Tomotherapy and Cyberknife

in Head & Neck cancer

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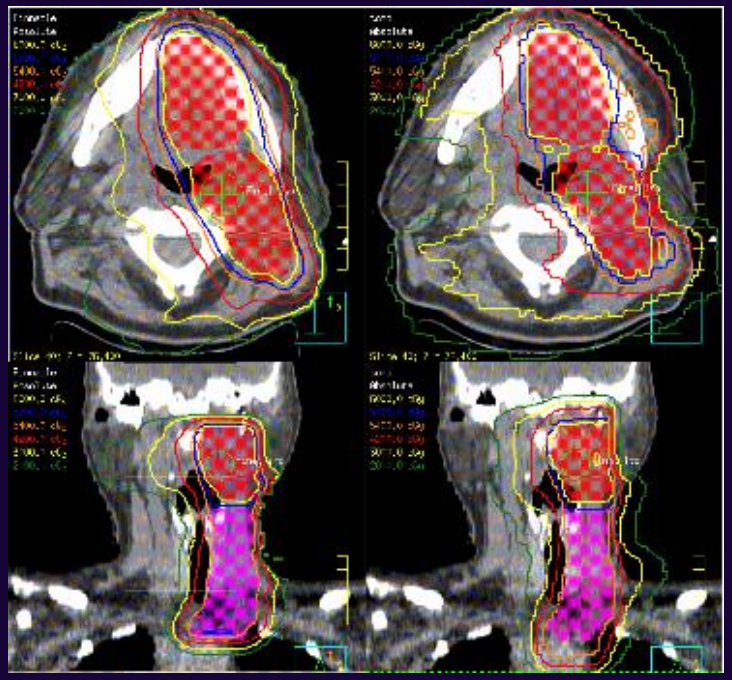
Treatment plan comparison between helical tomotherapy and MLC-based IMRT using radiobiological measures

Phys. Med. Biol. 52 (2007) 3817–3836

Panayiotis Mavroidis[1,2], Brigida Costa Ferreira[1,3], Chengyu Shi[4,5], Bengt K Lind[1] and Nikos Papanikolaou[4,5]

MLC-based IMRT



Helical Tomotherapy

The clinical effectiveness of the HT and MLC-based IMRT were evaluated using head and neck, lung and prostate cancers.

The evaluation was performed using both physical and biological criteria.

This evaluation shows that in the head and neck cancer case **the HT treatment is expected to have a better clinical outcome as compared to the MLC-based IMRT**

IMRT for head and neck cancer depends heavily on the accurate identification of target tissue, and the variations in CTV delineation have the potential to confound the results

Multiple aspects of IMRT planning, such as the optimization of beam angles to prioritization of constraints are dependent on the individual user

Wiezorek *et al. Radiation Oncology* 2011, **6**:20
http://www.ro-journal.com/content/6/1/20

Rotational IMRT techniques compared to fixed gantry IMRT and Tomotherapy: multi-institutional planning study for head-and-neck cases

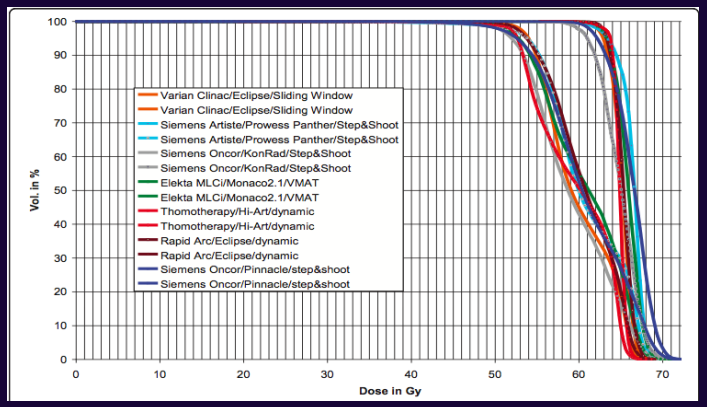
Tilo Wiezorek[1*], Tim Brachwitz[1], Dietmar Georg[2], Eyck Blank[3], Irina Fotina[2], Gregor Habl[5], Matthias Kretschmer[4], Gerd Lutters[6], Henning Salz[1], Kai Schubert[5], Daniela Wagner[7], Thomas G Wendt[1]

Methods: Treatment plans were created for 10 patients with head-and-neck tumours (oropharynx, hypopharynx, larynx) using the following treatment planning systems (TPS):

- for rotational IMRT: Monaco (ELEKTA VMAT solution), Eclipse (Varian RapidArc solution) and HiArt for the helical tomotherapy (Tomotherapy).
- for static gantry IMRT: KonRad, Pinnacle and Panther DAO based on step&shoot IMRT delivery and Eclipse for sliding window IMRT.

Table 4 MUs, treatment time, V_{50Gy} dependend on IMRT technology

	KonRad/S&S	Panther DAO/ S&S	Eclipse/SW	VMAT	Tomotherapy	Rapid Arc	Pinnacle/S&S
MU normalised	800.44 ± 100.90	408.27 ± 17.97	1139.86 ± 239.45	500.82 ± 71.59	x	436.92 ± 36.53	1059.63 ± 134.85
treatment time/ min	11.18 ± 2.64	7.07 ± 0.72	10.5 ± 1.00	11.8 ± 1.44	7.74 ± 0.80	2.48 ± 0.01	11 ± 0.45
Volume/ccm receiving >5 Gy	4524.94 ± 1969.67	5331.76 ± 1437.55	3802.11 ± 899.31	4497.85 ± 1196.30	5122.01 ± 1647.57	5479.37 ± 1524.97	5010.46 ± 1149.93



CONCLUSIONS

All IMRT delivery technologies with their associated TPS provide plans with satisfying target coverage while at the same time respecting the defined OAR criteria.

- SW-IMRT, RapidArc and Tomo techniques resulted in better target dose homogeneity.
- Rotational IMRT seem to be advantageous with respect to OAR sparing and treatment delivery efficiency, at the cost of higher dose delivered to normal tissues.
- The overall treatment plan quality using Tomo seems to be better than the other TPS technology combinations.

