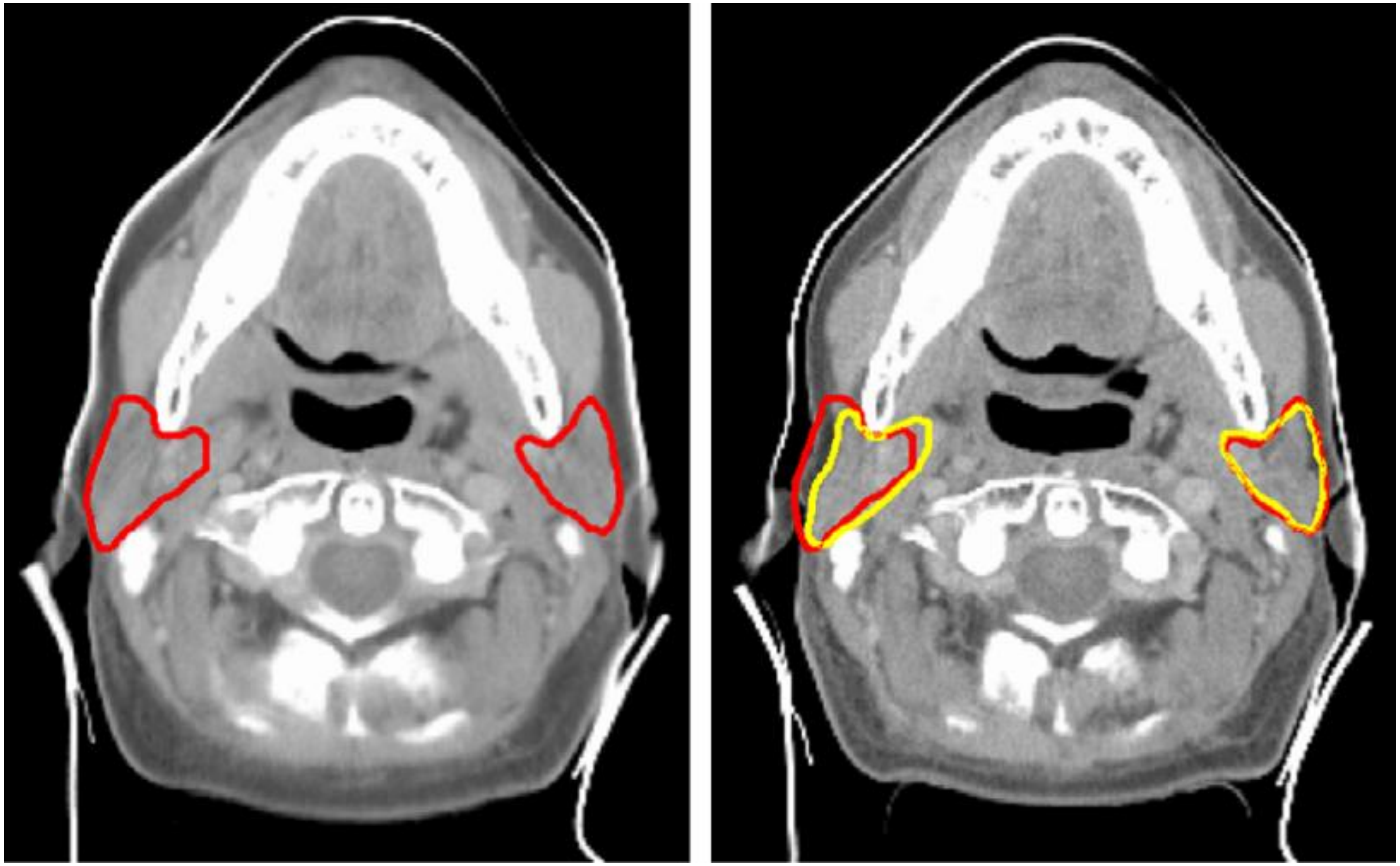
They are adjacent to a dose gradient because you are trying to spare them

The parotids represent the OAR that should be monitored during treatment because their anatomical changes are associated with an increase in received dose

Adaptive RT for HN SCC

- Which organs at risk to follow during tmt?
- Is it possible to predict which patients?
- When to adapt during tmt?

Parotid shrinkage vs dose



Unilateral tmt

Vasquez Osorio et al, IJROBP, 2008

Relative parotid shrinkage vs dose

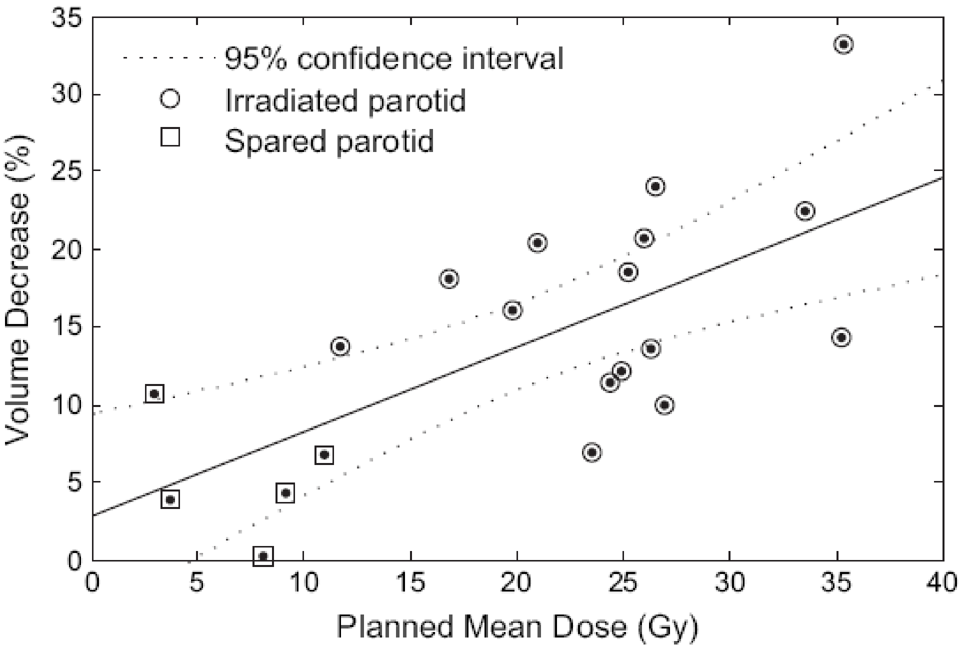
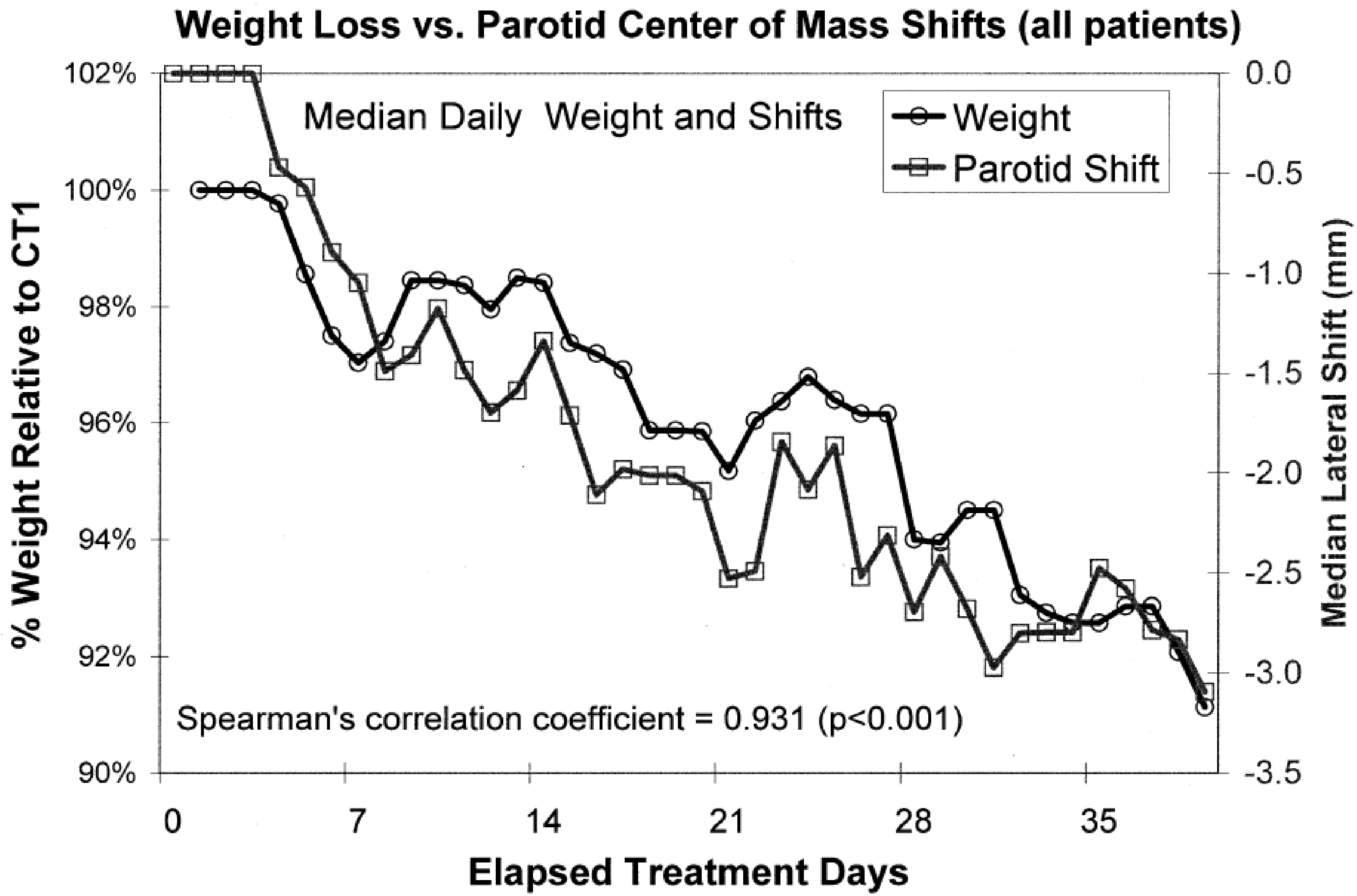


Fig. 6. Volume changes vs. planned mean dose for parotid glands. Solid line indicates linear regression ($p < 0.001$, $r = 0.68$).

