Adaptive radiotherapy in the head and neck: what is the clinical significance?

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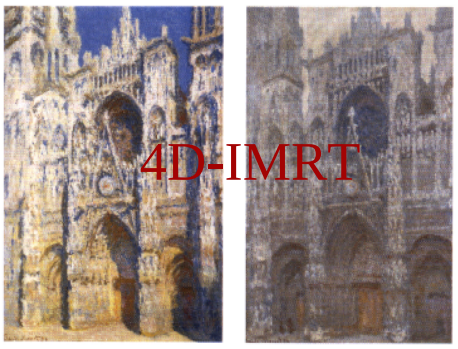
Adaptive radiotherapy in the head and neck: what is the clinical significance?

The facts, the needs and the solutions …

Adaptive radiotherapy in the head and neck: what is the clinical significance?

The facts,



4D-IMRT

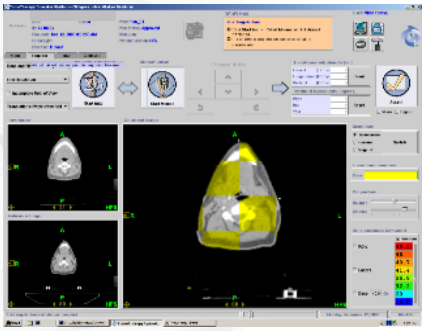
The Cathedral of Rouen

C. Monet, 1894

Geometric 4D-IMRT

MVCT

kVCT



AAPM
July 2009

Vaandering, 2006

CT MRI (T2) FDG-PET

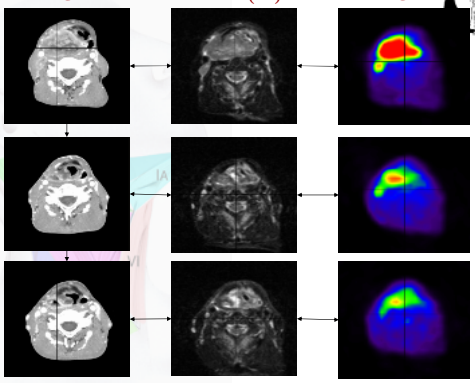
PRE-R/

(Week 2)

WEEK 3

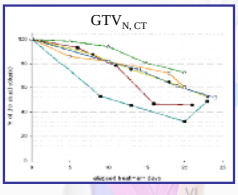
(Week 4)

WEEK 5



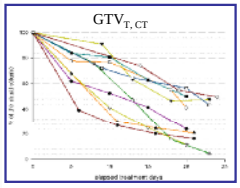
AAPM
July 2009

Variation in GTVs during RT-CH (70 Gy – 3 courses on w1, w4, w7)



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

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



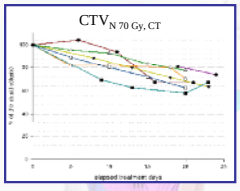
Mean slope: -3.18% / treat day ($p<0.05$)

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

AAPM
July 2009

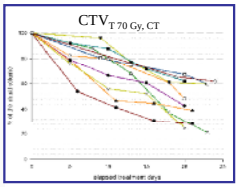
Castadot & Lee, 2008

Variation in therapeutic CTVs during RT-CH (70 Gy – 3 courses 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# ($p<0.05$)

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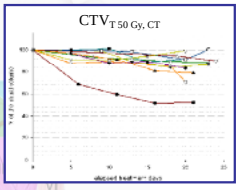
July 2009

Castadot & Lee, 2008

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

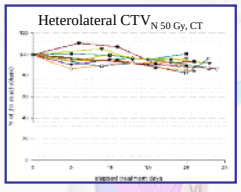


Mean slope: -0.63% / treat day (p<0.05)

No shift

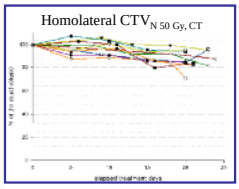
Castadot & Lee, 2008

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



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

No shift

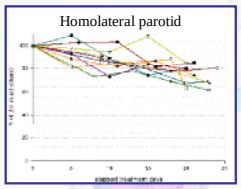


Mean slope: -0.41% / treat day (p<0.05)