There is no best technology with respect to all evaluation parameters, i.e. all techniques are connected with some advantages and with some disadvantages.

There were substantial differences in terms of usability to specify the planning goals for the different volumes

We expect a medical relevance of the results e.g. partial underdosage, different OAR sparing, dose burden with 5Gy or more; but this should be investigated in prospective studies

Wiezoreck 2011

Hong et al. demonstrated that significant "cold spots" could develop from daily setup error, which could adversely affect tumor control among those treated with IMRT for head and neck cancer. They showed that underdosing 1% of the tumor subvolume by just 20% could lead to a loss of 11% in expected tumor control.

Hong, Red Journal 2005

TOMOTHERAPY
=
Rotational IMRT and Volumetric IGRT

A lack of consensus currently exists regarding the optimal CTV-to-PTV expansion margins to be used in the treatment of head and neck cancer with IMRT.

Although the published literature on optimal CTV-to-PTV margins is extremely limited, it is becoming recognized that this depends largely on the method and frequency of verification imaging used in treatment

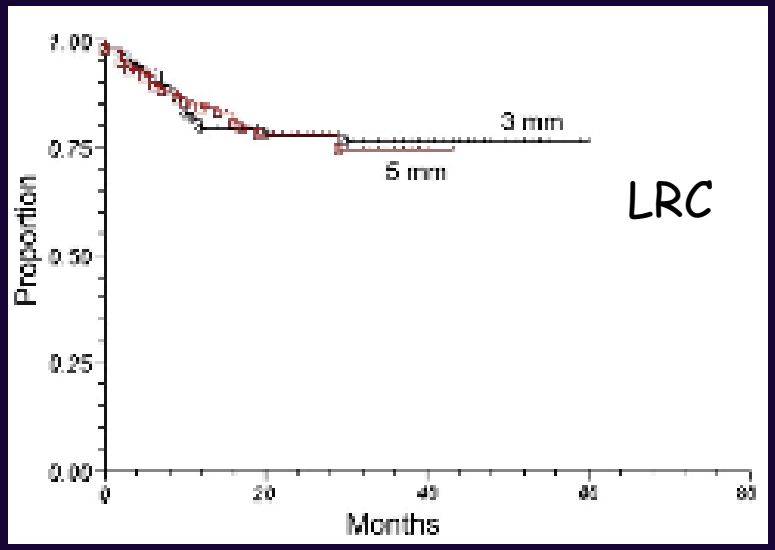
Int. J. Radiation Oncology Biol. Phys., Vol. 81, No. 4, pp. 943–949, 2011

EVALUATION OF THE PLANNING TARGET VOLUME IN THE TREATMENT OF HEAD AND NECK CANCER WITH INTENSITY-MODULATED RADIOTHERAPY: WHAT IS THE APPROPRIATE EXPANSION MARGIN IN THE SETTING OF DAILY IMAGE GUIDANCE?

Allen M. Chen, M.D.,* D. Gregory Farwell, M.D.,† Quang Luu, M.D.,† Paul J. Donald, M.D.,* Julian Perks, Ph.D.,* and James A. Purdy, Ph.D.*

Characteristic	CTV-PTV Margin	
	5 mm (%)	3 mm (%)
Initial KPS		
90–100	77 (81)	101 (78)
80	10 (11)	20 (15)
70	8 (8)	9 (7)
Gender		
Male	56 (59)	78 (60)
Female	39 (41)	52 (40)
Primary site		
OPX	43 (45)	55 (42)
OC	32 (34)	38 (29)
NPX	12 (13)	19 (15)
LYX/HPX	8 (8)	18 (14)
Pre-therapy PET scan		
Yes	33 (35)	61 (47)
No	62 (65)	69 (53)
Radiation approach		
Definitive	43 (45)	74 (57)
Postoperative	52 (55)	56 (43)
Concurrent chemotherapy		
Yes	59 (62)	70 (54)
No	36 (38)	60 (46)

The first study reporting patterns of failure according to CTV-to-PTV expansion margins for patients treated with IMRT for head and neck cancer,



LRC

46 LRRs
- 38 in field Rs
- 8 marginal Rs
    - 5 in 5mm group
    - 3 in 3mm group

In conclusion, our results, demonstrating no difference with respect to any of the clinical endpoints studied (OS, LRC, DFS), suggest that CTV-to-PTV expansion margins can safely be reduced from 5 mm to 3 mm when daily IGRT is used to guide dose delivery.

Whether or not CTV-to-PTV expansion margins of 3 mm could have safely been applied without daily IGRT remains speculative, and in our opinion, a questionable practice

Chen 2011

RTOG
RADIATION THERAPY ONCOLOGY GROUP

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RTOG 0920

A PHASE III STUDY OF POSTOPERATIVE RADIATION THERAPY (IMRT) +/- CETUXIMAB FOR LOCALLY-ADVANCED RESECTED HEAD AND NECK CANCER

					Arm 1: Radiation Therapy Alone
R	**For all**	**S**	**EGFR Expression**	**R**	RT, 2 Gy/day, in 30 fractions
E	**patients:**	**T**	1. High (≥ 80% of cells	**A**	for a total of 60 Gy[A]
G	Mandatory	**R**	staining positive for EGFR)	**N**	
I	submission	**A**	2. Low (< 80% of cells	**D**	**Arm 2: Radiation Therapy + Cetuximab**
S	of tissue for	**T**	staining positive for EGFR)	**O**	At least 5 days prior to RT:
T	EGFR[B]	**I**	3. Not evaluable	**M**	cetuximab: Initial dose, 400 mg/m^2
E		**F**		**I**	
R	**For**	**Y**	**Primary Site**	**Z**	RT, 2 Gy/day in 30 fractions for a total of 60 Gy[A]
	oropharyngeal		1. Oral cavity	**E**	plus cetuximab: 250 mg/m^2/week x 6 weeks
	cancer		2. Larynx		
	patients:		3. Oropharynx p16+		plus
	Mandatory		4. Oropharynx p16-		cetuximab: 250 mg/m^2/week
	analysis for		5. Oropharynx p16 not		x 4 weeks post-RT
	HPV[B]		evaluable		
					(cetuximab: 1 initial dose + 10 maintenance
			Use of IGRT		doses, a total of 11 doses)
			1. No		
			2. Yes		