Vasquez Osorio et al, IJROBP, 2008



Barker et al, IJROBP, 2004

A two-variable linear model of parotid shrinkage during IMRT for head and neck cancer

Sara Broggi [a,*], Claudio Fiorino [a], Italo Dell'Oca [b], Nicola Dinapoli [c], Marta Paiusco [d], Alessandro Muraglia [e], Eleonora Maggiulli [a,f], Francesco Ricchetti [g], Vincenzo Valentini [c], Giuseppe Sanguineti [g], Giovanni Mauro Cattaneo [a], Nadia Di Muzio [b], Riccardo Calandrino [a]

Radiotherapy and Oncology 94 (2010) 206–212

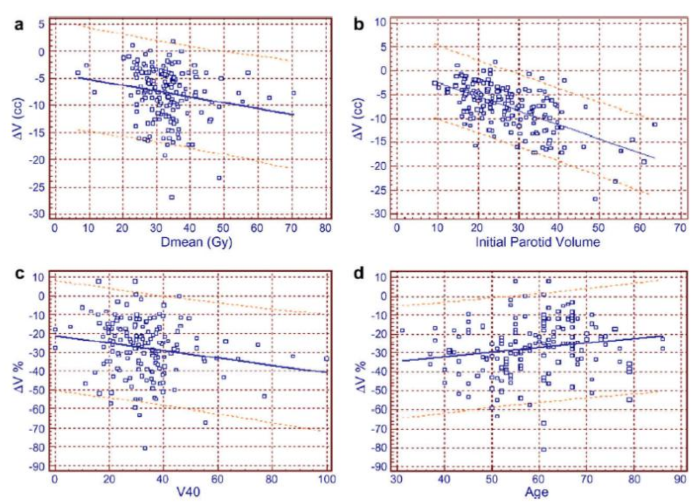
Data of 174 parotid glands of 87 patients from four institutions (IRCCS San Raffaele, Milan (HSR); University Cattolica S. Cuore, Roma (UCSC); Arcispedale S. Maria Nuova, Reggio Emilia (RE); John Hopkins University, Baltimore (JHU)) were pooled.

absolute change

Initial parotid volume (IVP)	OR = 1.100, 95% CI: 1.056–1.158, *p*-value = 0.0002
Parotid mean dose (*D*mean)	OR = 1.059, 95% CI: 1.003–1.118, *p*-value = 0.038

relative change

MVA analysis (p-value = 0.0030)	
Age	OR = 0.968, 95% CI: 0.939–0.999, *p*-value = 0.041
*V*40	OR = 1.0338, 95% CI: 1.007–1.061, *p*-value = 0.013



Predictors of parotid shrinkage

(85 pts)

Table 5. Logistic regression including selected covariates considering the whole treatment and each separate half.

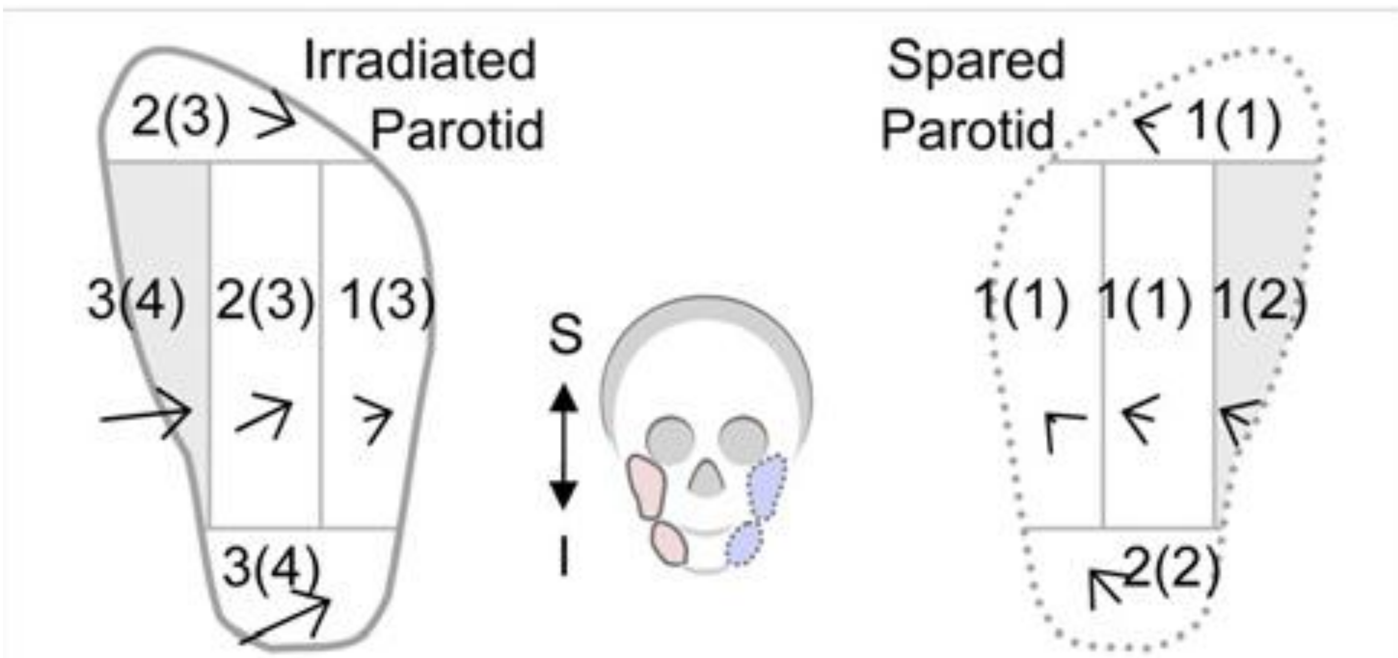
		Covariate		
		Weight loss (%)	Cumulative mean D (Gy)	Age (yrs)
Whole tmt	OR	1.19	1.01	0.95
	95% CI	1.09-1.31	0.97-1.05	0.92-0.99
	p value	**<0.001**	0.699	**0.011**
First half	OR	1.16	1.08	0.96
	95% CI	1.04-1.29	1.01-1.17	0.93-0.99
	p value	**0.007**	**0.038**	**0.033**
Second half	OR	1.36	1.02	0.94
	95% CI	1.18-1.58	0.94-1.10	0.90-0.98
	p value	**<0.001**	0.632	**0.005**

Sanguineti, unpublished data

LOCAL ANATOMIC CHANGES IN PAROTID AND SUBMANDIBULAR GLANDS DURING RADIOTHERAPY FOR OROPHARYNX CANCER AND CORRELATION WITH DOSE, STUDIED IN DETAIL WITH NONRIGID REGISTRATION

Eliana M. Vásquez Osorio, B.Sc., Mischa S. Hoogeman, Ph.D., Abrahim Al-Mamgani, M.D., David N. Teguh, M.D., Peter C. Levendag, Ph.D., and Ben J. M. Heijmen, Ph.D.

Int. J. Radiation Oncology Biol. Phys., Vol. 70, No. 3, pp. 875–882, 2008



Average 3D deformation vectors (millimeters) in frontal view. Solid lines represent irradiated glands; dashed lines represent spared glands

Quantifying deformation during (and after) RT using elastic registration

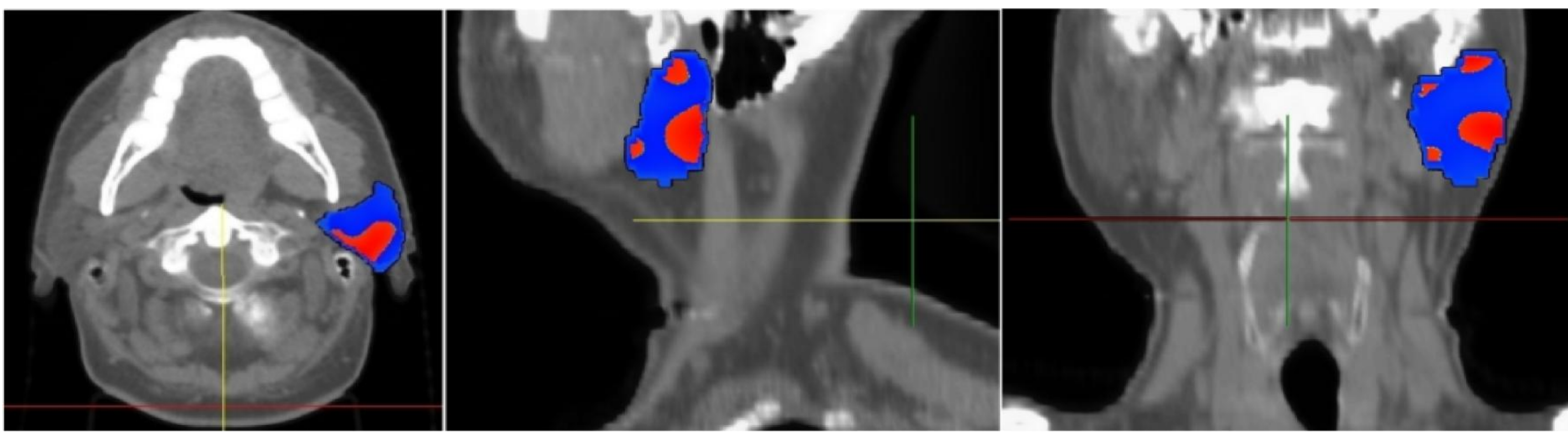
- The determinant of the transformation is the **jacobian** and represents the degree of expansion/compression of each voxel resulting from the elastic registration
- Jacobian (J) map restricted to organs to quantify local shape changes

J=1 no deformation
J<1 shrinkage (ex: 0.5=50% shrinkage)
J>1 expansion (ex: 2=100% expansion)

$$Jac(\Phi) = \det(\nabla x_B) = \det\left(\nabla\left(x_A + T(x_A)\right)\right) = \det\left(I + \nabla T(x_A)\right) =$$