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

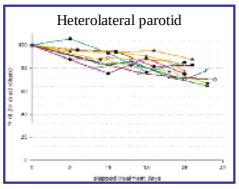
Castadot & Lee, 2008

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



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

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



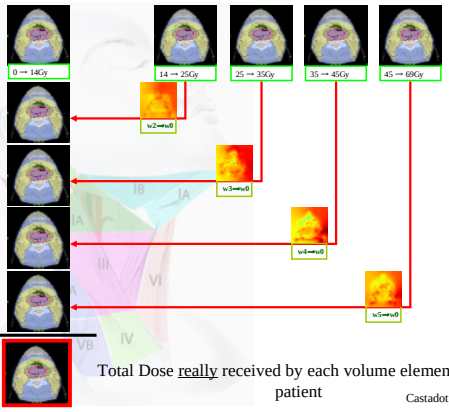
Mean slope: -1.03% / treat day (p<0.05)

No shift

Castadot & Lee, 2008

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 / w	4.9% / week	-	-
Han, 2008	MVCT	-	1.1% / day	-	-
Vasquez-Osorio, 2008	kVCT	3 mm medial	17% loss at 46 Gy	-	-

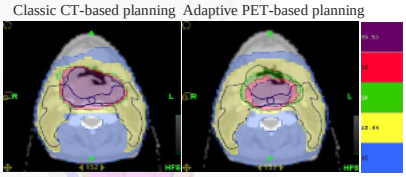


Total Dose really received by each volume element of the patient

Castadot & Lee, 2008

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

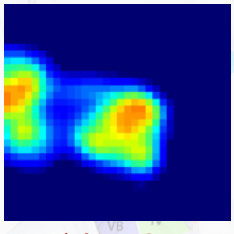
Dose distribution after adaptive RT-CH (n=5)

	« Classical » CT-based	« Classical » PET-based	« Real » CT-based	« Real » PET-based	Adaptive CT-based	Adaptive PET-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_4 (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_{2Gy} (cc)	11.66	8.78	12.08	9.25	10.25	7.24
V_{45Gy} (cc)	308.89	297.00	400.11	327.46	311.39	254.40

Castadot & Lee, 2008

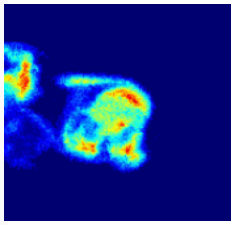
Biological heterogeneity

[^{18}F]-FDG TEP



Résolution 2.3 mm

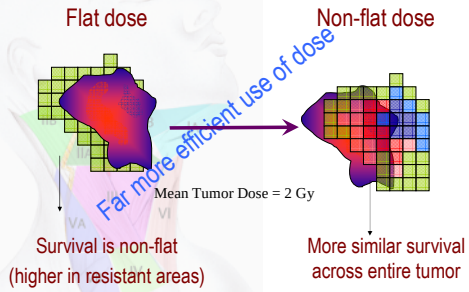
Registered autoradiography



Résolution 0.1 mm

N. Christian, 2007

“Dose painting” by number…



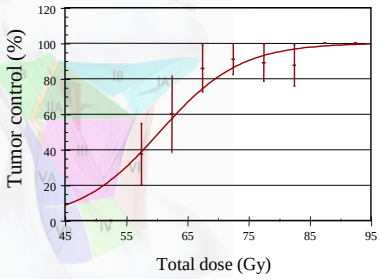
Courtesy of D. De Ruysscher

Adaptive radiotherapy in the head and neck: what is the clinical significance?

the needs

Tumor Control Probability (TCP)

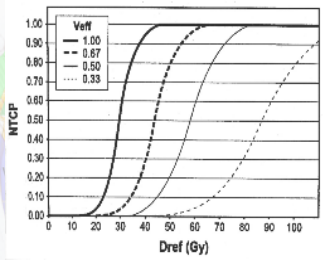
Dose-response curve for neck nodes ≤ 3 cm