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RTOG 0920

A PHASE III STUDY OF POSTOPERATIVE RADIATION THERAPY (IMRT) +/- CETUXIMAB FOR LOCALLY-ADVANCED RESECTED HEAD AND NECK CANCER

*PTV Expansion **Without** Daily IGRT*

For those institutions that are not using daily IGRT (see Section 6.2.2), the minimum CTV-to-PTV expansion should be 5 mm (a larger expansion may be necessary for a target volume subject to significant inter-fraction variability such as the tongue). In general, the CTV-to-PTV expansion (without IGRT) should not exceed 10 mm.

*PTV Expansion **With** Daily IGRT*

For those institutions that are using daily IGRT (see Section 6.2.2), the minimum CTV-to-PTV expansion is 2.5 mm (a larger expansion may be necessary for a target volume subject to significant intra-fraction variability, such as the non-immobilized oral tongue).In general, the CTV-to-PRV expansion (with IGRT) should not exceed 5 mm.

Tertiary Objectives (Exploratory)

Assess the impact of the addition of cetuximab to postoperative radiation therapy on the following:

- Local-regional control;
- Patient-reported quality of life (QOL), swallowing, xerostomia, and skin toxicity based on head and neck specific instruments, including: the Performance Status Scale for Head and Neck Cancer (PSS-HN), the Functional Assessment of Cancer Therapy-Head & Neck (FACT-H&N), the University of Michigan Xerostomia-Related Quality of Life Scale (XeQOLS), and the Dermatology Life Quality Index (DLQI);
- Cost-utility analysis using the EuroQol (EQ-5D).

To evaluate the utility of IGRT as a means of enhancing the efficacy (i.e., local-regional control) of IMRT while reducing the acute and/or late toxicity (particularly xerostomia) and improving patient-reported outcomes (particularly scores with the XeQOLS);

To retrospectively compare the local regional control rate for patients treated with IMRT alone (no IGRT or cetuximab) with similar patients treated with external beam radiation alone in the postoperative trial, RTOG 95-01.

Regione Emilia-Romagna

Osservatorio Regionale per l'Innovazione

Innovative Radiation Treatment in Cancer

IGRT/IMRT

**(Image Guided Radiation Therapy-
Intensity Modulated Radiation Therapy)**

HEALTH TECHNOLOGY ASSESSMENT

ORIentamenti

Programma di ricerca Regione-Università 2010-2012

Assessment of the role of image guided hypofractionated intensity modulated radiotherapy in the treatment of prostate, lung, oropharyngeal cancers, and glioblastoma

1. **G. Frezza (BO)**: A randomized phase III study of hypofractionated image guided radiation therapy (iIGRT) vs conventional fractionation in low and intermediate risk prostate cancer
2. **C. Iotti (RE)**: A randomized phase III study of chemo-radiation for stage III-IVA oropharynx cancer: IG-IMRT with dose/fraction escalation vs IMRT with conventional fractionation
3. **G. Zini (FE)**: impact on overall survival and disease free survival of image guided radiochemo- therapy and hypofractionation in stage IIIA-IIIB non small cell lung cancer: a randomized phase III study
4. **F. Bertoni (MO)**: A randomized phase II study: hypofractionated radiotherapy delivered every other day vs daily hypofractionated. IG-IMRT in patients with poor prognosis glioblastoma (V and VI RPA)

FUNDED

Head & Neck Helical Tomotherapy

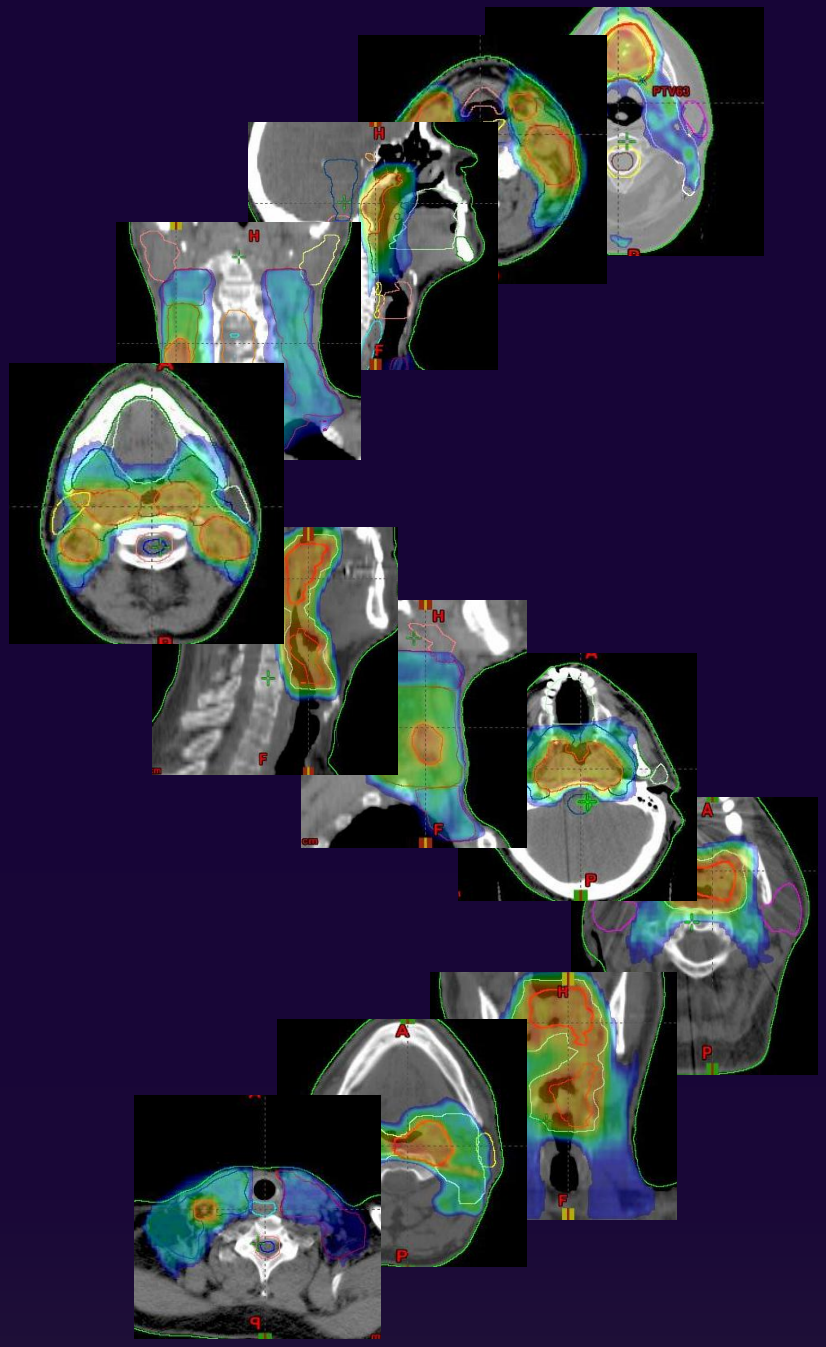
at Reggio Emilia Hospital
July 2008-June 2011