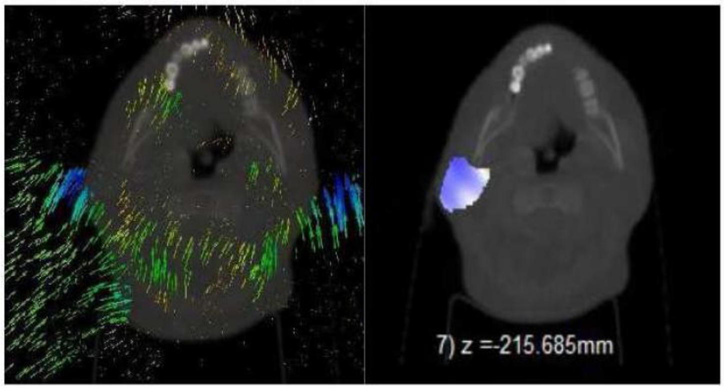
$$= \det\begin{bmatrix} 1+\frac{dT_x}{dx} & \frac{dT_x}{dy} & \frac{dT_x}{dz} \\ \frac{dT_y}{dx} & 1+\frac{dT_y}{dy} & \frac{dT_y}{dz} \\ \frac{dT_z}{dx} & \frac{dT_z}{dy} & 1+\frac{dT_z}{dz} \end{bmatrix}$$

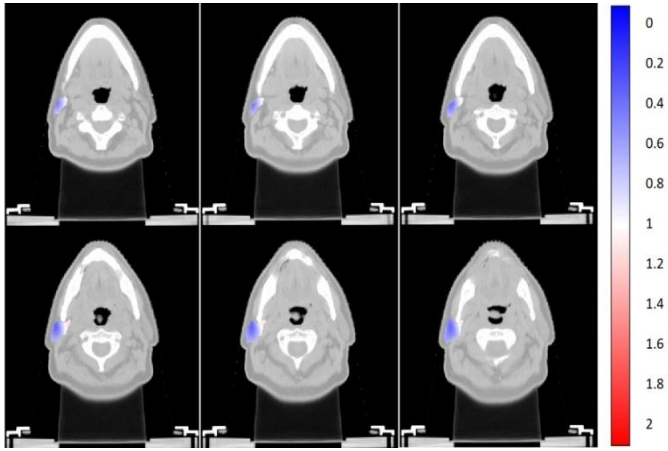
Example: In blue voxels with J<0.85

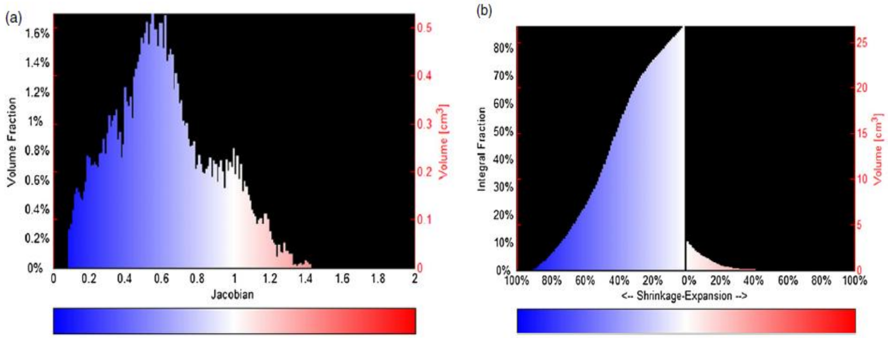


Predicting deformation before RT: quantifying by Jacobian map (and histogram)

32 pts,64 glands, 1 Institute (Helical MVCT)



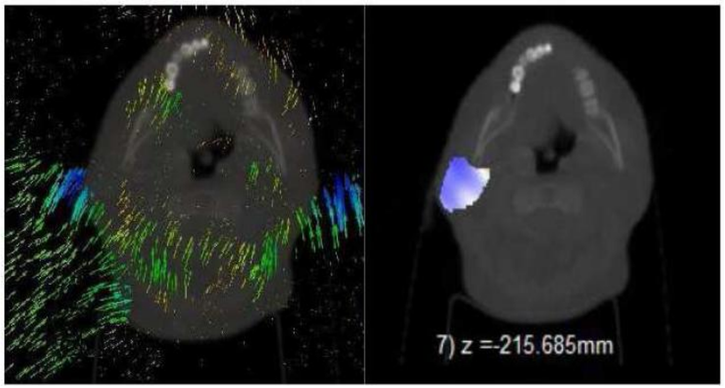


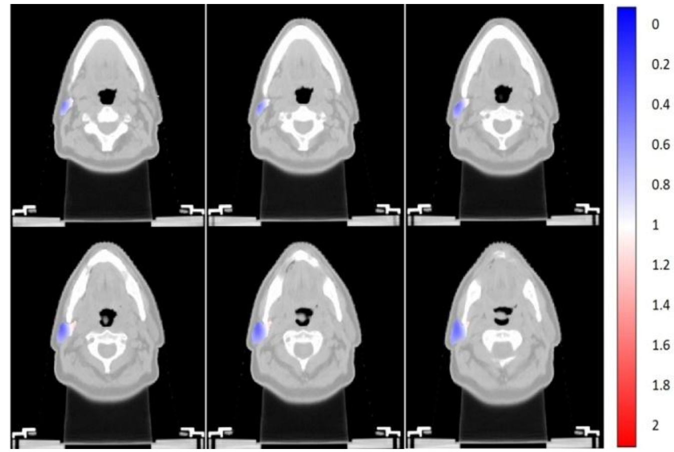


Introducing the Jacobian-volume-histogram of deforming organs: application to parotid shrinkage evaluation. ***C Fiorino, E Manggiulli, S Broggi, S Liberini, G M Cattaneo, I Dell'Oca, E Faggiano, N Di Muzio, R Calandrino, G Rizzo; Phys. Med. Biol. 56 (2011) 3301-3312***

Predicting deformation before RT: quantifying by Jacobian map (and histogram)

32 pts,64 glands, 1 Institute (Helical MVCT)

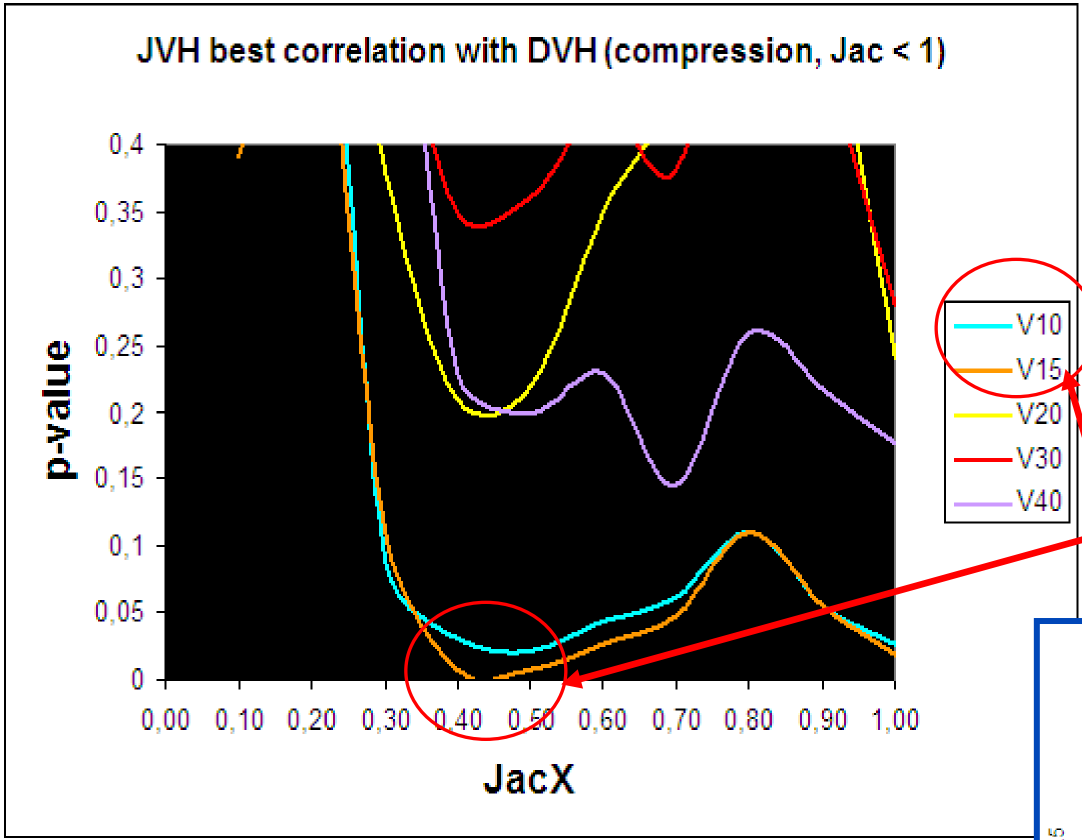




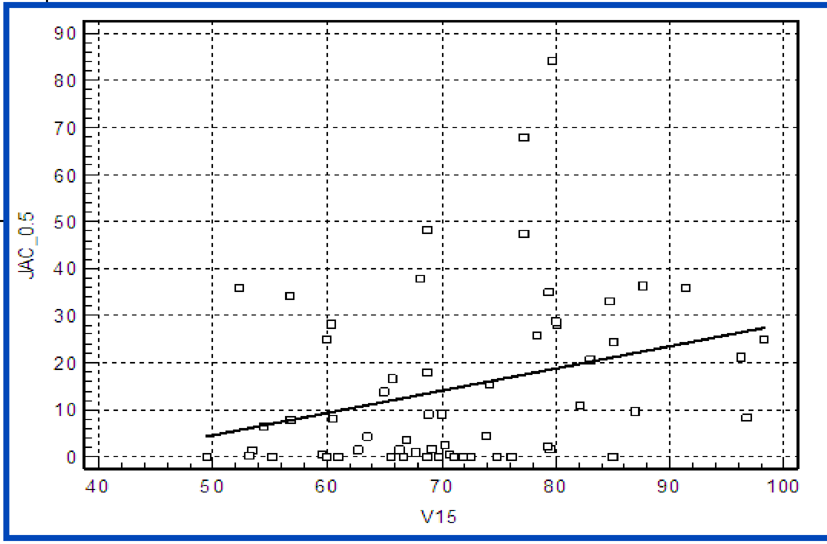
On average 82.6% (median value:86.6%; range: 19.02%-100%) of the voxels of parotid glands are affected by a shrinkage effect (Jac<1) and on average 13.7% (median:8.5%; range:0%-84.1%) of voxels show a compression >50% (Jac<0.5)