Bataini et al, 1982

Complication probability after parotid gland irradiation

Complication = stimulated flow rate ≤ 25% of the pre-RT rate at 12 months

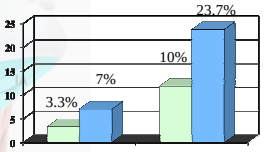


From Eisbruch, 1996

Clinical impact of the TLD QA program of the EORTC assessed by biological modeling

65 high-energy treatment units have been checked :

- 22 underdosing
- 41 overdosing

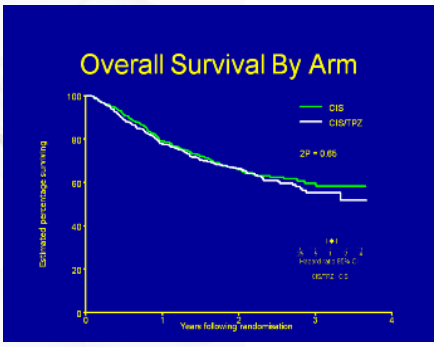


loss of local control

excess mild to moderate complications

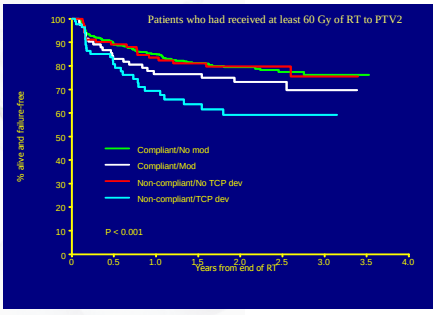
Bentzen, R & O, 48 (S1): 728, 1998

HeadSTART trial: OS (analysis by ITT)



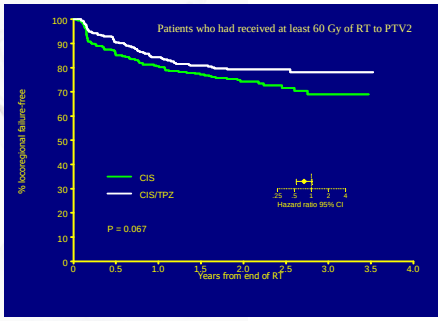
Peters, 2009

HeadSTART trial: DFS as a function of compliance to protocol



Peters, 2009

HeadSTART trial: LR-DFS for the compliant patients



Peters, 2009

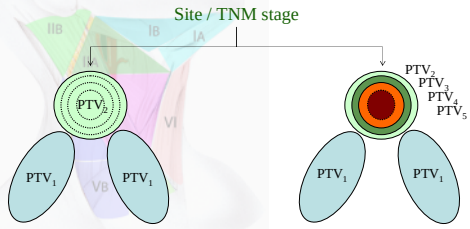
Adaptive radiotherapy in the head and neck: what is the clinical significance?

and the solutions …

A clinical trial ?

IMRT >< geometrical adaptive IMRT ?

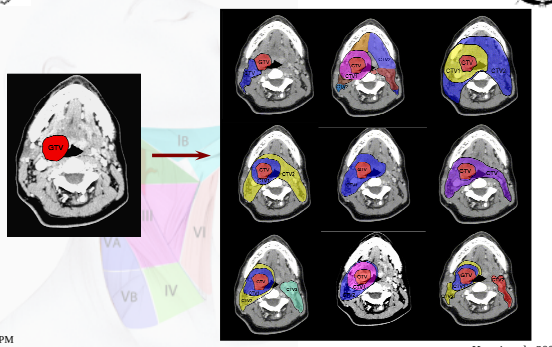
Geometric adaptive IMRT >< biological adaptive IMRT ?



"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 …

But … still a long way to go …



Harari et al., 2005

The reality…

- Adaptive IMRT: geometrical, biological & dosimetrical
  - which imaging modalities??
  - which biological pathways??
  - which volume/dose registration algorithms??
  - how frequently??