85 patients

Female 29
Male 57

Age 30-83, median 62

65 curative intent
20 postop intent



Postop Head & Neck Tomotherapy (20)

SITES

9 Oral cavity
4 Salivary glands
3 Paranasal sinus
2 Larynx
1 Hypopharynx
1 Thyroid

AJCC staging (7th Ed)

I	1	(5%)
II	1	(5%)
III	1	(5%)
IV	17	(85%)

RT schedules

SIB 30 x 2/1.8 Gy	12	(60%)
Unif 27-30X 2 Gy	7	(35%)
SIB 25 x 2.3/2 Gy	1	(5%)

5 conc. weekly P
2 conc. cetuximab

Follow up (months): 6-38.8, median 17

3 Distant Recurrences
Onset time (months): 5.1, 9.6, 11.0
No loco-regional failures

OS 85%

Alive w/o disease 16 (80%)
Alive w distant disease 1 (5%)
Dead of disease 2 (10%)
Dead w/o disease 1 (5%)

Curative Head & Neck Tomotherapy (65)

SITES

29 Oropharynx
15 Nasopharynx
7 Hypopharynx
7 Larynx
4 Oral Cavity
1 Paranasal sinus
1 Thyroid
1 Unknown

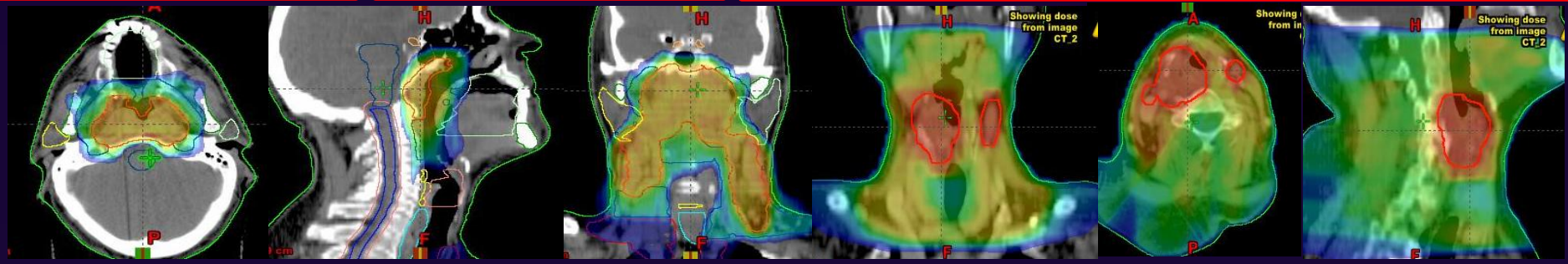
AJCC staging (7th Ed)

I	4	(6.2%)
II	5	(7.7%)
III	16	(24.6%)
IV	40	(61.5%)

RT schedules

SIB 30 x 2.2/2/1.8Gy	46 (70.8%)
SIB 30 x 2.3-/2/1.8Gy	10 (15.4%)
SIB 25 x 2.4/2Gy	4 (6.1%)
SIB 33 x 2.12/1.85/1.7Gy	3 (4.6%)
SIB 30 x 2/1.8Gy +5 x 2Gy	2 (3.1%)

30 neo-adjuvant + conc ChT/cetuximab
15 conc ChT/cetuximab



PTV_{HD} : Gross Tumor Volume plus 0.5 cm (CTV) plus 0.3 cm
PTV_{ID} : High-risk subclinical disease plus 0.3 cm
PTV_{LD} : Low-risk subclinical disease plus 0.3 cm

Curative Head & Neck Tomotherapy (65)

Follow up (months) 6.3-41.1, median 18.7

- 10 Local failure in field
- 1 Local failure marginal
- 1 Regional failure outside

Onset time (months): 0-20.2 median 8.7

Successfully salvage surgery in 8 patients

OS 93.8%

Alive w/o disease	57 (87.7%)
Alive w LR disease	2 (3.1%)
Alive w distant disease	2 (3.1%)
Dead of disease	4 (6.1%)

Local failure in field	*(>95% in high dose volume)*
Local failure marginal	*(20-95% in high dose volume)*
Local failure outside	*(<20 in high dose volume)*
Regional failure in field	*(>95% in low dose volume in uninvolved neck site)*
Regional failure marginal	*(20-95% in low dose volume in uninvolved neck site)*
Regional failure outside	*(<20% in low dose volume in uninvolved neck site)*

Toxicity (curative treatments)