Introducing the Jacobian-volume-histogram of deforming organs: application to parotid shrinkage evaluation. ***C Fiorino, E Manggiulli, S Broggi, S Liberini, G M Cattaneo, I Dell'Oca, E Faggiano, N Di Muzio, R Calandrino, G Rizzo; Phys. Med. Biol. 56 (2011) 3301-3312***

Predicting deformation before RT: quantifying by Jacobian map (and histogram)



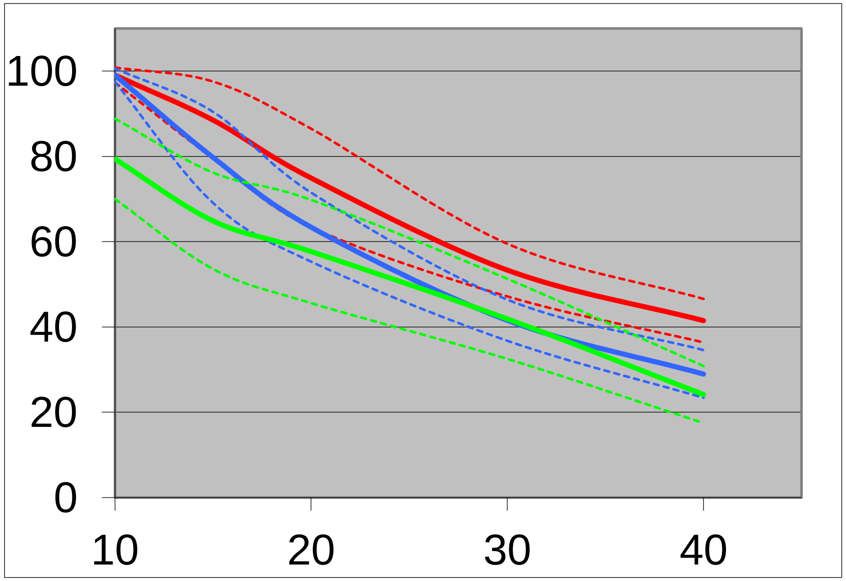
Best correlation between the fraction of largely compressing voxels (J=0.4-0.5) and the low-dose (10-15Gy)



Sparing the fraction of parotid receiving>15 Gy may translate into a drastically reduced risk of having large fractions of the gland showing large compression

Predicting deformation before RT: quantifying by Jacobian map (and histogram)

87pts,169 glands, 3 Institutions (2: dx kVCT, 1: H-MVCT)



- bad-DVH
V10>93% & V40>36%
Rate large deformations:
R=39,6%

- intermediate-DVH
V10>93% & V40<36%
R=19,6%

- good-DVH
V10<93%
R=11,3%

Shape of DVH highly predictive of the pattern of deformation expressed as R=risk of Jac_mean < 0.67 (quartile value)

QUANTITATIVE PARAMETERS OF PAROTID DEFORMATION DURING IMRT FOR HEAD-NECK CANCER CORRELATE WITH INDIVIDUALLY ASSESSED CLINICAL AND DOSIMETRY INFORMATION, ***S Broggi, C Fiorino, E Scalco, M L Belli, G Sanguineti, I Dell'Oca, N Dinapoli, V Valentini, N Di Muzio, G Rizzo, G M Cattaneo; submitted***

Parotid changes during RT: quantifying and predicting density variation

84 pts,168 glands, 3 Institutions (2: dx kVCT, 1: H-MVCT)

	All parotids	MVCT	kVCT
N°	168	76	92
ΔHU Mean	−7.3	−9.3	−5.6
Median	−4.6	−1.9	−5.0
SD	17.1	24.3	7.4
Max	+24.0	+24.0	+13.8
Min	−94	−94	−27.9
Lower quartile	−11.0	−12.7	−10.5
Higher quartile	+1.9	+4.5	−1.0
N° with ΔHU < 0	116	44	72

ΔHU=15 → Δρ=0.01 g/cm³

Difference between glandular and fat density:

70/80 HU → ρ=0.05 g/cm³

MVCT not accurate for individual prediction (w/o correct)

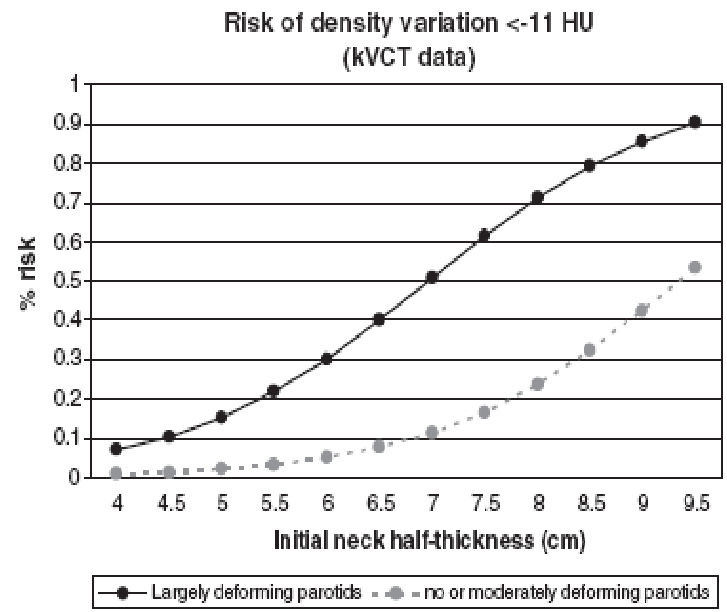
Density variation of parotid glands during IMRT for head-neck cancer: correlation with treatment and anatomical parameters. ***C Fiorino, G Rizzo, E Scalco, S Broggi, M L Belli, I Dell'Oca, N Di Napoli, F Ricchetti, A Mejia Rodriguez, N Di Muzio, R Calandrino, G Sanguineti, V Valentini, G M Cattaneo; Radiother. Oncol. 104 (2012) 224-229***

Parotid changes during RT: quantifying and predicting density variation

84 pts,168 glands, 3 Institutions (2: dx kVCT, 1: H-MVCT)

MVA – end-point: Δρ<quartile

		Jac mean < 0,68 (best cut off)	Initial neck half-thickness
kVCT & MVCT	OR	3,8	1,61
	95% CI	1,8-7,9	0,99-2,62
(p=0,0002)	p-value	0,0004	0,05
	AUC	0,683 (95%CI: 0,607-0,752)	
kVCT	OR	8,0	2,39
	95% CI	2,7-24,2	1,07-5,33
(p=0,0001)	p-value	0,0002	0,03
	AUC	0,776 (95%CI: 0,677-0,856)	



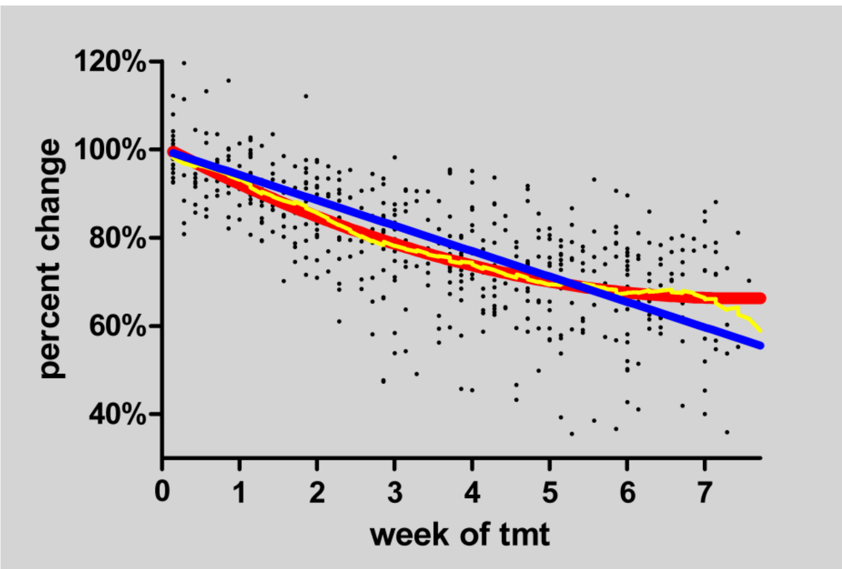
Density reduction well described by a two-variable model including parotid deformation and initial neck thickness

Density variation of parotid glands during IMRT for head-neck cancer: correlation with treatment and anatomical parameters. ***C Fiorino, G Rizzo, E Scalco, S Broggi, M L Belli, I Dell'Oca, N Di Napoli, F Ricchetti, A Mejia Rodriguez, N Di Muzio, R Calandrino, G Sanguineti, V Valentini, G M Cattaneo; Radiother. Oncol. 104 (2012) 224-229***

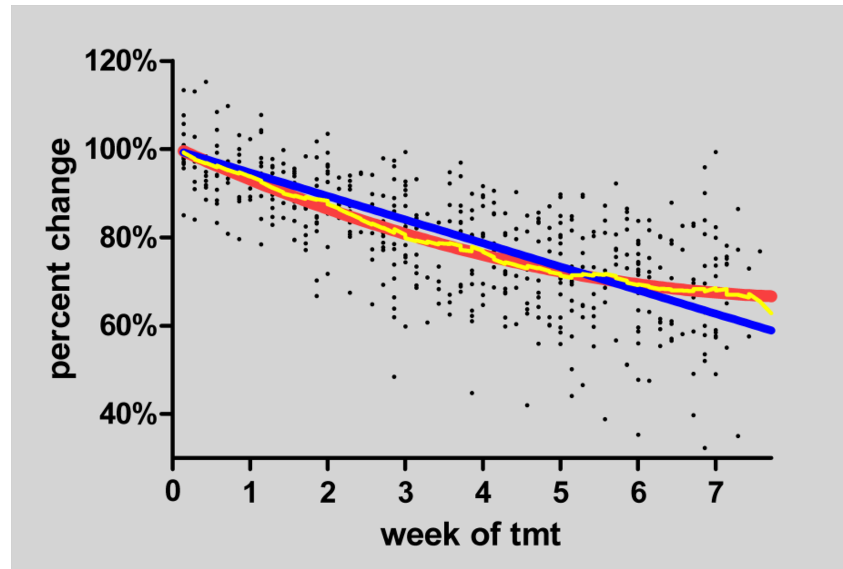
Adaptive RT for HN SCC

- ♦ Which organs at risk to follow during tmt?
- ♦ Is it possible to predict which patients?
- ♦ When to adapt during tmt?