Challenges in Head & Neck loco-regional treatment

The Bridge at Argenteuil

C. Monet, 1874

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• Communication and Remote Sensing Lab.	**Adriana PARRAGA, Eng.** Benoit MACQ,Eng., Ph.D.
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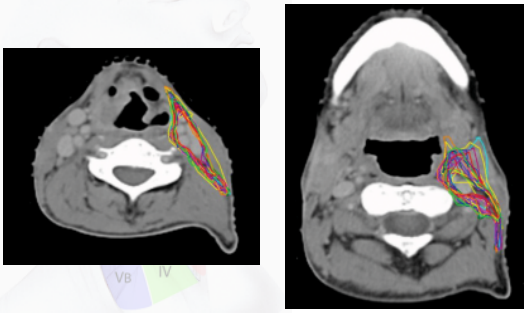
"My" vision of Radiation Oncology in 2009 and beyond …

- 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

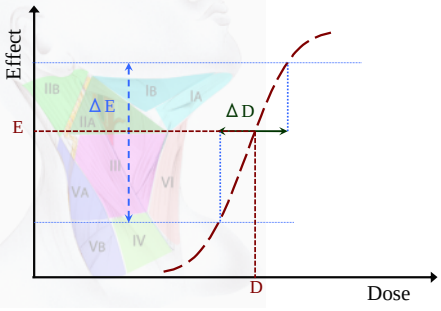
- Target selection and delineation
- Adaptive IMRT: geometrical, biological & dosimetrical
  - which imaging modalities?
  - which biological pathways?
  - which volume/dose registration algorithms?
  - how frequently?
- Concomitant association with drugs and/or "small molecules"

H&N IMRT practice heterogeneity among Dutch Radiation Oncologists



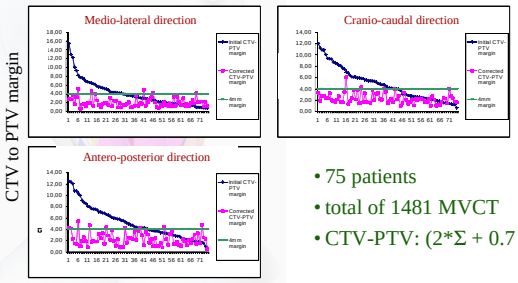
Rasch et al., 2007

Tumor Control Probability (TCP)



Geometric 4D-IMRT

Alternate week MVCTs: CTV-PTV margins



- 75 patients
- total of 1481 MVCT
- CTV-PTV: (2*Σ + 0.7 σ)

Vaandering, 2007

Parotid gland sparing in IMRT for HNSCC

PARSPORT Trial Design

Head and neck cancer patients at risk of radiation induced xerostomia (oropharynx/hypopharynx)

↓

Randomisation 1:1

Conventional radiotherapy (CRT) | Parotid-sparing IMRT

65Gy/30 fractions in 6 weeks - radical and post-operative R1/R2
60Gy/30 fractions in 6 weeks - post-operative R0

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

Parotid gland sparing in IMRT for HNSCC

Treatment Received

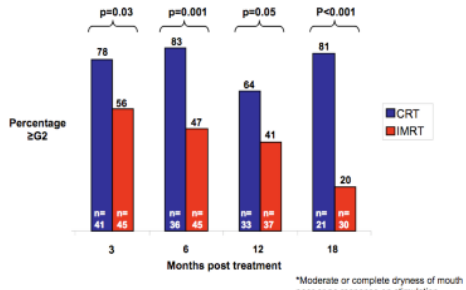
	CRT n=47		IMRT n=47	
Radiotherapy delivery as per protocol	43*	91%	46†	98%
Radiotherapy given as radical treatment	29	62%	38	81%
Mean (SD) radiotherapy dose PTV1	65 Gy	(0.5)	65 Gy	(0.4)
Ipsilateral Parotid mean (SD) dose	59 Gy	(6.3)	45 Gy	(10.6)
Contralateral Parotid mean (SD) dose	60 Gy	(6.5)	26 Gy	(6.8)
Radiotherapy given post-operatively	15	32%	8	17%
Mean (SD) radiotherapy dose PTV1	64 Gy	(2.3)	61 Gy	(2.2)
Ipsilateral Parotid mean (SD) dose	61 Gy	(5.0)	50 Gy	(12.9)
Contralateral Parotid mean (SD) dose	57 Gy	(10.3)	27 Gy	(3.7)
Received neoadjuvant chemotherapy	19	40%	20	43%

* 1 received IMRT due to coverage; 1 ineligible; 2 refused;
† 1 deviated due to rectal bleed

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

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)