ACUTE

grade	Dermatitis	Mucositis
0	1,5%	-
1	17%	12.3%
2	67.7%	64.6%
3	13.8%	23.1%

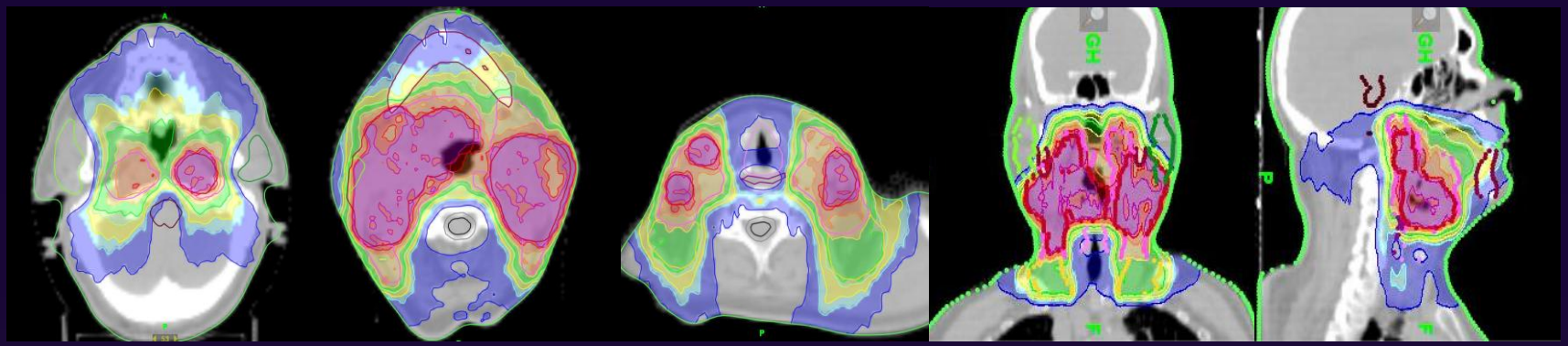
LATE

grade	Xerostomia	Dysphagia
0	20%	40%
1	66.2%	32.3%
2	13.8%	6.2%
3	-	-

No grade ≥ 3 late toxicity
No toxic deaths

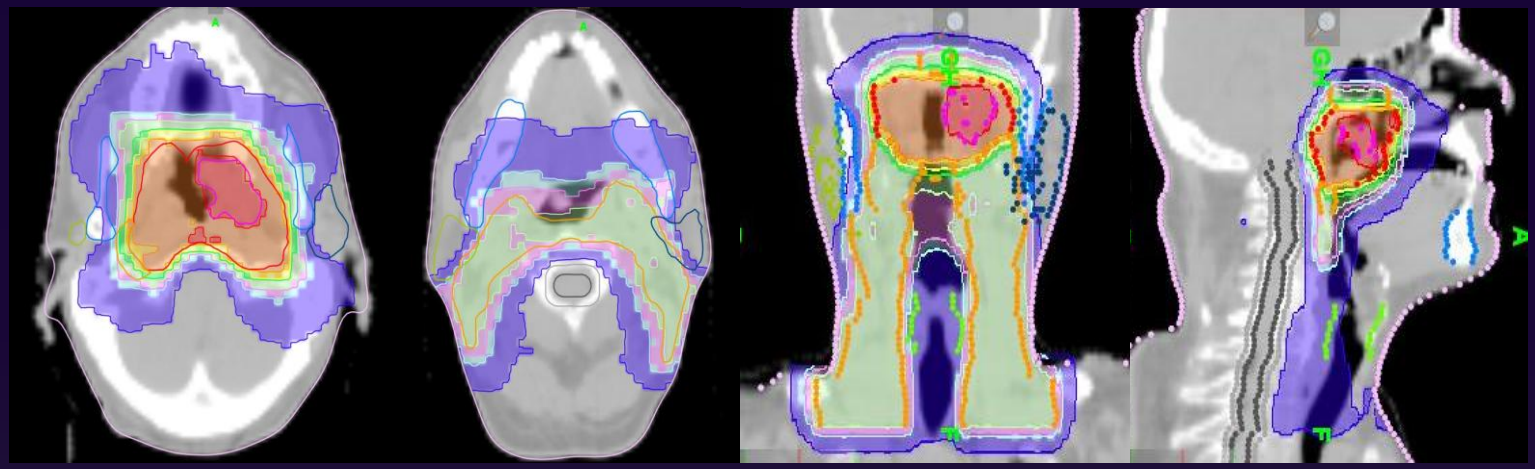
OROPHARYNX cancer (curative RT)
Comparison between D-MLC IMRT and Tomotherapy

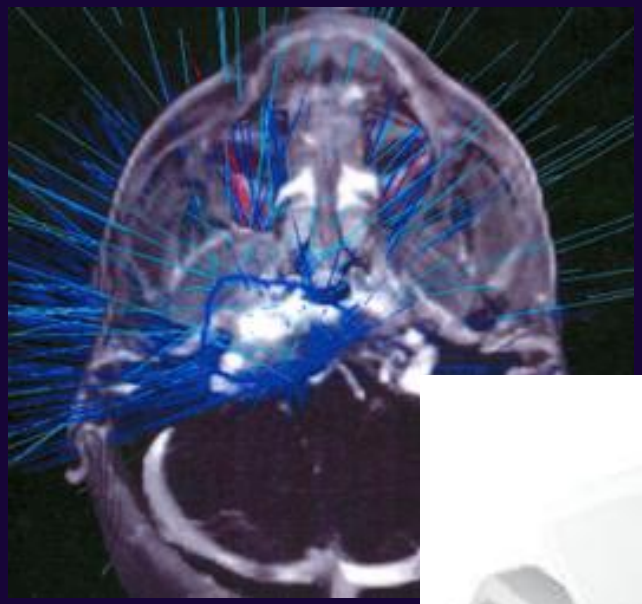
	D-MLC	HT
# patients	68	29
Follow-up (months)	6.1-122.7 (median 48.6)	6.3-42 (median 26.4)
Advanced stage (III-IV)	53 (78%)	27 (93.1%)
LR failure	14 (20.5%)	5 (17.2%)
Marginal failure	1 (regional)	1 (local)