Pattern of shrinkage of Parotids during IMRT 85 pts, 180 parotids



High dose side



Low dose side

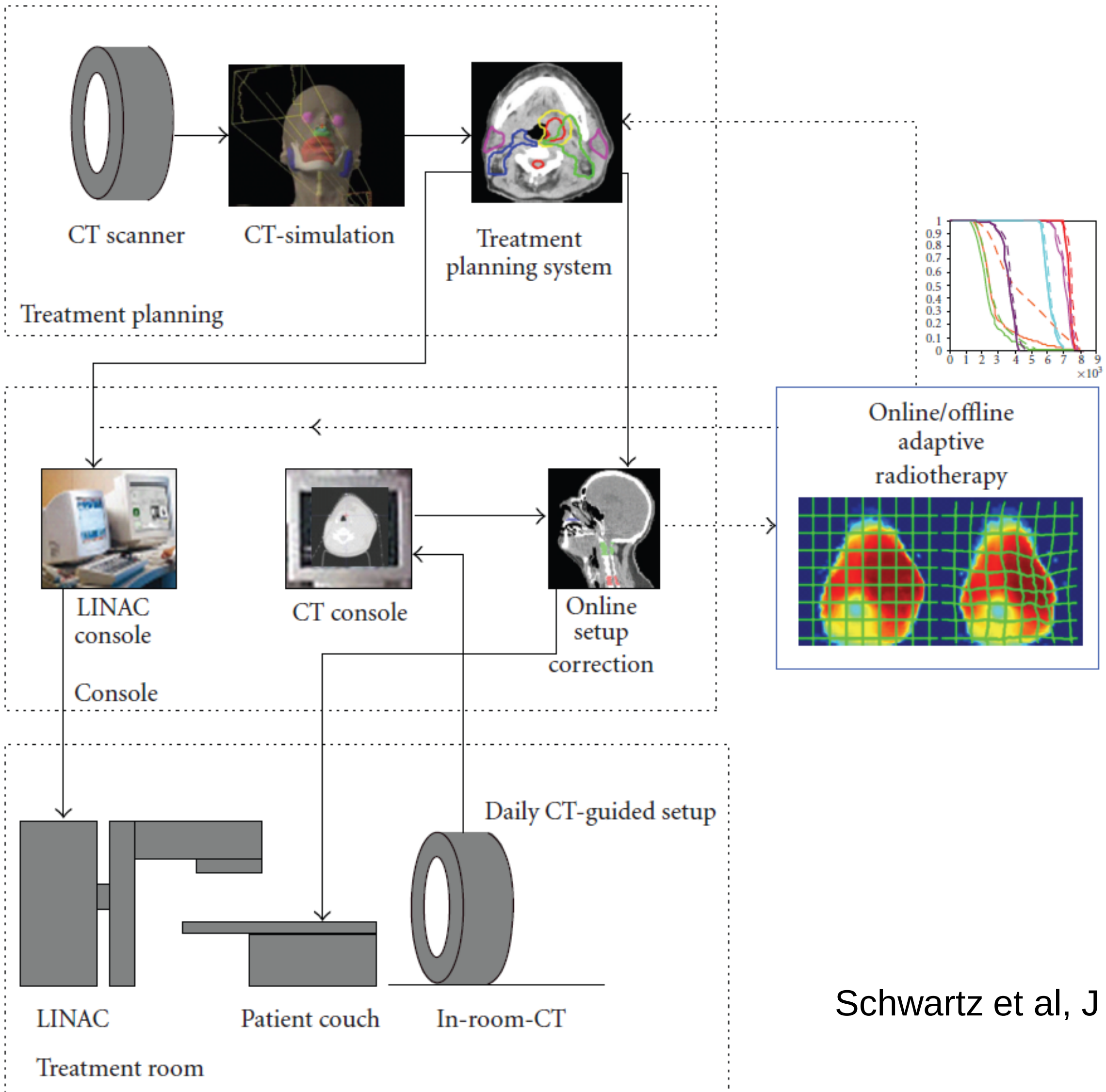
Sanguineti et al, most rejected paper…..

In summary

♣ Changes occur in all OAR during IMRT for oropharyngeal SCC;
♣ The parotids seems (most) suitable for adaptive RT;
♣ WL, age and dose are correlated with parotid volume change at the end of tmt
♣ The first part of the tmt seems the most critical for shrinkage

- It is unknown whether or not it is safe (in terms of local-regional control) to decrease the size of the GTV during the course of radiotherapy
- Adaptive RT could be considered in a selected group of patients (those with an anisotropic shape change)
- Current limitations to the implementation of repeat CT imaging and IMRT replanning (increased workload for staff, cost, etc.)

Adaptive radiotherapy workflow



Schwartz et al, J Oncol 2011

Useful tools

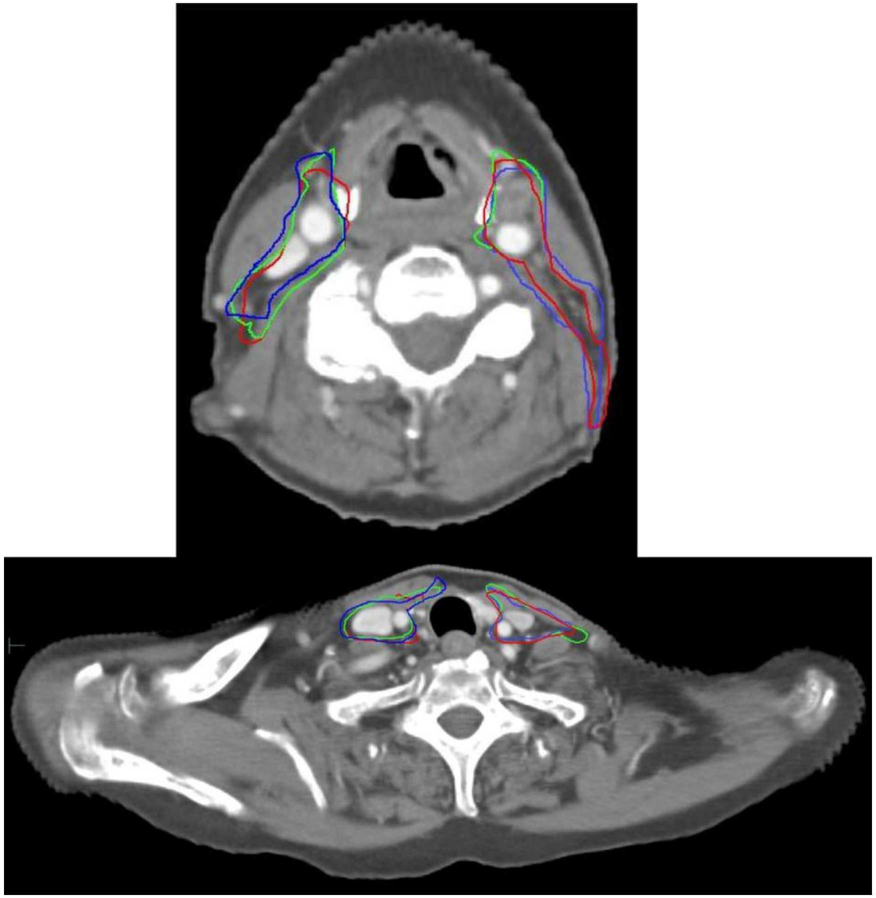
Fully Automated Simultaneous Integrated Boosted—Intensity Modulated Radiation Therapy Treatment Planning Is Feasible for Head-and-Neck Cancer: A Prospective Clinical Study

Binbin Wu, PhD,[*,§] Todd McNutt, PhD,[*] Marianna Zahurak, MS,[‡]
Patricio Simari, PhD,[||] Dalong Pang, PhD,[§] Russell Taylor, PhD,[†]
and Giuseppe Sanguineti, MD[*]

“Application-generated plans achieve statistically better dosimetric results and efficiency than plans created by dosimetrists; physician review further confirms that they can be delivered to patients”

Useful tools

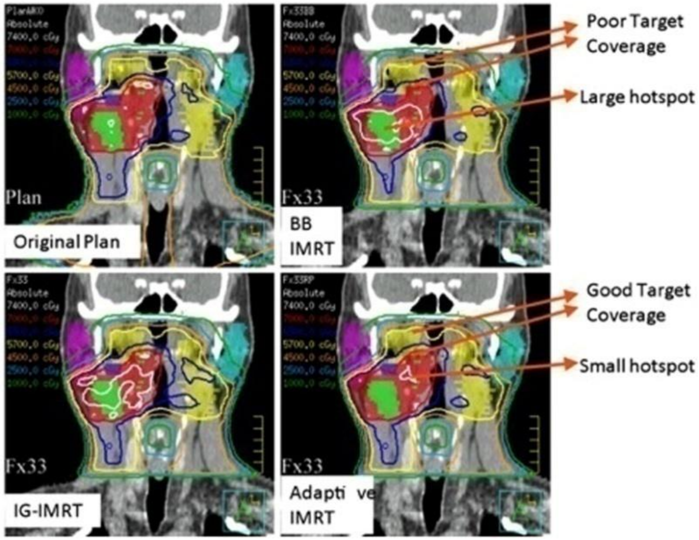
Atlas-based autosegmentation



Teguh et al, IJROBP 2011

Dosimetric benefits of adaptive radiotherapy (at least in some patients):

Are they clinically relevant?



Radiother Oncol 2013

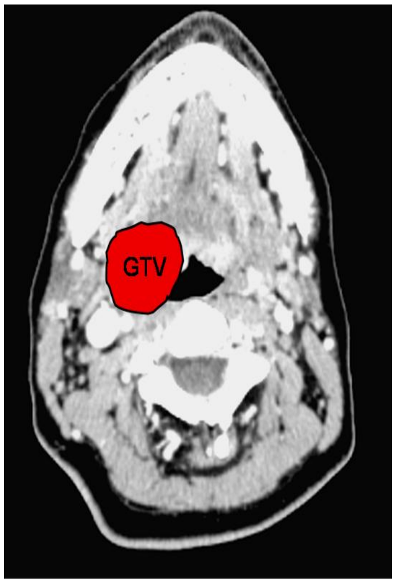
Adaptive radiotherapy for head and neck cancer—Dosimetric results from a prospective clinical trial

David L. Schwartz [a,b,c,*], Adam S. Garden [c], Shalin J. Shah [c], Gregory Chronowski [c], Samir Sejpal [c], David I. Rosenthal [c], Yipei Chen [d], Yongbin Zhang [d], Lifei Zhang [d], Pei-Fong Wong [c], John A. Garcia [c], K. Kian Ang [c], Lei Dong [d,e]

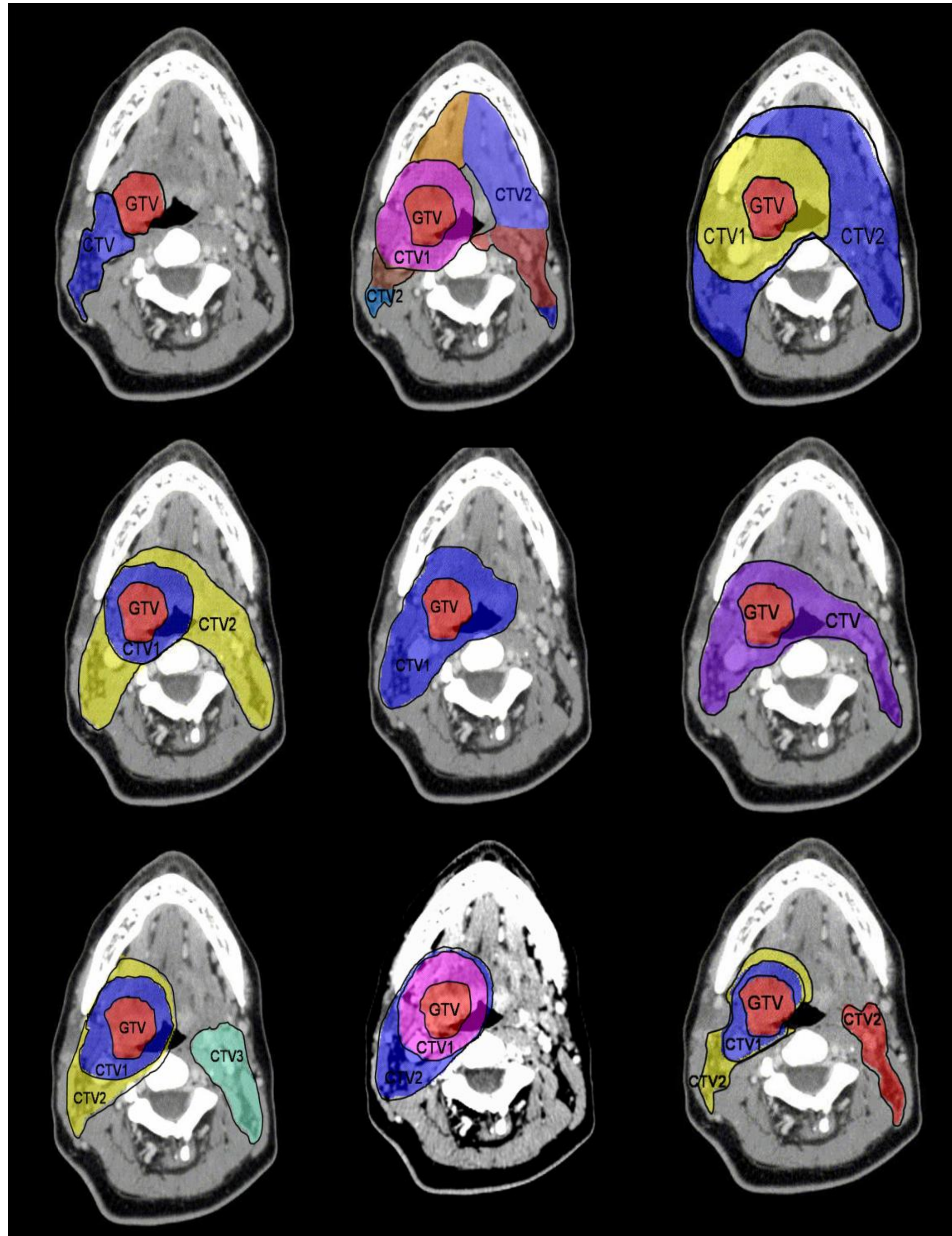
- One replanning reduced mean dose to contralateral parotid by 0.6 Gy (p = 0.003) over the IGRT alone.

- Two replannings further reduced the mean contralateral parotid dose by 0.8 Gy (p = 0.026)