NASOPHARYNX cancer (curative RT)
Comparison between D-MLC IMRT and Tomotherapy

	D-MLC	HT
# patients	26	15
Follow-up (months)	4.6-106.9 (median 62.2)	11.7-46.6 (median 22.5)
Advanced stage (III-IV)	16 (62%)	9 (60%)
LR failure	4 (15.4%)	0
Marginal failure	2 (local)	0





A robotic stereotactic radiosurgery system

Synthèse
General review

Bulletin du Cancer Volume 96 • N° 9 • septembre 2009
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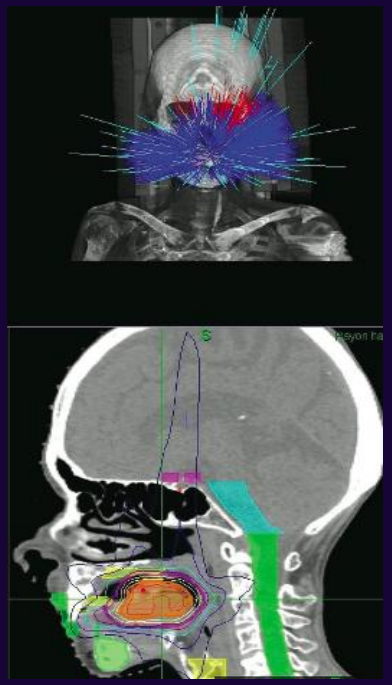
Indications du CyberKnife® et essais cliniques en cours en 2009

Current indications and ongoing clinical trials with CyberKnife® stereotactic radiotherapy in France in 2009

J. Thariat, G. Li, G. Angellier, S. Marchal, G. Palamini, G. Rucka, K. Bénézery, J. Castelli, R. Trimaud, H. Mammar, S. Marcie, J.-P. Gérard, P.-Y. Bondiau



Indications de radiothérapie extracrânienne en condition stéréotaxique reconnues par la HAS → Tumeurs pulmonaires primitives — stade précoce ; Tumeurs pulmonaires secondaires ; Lésions médullaires et paramédullaires

Indications en cours d'évaluation dans le cadre de la recherche clinique → Tumeurs hépatiques primitives ou secondaires ; Tumeurs mammaires → Néoadiuvant Boost hypofractionné ; Tumeurs pulmonaires localement avancées ou récidivantes

Indications pour lesquelles il n'existe pas de protocole en cours au 1er avril 2009 en France → Tumeurs ORL — réirradiation ; Tumeurs prostatiques

La radiothérapie stéréotaxique extracrânienne représente une voie de progrès majeure, notamment pour les tumeurs mobiles grâce au système de tracking. La précision de l'irradiation est également un avantage majeur pour les tumeurs proches d'OAR. L'hypofractionnement utilisé a de nombreux avantages, qui ne doivent pas faire omettre le risque de complications tardives, notamment lorsque de grands volumes sont irradiés

J. Radiat. Res., 52, 24–31 (2011)

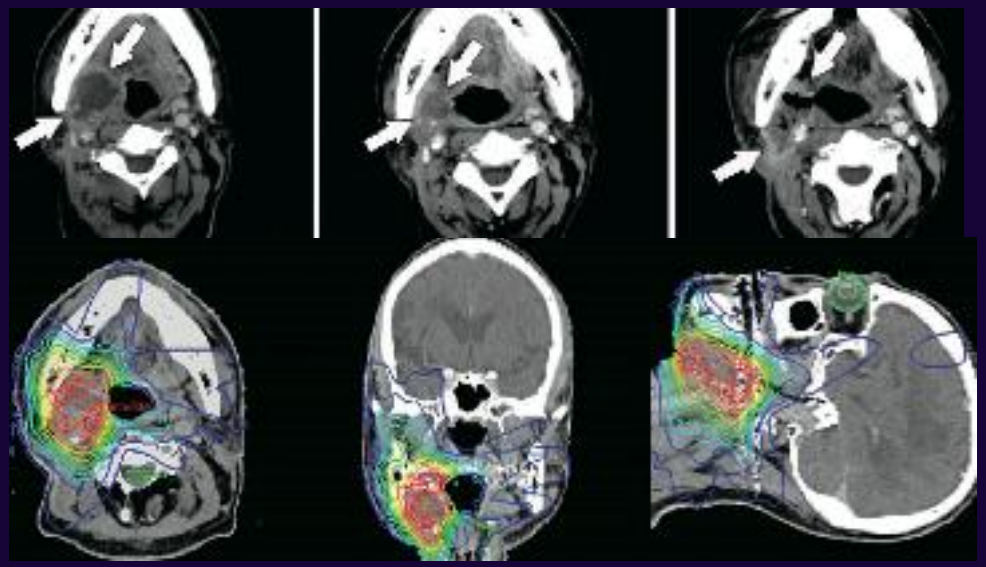
Stereotactic Body Radiation Therapy for Head and Neck Tumor: Disease Control and Morbidity Outcomes

Naohiro KODANI[1]*, Hideya YAMAZAKI[1], Takuji TSUBOKURA[1], Hiroya SHIOMI[2], Kana KOBAYASHI[1], Takuya NISHIMURA[1], Norihiro AIBE[1], Hiroyasu IKENO[1] and Tsunehiko NISHIMURA[1]