Contouring variability



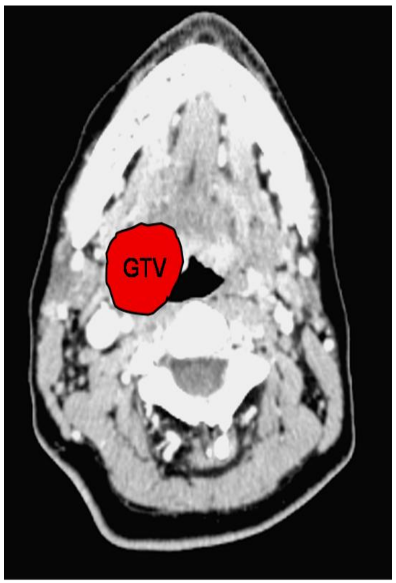
Tonsil T2 N1



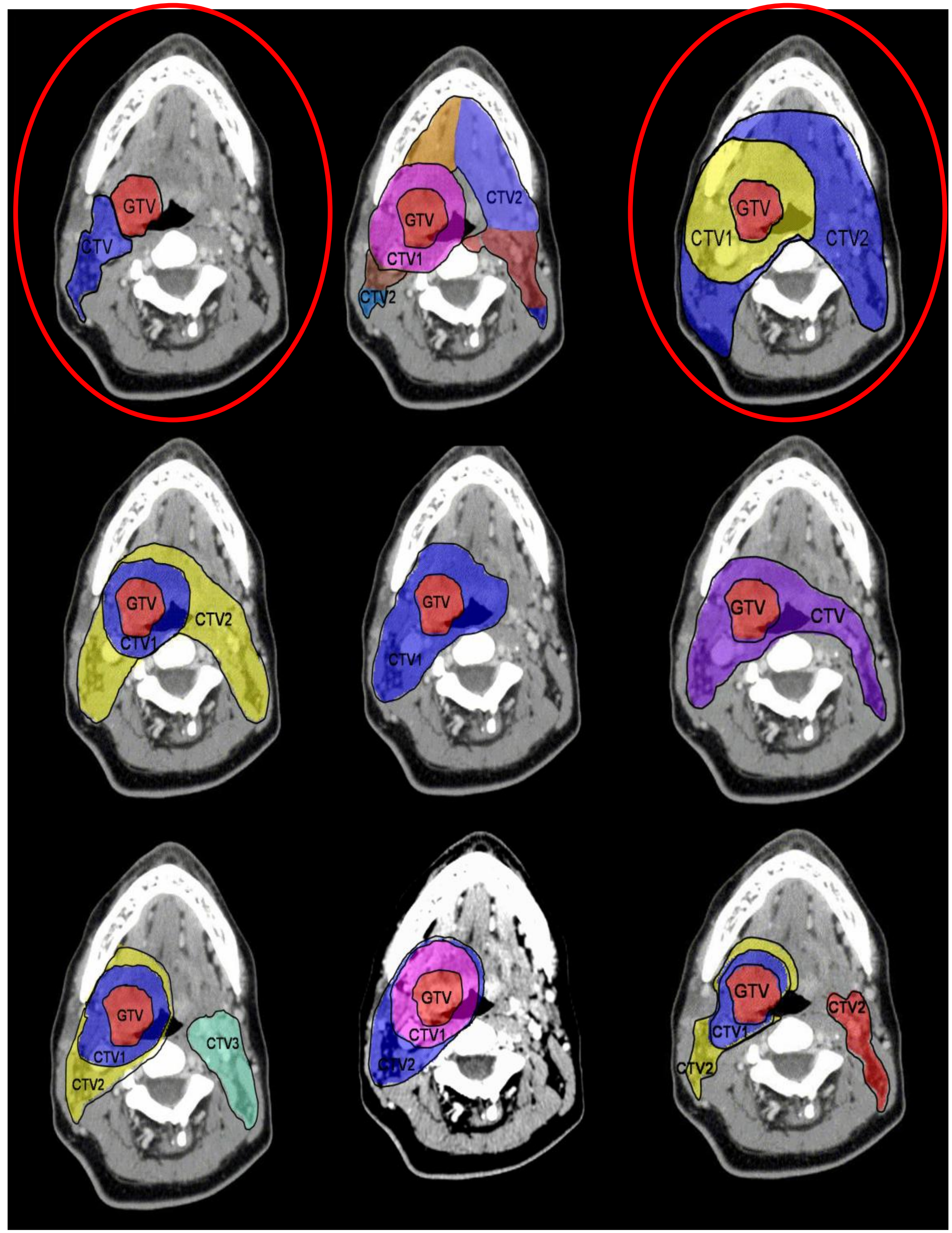
Harari et al., 2005

Courtesy of V. Gregoire

Contouring variability



Tonsil T2 N1

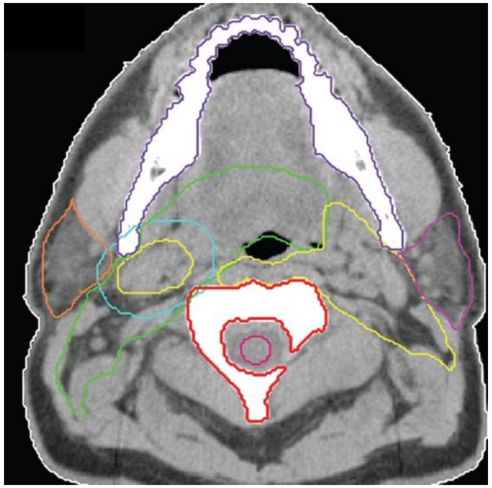


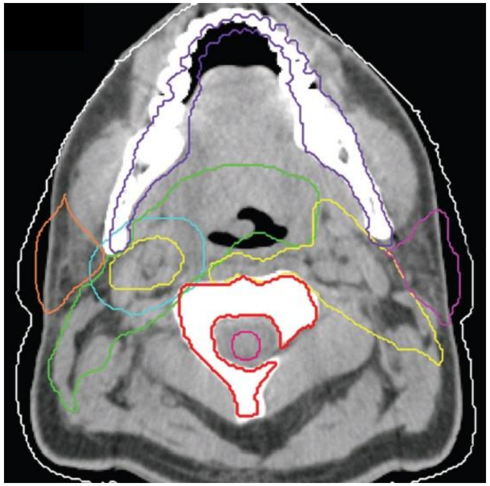
Harari et al., 2005

Courtesy of V. Gregoire

- The optimal frequency and utilization and the ultimate clinical impact of ART remain undefined

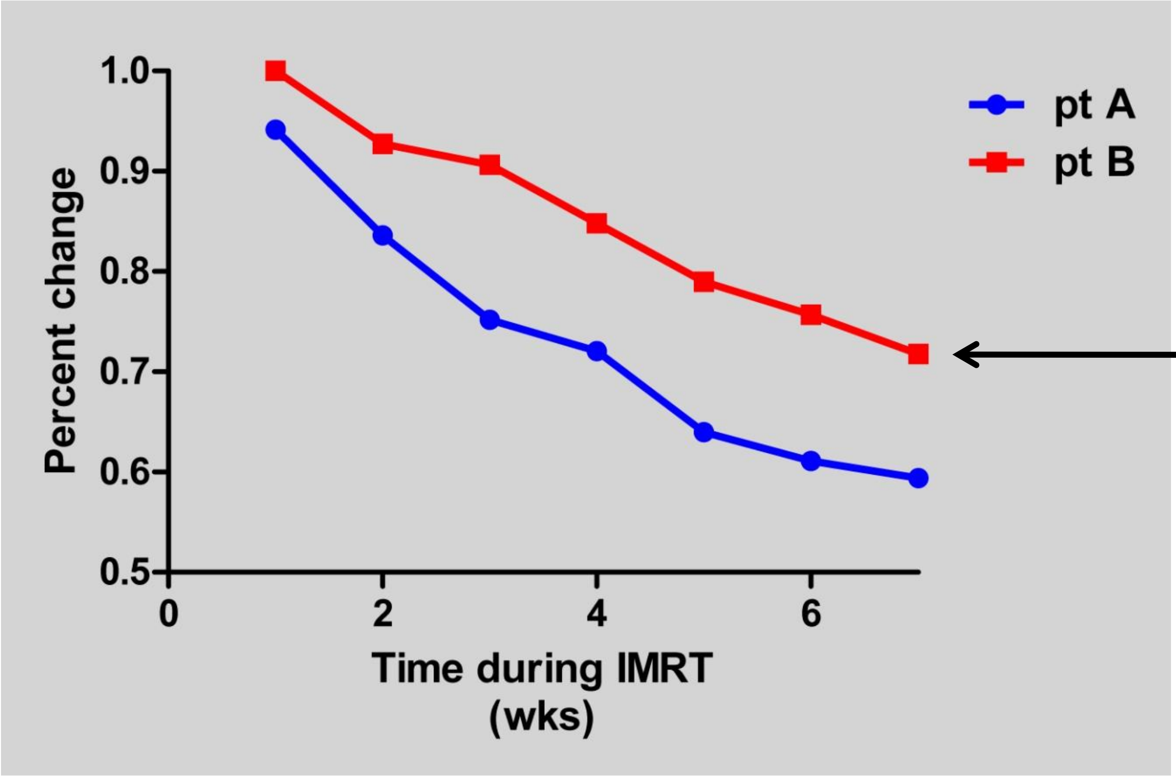
- Prospective clinical trials will be necessary to incorporate ART into a future treatment standard





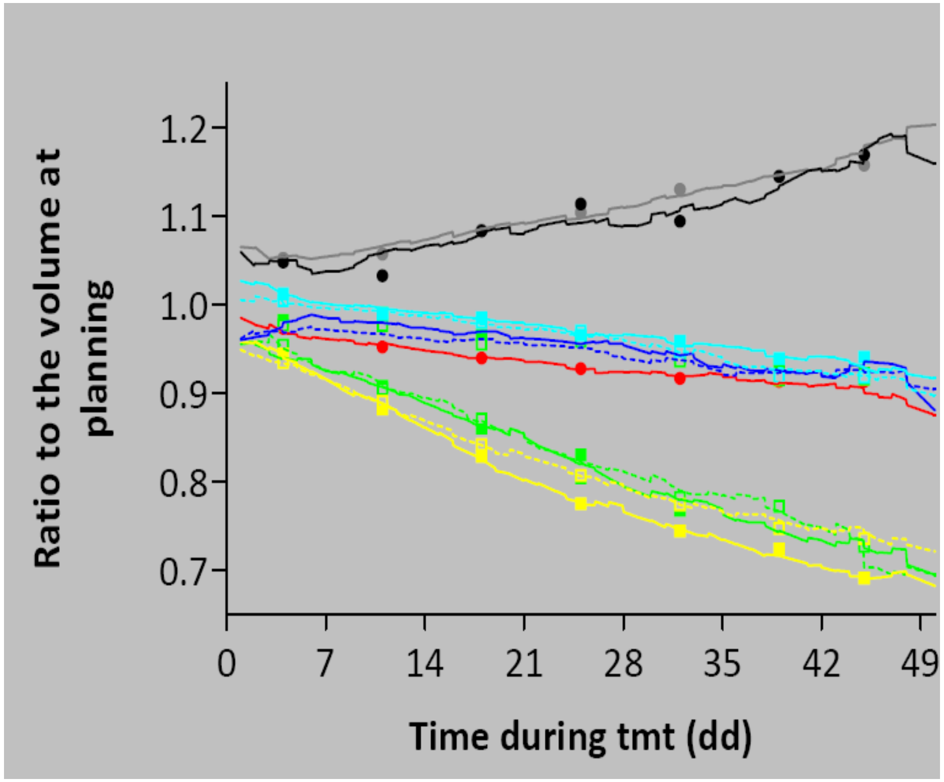
Prediction of (late) toxicity based on changes that occur during treatment

Prediction of (late) toxicity based on (morphological) changes that occur during treatment



Less toxicity?

Prediction of (late) toxicity based on (morphological) changes that occur during treatment



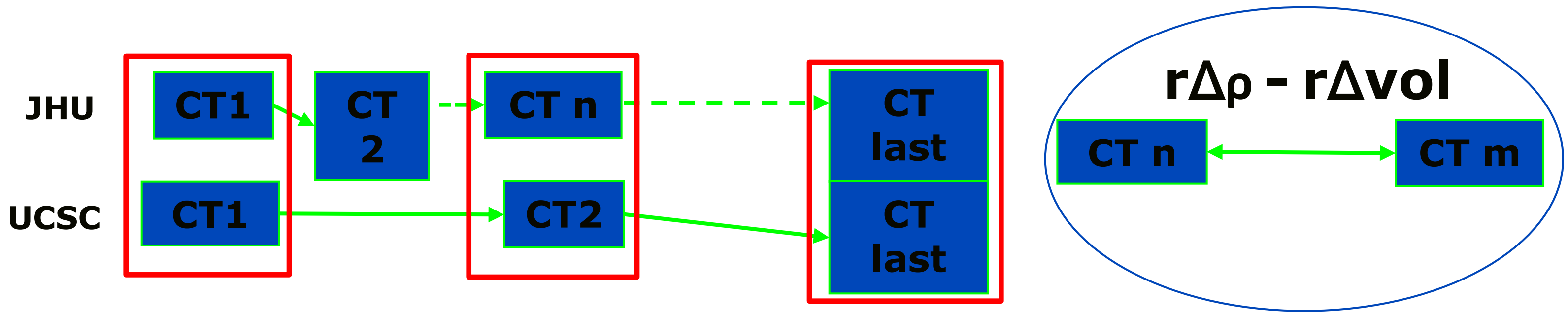
3 mths

Image-based scoring of toxicity: a tool for selecting patients for ART ?

- IGRT widely available means a large amount of available (mainly CT) imaging information describing how anatomical changes occur during RT….for the first time in the history of RT (!)
- Quantitative assessment of <u>organ deformation</u> as a potentially powerful tool for scoring and predicting toxicity
- Early assessment of anomalous organ deformation as a tool to correct/adapt the treatment to reduce toxicities !!

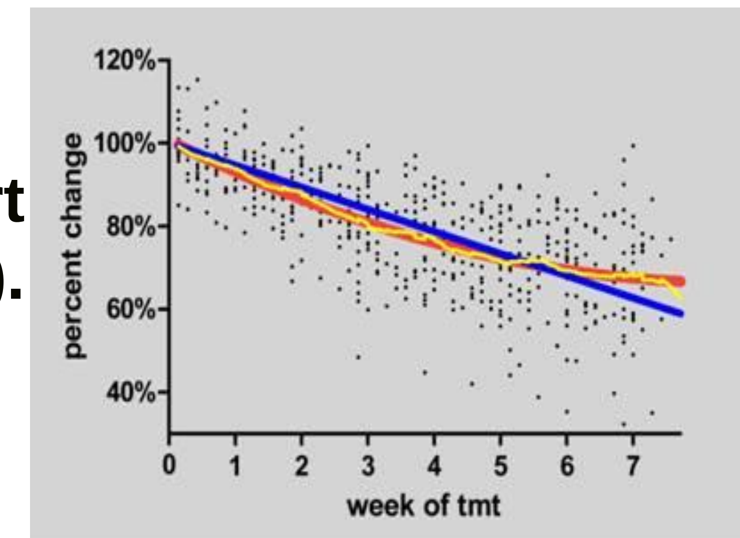
Parotid changes during RT: predicting modifications from early reactions

45 pts, 90 glands, 2 Institutions (2: dx kVCT)



Volume/jacobian and density variations are larger in the early phase compared to the second part (more evident for density changes).

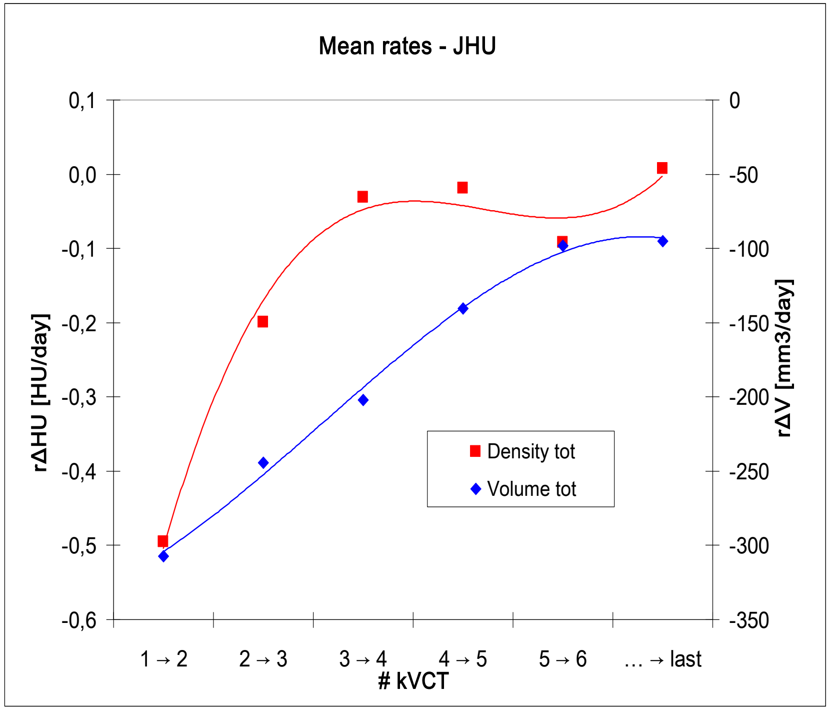
<u>Early variations are correlated with the final ones</u> (more evident for density changes)



M L Belli, G Sanguineti, G Rizzo, E Scalco, C Fiorino, et al. *Early density and volumetric parotid changes predict for variations at the end of therapy and for development of xerostomia (Submitted)*

Parotid changes during RT: predicting modifications from early reactions

- Kinetic of density and volume variations during treatment: daily rates of variations decrease during treatment (JHU data)
- Density variations are mainly concentrated in the first two weeks; stable values after week 3
- Early predictor of acute xerostomia ??
- Testing on clinical data…



M L Belli, G Sanguineti, G Rizzo, E Scalco, C Fiorino, et al. Early density and volumetric parotid changes predict for variations at the end of therapy and for development of xerostomia (Submitted)

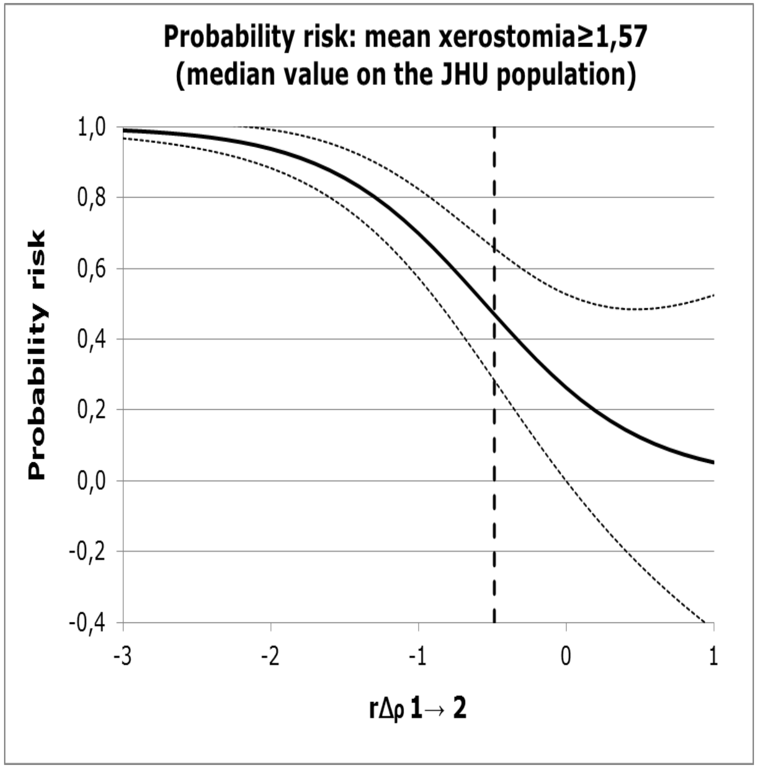
Early density changes correlate with acute xerostomia

- CTC-based prospective assessment of acute xerostomia (weekly) of 25 JHU pts
- Peak and longitudinal scores (mean score) representing both severity and persistence

Logistic fit: end-point mean xerostomia score > 1,57 (median value)

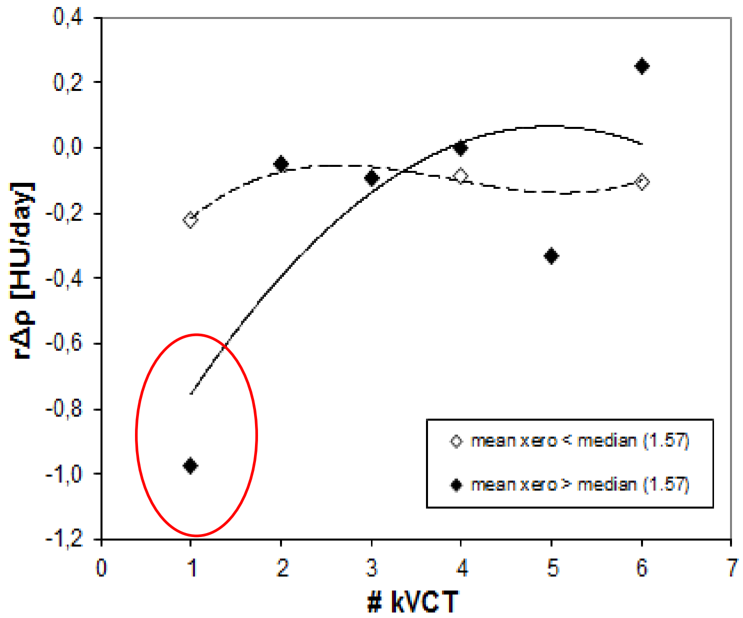
	OR	CI 95%	p-value
rΔρ 1 → 2 (ext)	0,11	0,02 to 0,81	0,01

AUC	95% CI	p-value	Best Cut-Off
0,76	0,55 to 0,91	0,01	-0,31

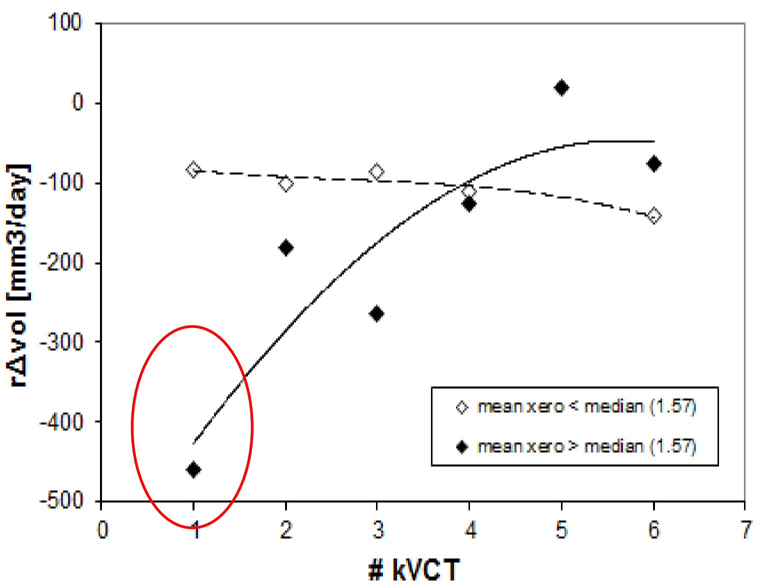


M L Belli, G Sanguineti, G Rizzo, E Scalco, C Fiorino, et al. Early density and volumetric parotid changes predict for variations at the end of therapy and for development of xerostomia (Submitted)

Median density rates



Median volume rates



Rates of density/volume change in the first 2 weeks correlate with worse acute xerostomia profile (severity/persistence) !!

Detecting sensitive pts! ...potential for ART ??

Conclusions and future trends…

Patients with larger parotid shrinkage may be predicted with a moderate predictive value (AUC: 0.70-0.80) by parotid DVH and age….(reducing V10…stem cells hypothesis ? Van Lujik 2012)

Early variations correlate with final changes; density seems to be the most sensitive and promising parameter (in-vivo measurement of the reduction of acinal cells ??)

Early density/volume changes predict worse acute xerostomia profile: what to do ?...adapt ? supportive care ? ...2 weeks is too late for reducing the acute damage ??..and late effects ??

Need of prospective ART trials testing predictive value on reducing acute (and late?) tox…CT @ second week good timing to already see sensitive pts…(again, to be confirmed in prospective trials…)