Characteristics	No prior RT (n = 13)	Prior RT (n = 21)
CyberKnife SBRT		
D90 (Gy)	35 (25–42)	30 (21–36)
D100 (Gy)	26.0 (12.2–38.4)	26.1 (5.0–32.1)
Max tumor dose (Gy)	38.0 (27.7–52.1)	35.7 (26.2–42.8)
BED-D90 (Gy)		7–79.2)
BED-D100 (Gy		9–62.1)
V100 (%)	90	90
V110 (%)	25.5 (0–65.4)	26.0 (0–86.0)
V95 (%)	98.3 (92.5–99.8)	98.3 (91.1–99.8)
Fractions	5 (3–8)	5 (3–7)
Treatment duration (day)	5 (3–9)	5 (3–9)
Cumulative BED (Gy_2)	140.0 (87.5–252.0)	242.5 (94.5–372.0)
Target volume (cm^3)	22.0 (0.7–78)	10.0 (0.9–58)

34 patients

19,5-42 Gy in 3-8 fx



CR 32.4% PR 38.6% 1yOS 70.6% 2yOS 58.3%

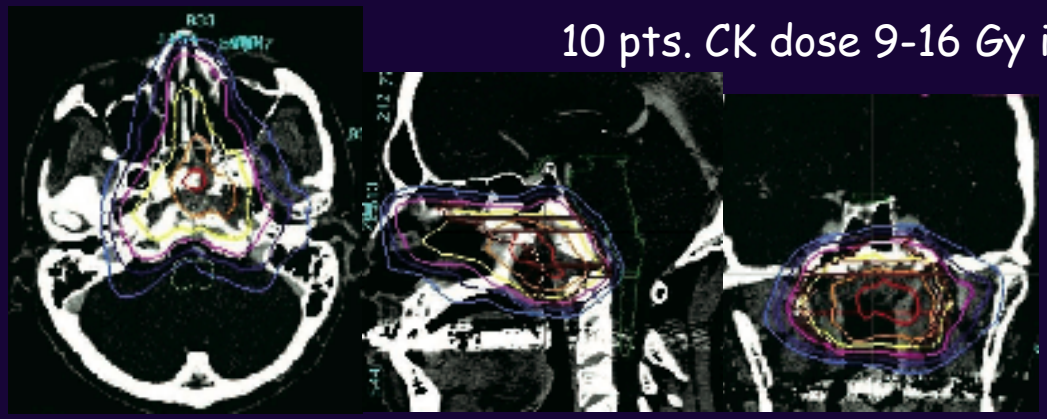
The overall survival was better in patients without prior RT within the previous 2y or in case of smaller target volume. Six patients suffered severe late complications. All these patients had prior RT, and 2 of them developed massive hemorrhage in the pharynx and both died of this complication

J. Radiat. Res., 51, 449–454 (2010)

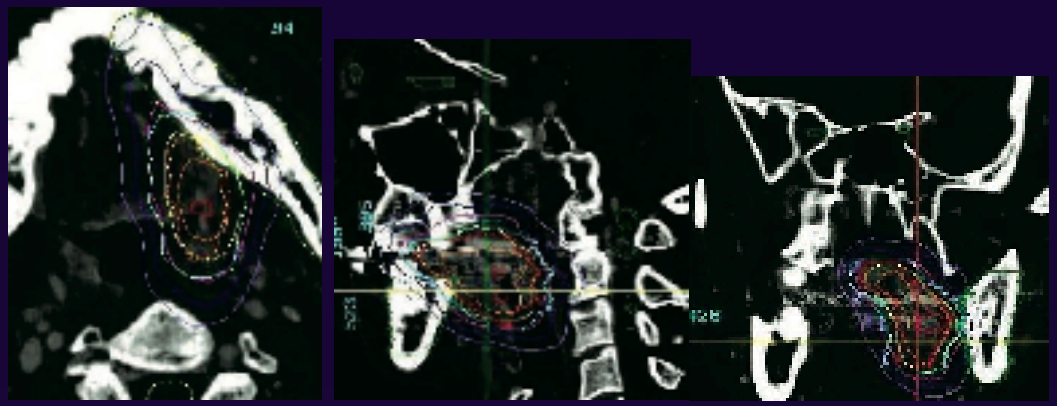
Fractionated Stereotactic Radiotherapy as a Boost Treatment for Tumors in the Head and Neck Region

Takashi UNO[1]*, Kouichi ISOBE[1], Naoyuki UENO[1], Ataru FUKUDA[2], Satoshi SUDO[2], Hiroaki SHIROTORI[2], Isao KITAHARA[2], Takanori FUKUSHIMA[2] and Hisao ITO[1]

10 pts. CK dose 9-16 Gy in 3-4 fxs



Nasopharyngeal cancer invading broadly the bony skull base (T3N0M0)
50Gy/25 + 15Gy/4



Oropharyngeal cancer
Close proximity to the mandible
50Gy/25 + 15Gy/4

Although a small volume high dose area within the normal structure could be observed in several patients, results of the present study showed potential benefits of the CyberKnife SRT boost

Head & Neck re-irradiation with Tomotherapy

at Reggio Emilia Hospital

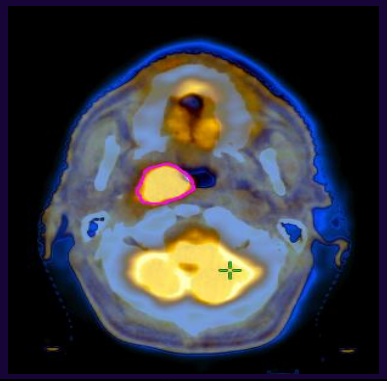
October 2008-September 2011

- 12 patients

male 10; female 2 Age: 49-83, median 65

5 second primary tumors

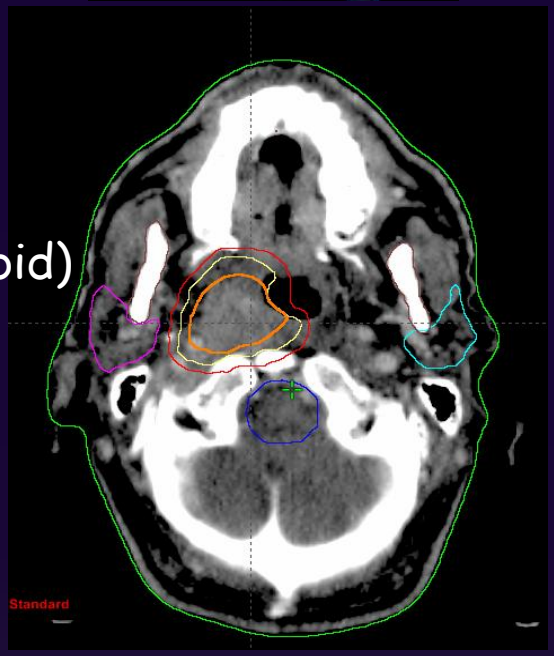
7 recurrent tumors



- Prior RT dose (Gy): 50-70, median 62

- Interval (months): 11-474, median 81

- Work-up: c.e.CT + $_{FDG}$PET/CT ± MR



- RT dose (Gy): 60-66, median 61.5 (all but one 1.5Gy bid)

- PTV (GTV+3mm) cc: 8.2-145.3, median 52.7

- All patients completed the planned course

- FU (months): 3-34, median 10

	Disease sub-sites	Prior RT dose	Interval months	RT dose	FU months	PTV cc	CT	LR response to RT	Status
1	oroph	50	46	63	20	54,1	+	PR	AwD §
2	RP N	60	16	60	9	8.2	-	CR	NED
3	oroph	54	81	60	3	51.3	+	PR	AwD §§
4	oroph	66	47	60	4	64.5	+	PR	AwD §§
5	2°lev N	60	105	66	27	55.9	-	CR	NED
6	hypoph	50	166	60	4	29.5	-	CR	NED
7	nasoph	57	474	60	4	95.4	+	NE	Dead *
8	oroph	66	69	60	34	25.9	+	CR	AwD §§§
9	nasoph	70	81	66	14	70.8	-	CR	AwD §§§
10	oroph	66	122	66	12	23.4	-	NE	Dead **
11	hypoph	64	199	66	5	145.3	+	SD	Dead *
12	oroph	66	11	66	10	33.0	+	PD	Dead ***

§ LR and distant disease
§§ LR disease
§§§ Distant disease

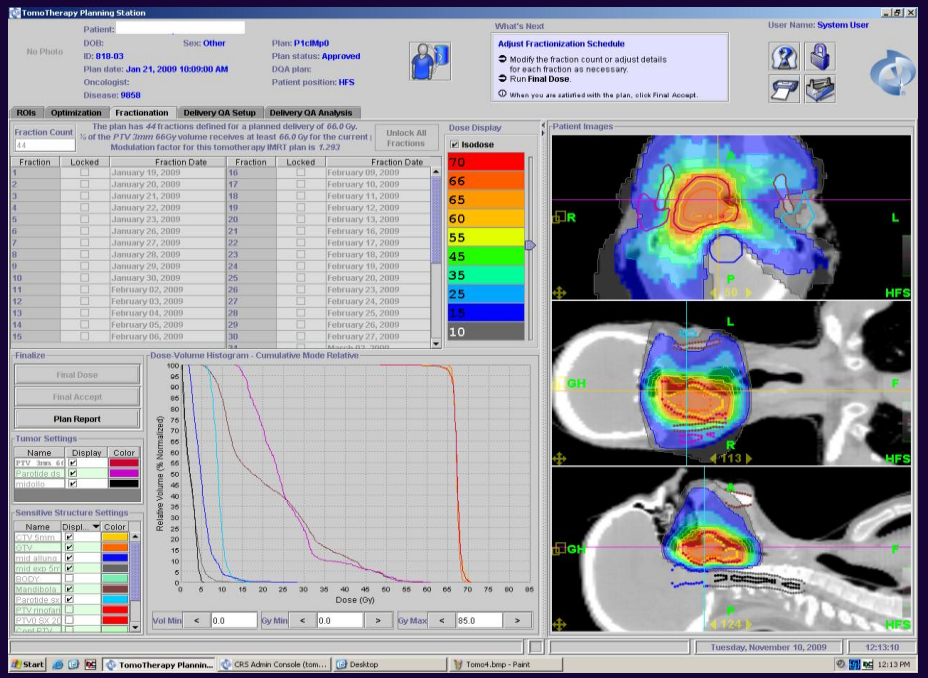
* Dead of complication
** Dead of unknown cause
*** Dead of local progression

Complete response 41.7%
Partial response 25% } 66.7%
Stable disease 8.3%
Progressive disease 8.3%
Not evaluable 16.7%

Alive 8 (66,7%)
- 4 patients surviving >1 years
- 3 patients surviving >2 years

Dead 33,3%

2 Radiation-related deaths
- •Massive hemorrhage (4 months)
- •Massive hemorrhage (5 months)



Disease sub-sites	Prior RT dose	Interval months	RT dose	PTV cc	CT	LR response to RT
Nasopharynx (2°P)	57	474	60	95.4	yes	NE
Hypopharynx (2°P)	64	199	66	145.3	yes	SD

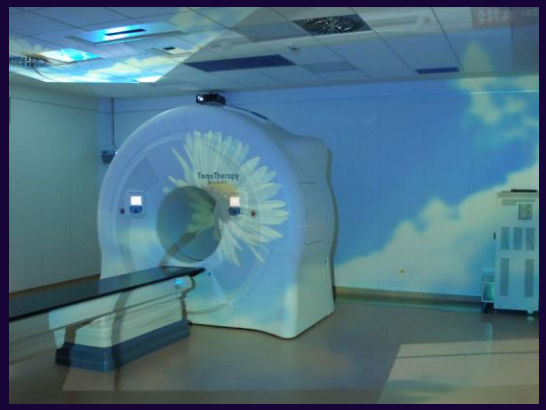
CONCLUSION

Helical Tomotherapy for head and neck cancer is safe, effective and efficient.
However, its clinical superiority with respect other IMRT planning and delivery systems is unproven.

Cyberknife is a promising approach for stereotactic irradiation of H&N tumor arising in previously irradiated sites. However, the data are very limited and further studies are needed.

Tomotherapy Hi-Art

2012 Spring Collection



I tagli alla sanità